

# VA/DoD CLINICAL PRACTICE GUIDELINE FOR THE MANAGEMENT OF ISCHEMIC HEART DISEASE CORE MODULE SUMMARY

## INITIAL EVALUATION AND TRIAGE

### KEY ELEMENTS

- Triage patients with possible acute myocardial infarction (MI) or unstable angina for evaluation and treatment
- Initiate O<sub>2</sub>, intravenous access and continuous ECG monitoring
- Institute advanced cardiac life support (ACLS), if indicated
- Obtain 12-lead electrocardiogram (ECG)
- Perform expedited history & physical to:
  - R/O alternative catastrophic diagnoses (pericarditis, pericardial tamponade, thoracic aortic dissection, pneumothorax, pancreatitis, & pulmonary embolus)
  - Elicit characteristics of MI
  - Determine contraindications to reperfusion therapy
- Administer the following:
  - Non-coated aspirin (160 to 325 mg).
  - Nitroglycerin (spray or tablet, followed by IV, if symptoms persist).
  - Beta-blockers in the absence of contraindications
- Determine if patient meets criteria for emergent reperfusion therapy:
  - History of ischemia or infarction, and
  - ECG finding of ongoing ST-segment elevation in 2 or more leads or left bundle branch block (LBBB)
- Ensure adequate analgesia (morphine, if needed)
- Obtain serum cardiac markers (troponin or CK-MB)
- Identify and treat other conditions that may exacerbate symptoms

### Risk Stratification: Non-Invasive Evaluation (Cardiac Stress Test)

#### Indications for Non-Invasive Evaluation:

- Establish or confirm a diagnosis of ischemic heart disease.
- Estimate prognosis in patients with known or suspected IHD.
- Assess the effects of therapy.

*Patients with contraindications to exercise testing should undergo pharmacologic stress testing with an imaging modality.*

#### Establishing diagnoses:

- Is most useful if the pre-test probability of coronary artery disease (CAD) is intermediate (10% to 90%).
- Should generally not be done in patients with very high or very low probabilities of CAD.

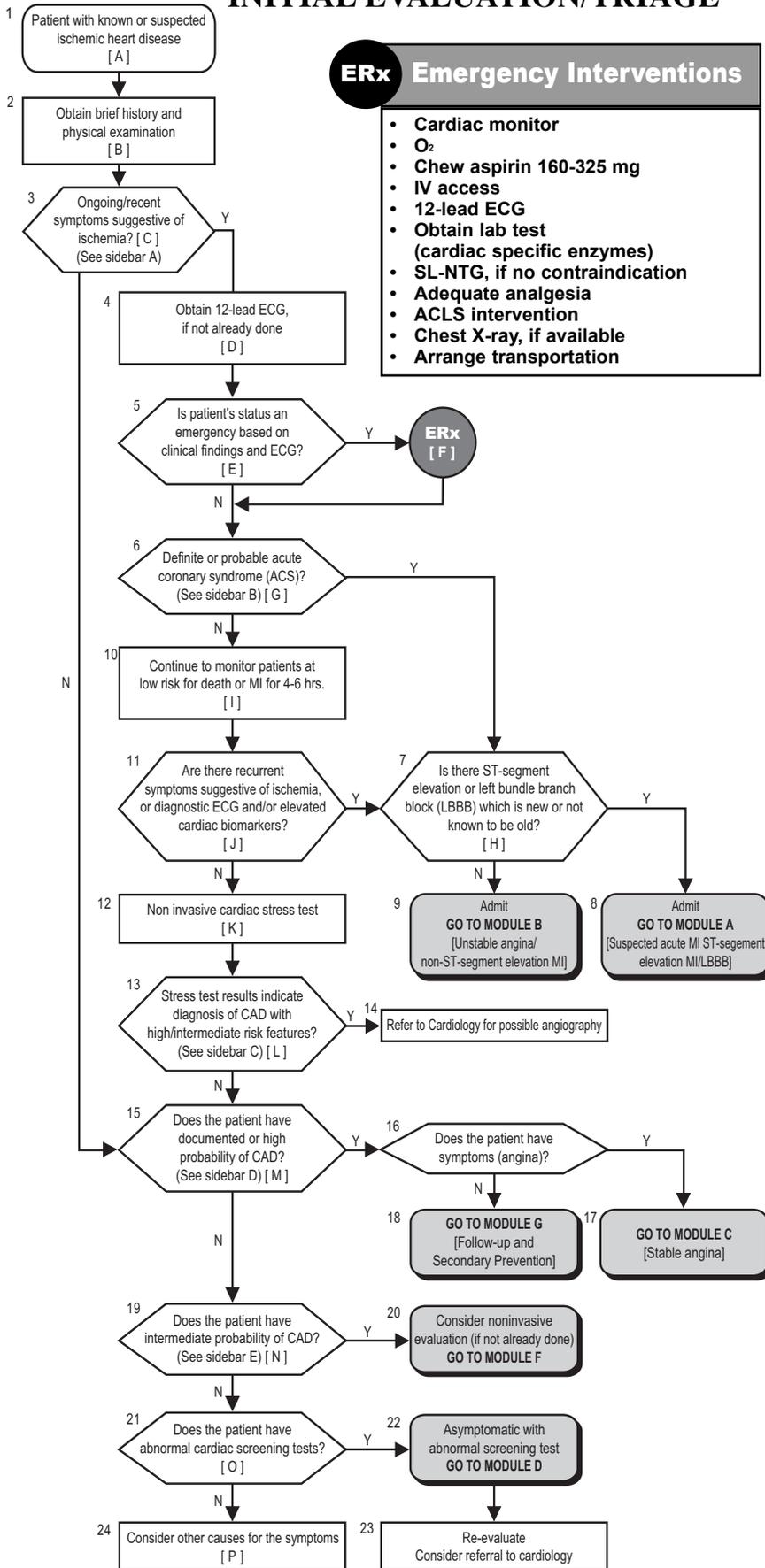
#### Variables useful in estimating prognosis include:

- Maximum workload achieved
- Heart rate and blood pressure responses to exercise
- Occurrence and degree of ST-segment deviation
- Occurrence and duration of ischemic symptoms
- Size and number of stress-induced myocardial perfusion or wall motion abnormalities

# MANAGEMENT OF ISCHEMIC HEART DISEASE

## CORE MODULE

### INITIAL EVALUATION/TRIAGE



**ERx Emergency Interventions**

- Cardiac monitor
- O<sub>2</sub>
- Chew aspirin 160-325 mg
- IV access
- 12-lead ECG
- Obtain lab test (cardiac specific enzymes)
- SL-NTG, if no contraindication
- Adequate analgesia
- ACLS intervention
- Chest X-ray, if available
- Arrange transportation

**Sidebar A (Box 3): Symptoms/Signs Suggesting Ischemia**

- Chest pain or severe epigastric pain, nontraumatic in origin, characterized by:
  - Central/substernal compression or crushing chest pain/discomfort
  - Pressure, tightness, heaviness, cramping, burning, aching sensation
  - Unexplained indigestion, belching, epigastric pain
  - Radiating pain in neck, jaw, shoulders, back, or arm(s)
- Associated dyspnea
- Associated nausea and/or vomiting
- Associated diaphoresis

**Sidebar B (Box 6): Acute Coronary Syndrome**

Any item of LIST A, OR  
One item from both LIST B and LIST C

**LIST A**

- ST-elevation or LBBB and recent (<24 hr) or ongoing angina
- New, or presumably new, ST-segment depression (>0.05 mV) or T-wave inversion (>0.2 mV) with rest symptoms
- Elevated biomarkers (i.e., troponin I, troponin T, and CK-MB)

**LIST B**

- Prolonged (>20 min.) chest, arm, or neck discomfort
- New onset chest, arm, or neck discomfort during minimal exertion or ordinary activity (CCS class III or IV)
- Previously documented chest, arm, or neck discomfort which has become distinctly more frequent, longer in duration, or lower in precipitating threshold (i.e., increased by one CCS class or more to at least CCS class II)

**LIST C**

- Typical or atypical angina
- Male age >40 or female age >60
- Known CAD
- Heart failure, hypotension, or transient mitral regurgitation by examination
- Diabetes mellitus
- Documented extracardiac vascular disease
- Pathologic Q-waves on ECG
- Abnormal ST-segment or T-wave abnormalities not known to be new

**Sidebar C (Box 13): Cardiac Stress Test: High or Intermediate Risk for Cardiac Event**

**HIGH**

- Duke treadmill score ≤-11 (estimated annual mortality >3%)
- Large, stress-induced perfusion defect
- 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 >2 segments at ≤10 mg/kg/min dobutamine or HR <120/min

**INTERMEDIATE**

- Mild/moderate resting left ventricular dysfunction (LVEF = 0.35 to 0.49)
- Intermediate-risk Duke treadmill score (greater than -11 and less than 5)
- Stress-induced moderate perfusion defect without LV dilation or increased lung uptake (thallium-201)
- Limited stress echocardiographic ischemia with wall motion abnormality only at higher doses of dobutamine involving ≤ two segments

**Sidebar D (Box 15): Definite or High Probability of CAD**

- Typical angina in a males age >50 or females age >60
- Prior myocardial infarction or pathologic Q-waves
- Coronary arteriogram with >50% stenosis in >1 vessel(s)
- Prior coronary revascularization (PCI or CABG)
- Left ventricular segmental wall motion abnormality
- Diagnostic evidence of ischemia or infarction on cardiac stress testing

**Sidebar E (Box 19): Intermediate Probability of CAD**

- Typical angina in female (age <60) male (age <50)
- Atypical/probable angina in male of any age
- Atypical/probable angina in female age >60
- Noncardiac chest pain in male (age >40) female (age >60)
- Indeterminate finding on cardiac stress testing

## **CORE MODULE: INITIAL EVALUATION**

The purpose of the Core Module is to guide the initial evaluation and treatment of a patient presenting with symptoms possibly due to myocardial ischemia or infarction. Primary emphasis is placed on the rapid identification and early treatment of patients with ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI), and unstable angina. It also provides guidance for the initial diagnosis of stable angina, the asymptomatic patient with an abnormal cardiac screening test, the patient with known coronary artery disease who requires follow-up and attention to prevention of recurrent coronary events, and the non-invasive evaluation of the patient with suspected coronary artery disease. Symptoms of heart failure and arrhythmias are commonly associated with presentation of ACS, however this guideline is not primarily intended to address congestive heart failure (CHF), arrhythmias, or valvular heart disease.

## ANNOTATIONS

### A. Patient With Known Or Suspected Ischemic Heart Disease (IHD)

Patients managed by this guideline are presenting with non-traumatic chest discomfort or other symptoms that may represent cardiac ischemia or ACS. Symptoms of heart failure and arrhythmias are commonly associated with presentation of ACS, however this guideline is not intended primarily to address congestive heart failure (CHF), arrhythmias, or valvular heart disease.

#### ANNOTATION

IHD conditions are caused by relative lack of blood flow to the heart. Acute coronary syndromes, such as MI and unstable angina, are acute events precipitated by an unstable atherosclerotic plaque and intra coronary thrombus.

Generally accepted criteria for a diagnosis of IHD, include the following:

- Prior myocardial infarction (MI) and/or pathologic Q-waves on the resting electrocardiogram (ECG)
- Typical stable angina in males age >50 or females age >60
- Cardiac stress test showing evidence of myocardial ischemia or infarction
- Left ventricular (LV) segmental wall motion abnormality by angiography or cardiac ultrasound
- Silent ischemia, defined as reversible ST-segment depression by ambulatory ECG monitoring
- Definite evidence of coronary artery disease (CAD) by angiography
- Prior coronary revascularization (percutaneous coronary intervention [PCI] or coronary artery bypass graft surgery [CABG])

IHD may be suspected in patients who do not meet one of the above criteria, if they have symptoms suggestive of myocardial ischemia or infarction. Although chest pain or discomfort is the classic presentation for stable and unstable angina and for acute myocardial infarction (AMI), other symptoms such as chest heaviness; arm, neck, jaw, elbow, or wrist pain or discomfort; dyspnea; nausea; palpitations; syncope; or nonspecific symptoms

(e.g. change in exercise tolerance) can all represent symptoms of IHD. Furthermore, patients may present with non-cardiac problems and undergo an evaluation that reveals significant CAD for which they are asymptomatic.

### B. Obtain Brief History And Physical Examination OBJECTIVE

Obtain the chief complaint and a brief, directed medical history and perform a physical examination, as required, to appropriately triage the patient with known or suspected IHD.

#### ANNOTATION

Triage personnel (in the clinic, emergency department [ED]), or even over the telephone) must rapidly assess the urgency of a complaint of chest pain or other symptoms that could represent acute ischemia. Vital signs are an essential part of the assessment. Factors such as hypotension, excessive bradycardia or tachycardia, or diaphoresis should prompt triage personnel to initiate emergency interventions (see Annotation D). The physician's physical examination should concentrate on the heart, lungs, and pulses. Historical features of importance include the following: the nature of the pain, onset, duration, provocative and palliative factors, and radiation patterns. The clinician should obtain the following (NHLBI, 1993):

#### Chief Complaint and History of Present Illness

The history, particularly the chief complaint, is one of the most important steps in the evaluation of the patient with chest pain. A detailed description of the symptom complex enables the clinician to characterize the chest pain (for typical symptoms of myocardial ischemia see Annotation A). Relationship of chest discomfort to exercise or emotion should be ascertained. It is often useful to quantitate the amount of exercise required to precipitate the symptoms and to record the Canadian Cardiovascular Society class (see Table 1). Chest discomfort occurring at rest or awakening the patient from sleep is usually an ominous finding and one of the criteria for ACS.

## Past Medical History

The triage nurse or physician should take a brief, targeted, initial history with an assessment of current or past history of the following (this brief history must not delay entry into the Advanced Cardiac Life Support [ACLS] protocol if required):

- Evidence of existing CAD: prior CABG, angioplasty, MI, or abnormal stress test or coronary arteriography
- Change in frequency of nitroglycerin (NTG) use to relieve chest discomfort
- Advanced age and other risk factors (smoking, hyperlipidemia, hypertension, diabetes mellitus, family history, and cocaine use).

## Physical Examination

The major objectives of the physical examination are to identify the hemodynamic status and possible comorbid conditions that precipitate or aggravate myocardial ischemia (e.g., aortic stenosis, hypertension, thyrotoxicosis, hypoxia etc.), and the presence of other comorbid conditions that might impact the risk of performing coronary revascularization. Several important aspects of the examination are listed below:

- Vital signs (i.e., blood pressure in both arms, heart rate, respiratory rate, and temperature)
- Evidence of heart failure (i.e., S3 gallop, rales, and elevated jugular venous pressure)
- Evidence of significant mitral or aortic valvular disease
- Evidence of extra-cardiac vascular disease (i.e., bruits or diminished pulses)
- Evidence of non-coronary causes of chest pain (i.e., chest wall tenderness, pericardial or pleural rub, etc.)

## C. Ongoing/Recent Symptoms Suggestive Of Ischemia? OBJECTIVE

Identify patients with myocardial ischemia.

## ANNOTATION

Symptoms and signs that may represent myocardial ischemia (NHLBI, 1993; ACC/AHA UA - NSTEMI, 2002) include the following:

- Chest pain or severe epigastric pain, nontraumatic in origin, characterized by:
  - Central/substernal compression or crushing chest pain/discomfort

- Pressure, tightness, heaviness, cramping, burning, aching sensation
- Unexplained indigestion, belching, epigastric pain
- Radiating pain in neck, jaw, shoulders, back, or 1 or both arms
- Associated dyspnea
- Associated nausea and/or vomiting
- Associated diaphoresis

The ACC/AHA UA - NSTEMI (2000) describes the different classes of the Canadian Cardiovascular Society (CCS) classifications as follows:

**Table 1. Canadian Cardiovascular Society (CCS) Classification of Angina \***

<b>Class I:</b>	<b>Angina only with <i>strenuous</i> exertion</b> Ordinary physical activity; such as walking or climbing stairs, does not cause angina. — Angina occurs with strenuous, rapid, or prolonged exertion at work or recreation.
<b>Class II:</b>	<b>Angina with <i>moderate</i> exertion</b> 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 two blocks on the level and climbing more one flight of ordinary stairs at a normal pace and under normal conditions.
<b>Class III:</b>	<b>Angina with <i>minimal</i> exertion or ordinary activity</b> 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.
<b>Class IV:</b>	<b>Angina <i>at rest</i> or with <i>any</i> physical activity</b> Inability to carry on any physical activity without discomfort. — Anginal symptoms may be present at rest.

\* (Campeau, 1976)

## **D. Obtain 12-Lead ECG, If Not Already Done**

### **OBJECTIVE**

Obtain key diagnostic information.

### **ANNOTATION**

A 12-lead ECG is an essential component of the evaluation of the patient with known or suspected IHD. For patients with ongoing symptoms, an urgent ECG should be obtained in the first 10 minutes of the initial evaluation. For patients without ongoing symptoms, an elective 12-lead ECG should be obtained if no prior ECG performed within the past year is available for review, or if there has been an interval worsening of the patient's symptoms. A right-sided ECG should be performed if a standard ECG suggests an inferior wall MI.

## **E. Is Patient's Status An Emergency Based On Vital Signs And Appearance?**

### **OBJECTIVE**

Rapidly triage patients with possible AMI, unstable angina, or unstable hemodynamic status from other causes to a high-acuity setting for rapid diagnostic evaluation and treatment.

### **ANNOTATION**

A patient presenting with chest pain/discomfort in the emergency department should be considered an emergency, if the evaluation reveals (ACEP, 1995):

#### **Patient's vital signs (including one or more of the following):**

- Pulse  $\geq 110$  or  $\leq 55$  beats per minute
- Systolic blood pressure  $\geq 200$  or  $\leq 90$  mm Hg
- Diastolic blood pressure  $\geq 110$  mm Hg
- Respiratory rate  $>24$  or  $<10$  inspirations per minute
- Oxygen saturation  $<90\%$
- Irregular pulse

#### **AND/OR**

#### **Patient's appearance (including one or more of the following):**

- Is unconscious or lethargic and/or confused
- Has severe respiratory distress or respirations appear labored
- Appears cyanotic, pale or gray

- Appears diaphoretic
- Is in extreme pain or exhibits visible distress

Sudden cardiac death can occur early in any ischemic syndrome. The goals of rapid treatment of MI are to preserve as much myocardium as possible, avoid later complications of heart failure and dysrhythmias, and decrease risk of death.

## **F. Initiate Emergency Interventions For Patients With Possible Acute Coronary Syndrome (ACS) And Emergent Status**

### **OBJECTIVE**

Institute specific interventions that are necessary early in the evaluation and treatment of AMI and unstable angina.

### **ANNOTATION**

#### **1. Oxygen (O<sub>2</sub>)**

Supplemental oxygen should be administered to all patients with respiratory distress, those with cyanosis or those with documented desaturation. Oxygen should start on initial presentation and during the first 2 to 3 hours and continued if necessary to maintain O<sub>2</sub> saturations of at least 90%. Oxygen may be considered for all patients with suspected ACS. Because oxygen can actually cause systemic vasoconstriction, continued administration should be reassessed for uncomplicated patients. CO<sub>2</sub> retention is not usually a concern with low flow nasal oxygen, even in patients with severe chronic obstructive pulmonary disease (COPD).

#### **2. Chew aspirin**

- All patients should chew non-coated aspirin, 160 mg to 325 mg, within 10 minutes of presentation to accelerate absorption
- If a patient is unable to take aspirin by mouth because of nausea, vomiting, or other gastrointestinal disorders, 325 mg may be given as a suppository.
- Patients should be given aspirin, even if they are receiving anticoagulation (e.g., warfarin) or antiplatelet (e.g., aspirin or clopidogrel) at the time of presentation.
- Contraindications to aspirin include a documented allergy to salicylates, active bleeding or active peptic ulcer disease.

- Subsequent aspirin dose of 81-325 mg per day should be given for chronic therapy. Chronic therapy with doses above 81 mg/day is associated with increased bleeding risk without incremental benefit.
- Patients who have an allergy to aspirin and no contraindication to antiplatelet therapy should be given clopidogrel 300 mg loading dose followed by 75 mg daily for at least a month.

### 3. 12-Lead ECG

A 12-lead ECG is an essential component of the evaluation of the patient with known or suspected IHD. For patients with ongoing symptoms, an urgent ECG should be obtained and interpreted within the first 10 minutes of the initial evaluation and followed up with 2 to 3 serial ECGs in the first 24 hours. EKG should be repeated for recurrent chest pain. For patients without ongoing symptoms, an elective 12-lead ECG should be obtained if no prior ECG performed within the past year is available for review or if there has been a worsening of the patient's symptoms.

### 4. Intravenous (IV) access

Intravenous access for the delivery of fluids and drugs should be obtained, with both antecubital veins used if possible for multiple infusions, especially if thrombolytic therapy is being considered. While the IV is being started, blood samples for cardiac enzymes/markers (troponin, CK, and CK-MB), lipid profile, complete blood count (CBC), electrolytes, renal function, international normalized ratio (INR), and activated partial thromboplastin time (aPTT) can be obtained. Immediate treatment of ACS should not depend on waiting for these tests.

### 5. Nitroglycerin (NTG)

NTG should be given for ongoing chest pain or other ischemic symptoms, unless the patient is hypotensive or bradycardic, has taken sildenafil within the last 24 hours, or there is a strong suspicion of right ventricular infarction.

Intravenous nitroglycerin should be considered for 24 to 48 hours in patients with a large MI, persistent ischemia, CHF, or hypertension.

### 6. Cardiac monitor

Patients with a possible ACS should be placed on continuous electrocardiographic monitoring as soon as possible. Potentially lethal ventricular arrhythmias can occur within seconds to minutes of the onset of coronary ischemia and monitoring will allow their immediate detection and treatment.

### 7. Adequate analgesia

Adequate analgesia should be given promptly; IV morphine is effective, decreases the often excess sympathetic tone and is a pulmonary vasodilator. Some patients may require a large dose. The patient should be monitored for hypotension and respiratory depression, but these are less likely in the anxious, hyperadrenergic patient who is kept supine.

### 8. Advanced cardiac life support (ACLS, 2000):

ACLS algorithm should be applied, as indicated.

### 9. Chest X-ray

A chest x-ray should be obtained in the ED, particularly if there is concern about aortic dissection; however, the treatment of hypotension, low cardiac output, arrhythmias, etc., usually has higher priority.

### 10. Transportation

In some settings within the DoD or the VA system, the patient will need to be urgently transported to a setting where an appropriate level of monitoring, evaluation and treatment is available.

## G. Definite or Probable Acute Coronary Syndrome (ACS)?

### OBJECTIVE

Identify patients who may have an ACS (MI or Unstable Angina).

### ANNOTATION

New or worsening symptoms suggestive of myocardial ischemia, especially when prolonged or ongoing, should prompt consideration of a possible ACS.

The diagnosis of ACS may be suspected on the basis of a compelling clinical history, specific ECG findings and/or elevations in serum markers of cardiac necrosis (e.g. troponin I, or troponin T, or CPK-MB). The acute coronary syndromes consist of the following three subgroups:

- ST-segment elevation myocardial infarction (STEMI)
- Non-ST-segment elevation myocardial infarction (NSTEMI)
- Unstable angina.

Details regarding the diagnosis and treatment of STEMI are provided in Module A. The pathogenesis and treatment of NSTEMI and unstable angina are similar and are covered in Module B. The following presents a

logical means by which the primary care provider may reach a decision with respect to whether the patient has an ACS and therefore be referred to either Modules A or B for specific management.

Symptoms and signs that may represent acute coronary syndrome (NHLBI, 1993; ACC/AHA UA - NSTEMI, 2002) include the following:

- New onset or worsening prolonged (i.e., >20 minutes) chest, shoulder, arm/shoulder, neck, or epigastric pain, discomfort, pressure, tightness, or heaviness
  - “New onset” is defined as symptoms being evaluated for the first time or the patient with a complaint of chest pain is new to the clinic.
  - “Worsening” is defined as at least a one-class increase (Canadian Cardiovascular Society angina classification) (see Table 1) in a patient with known previous symptoms attributed to myocardial ischemia.
- Radiating pain to the neck, jaw, arms, shoulders, or upper back
- Unexplained or persistent shortness of breath

- Unexplained epigastric pain
- Unexplained indigestion, nausea or vomiting
- Unexplained diaphoresis
- Unexplained weakness, dizziness or loss of consciousness

### **Diagnosis of Acute Coronary Syndrome**

The decision process can be achieved using information derived from a brief, targeted history and physical examination; a 12-lead ECG; and a lab test for cardiac markers. The following two interrelated questions form the basis of the decision process:

1. Do the clinical findings satisfy criteria for an ACS?
2. In the absence of definitive criteria, what is the likelihood (i.e., low, intermediate or high) that the patient’s symptoms are due to myocardial ischemia or infarction?

These two questions can be synthesized into a diagnosis of ACS, using Table 5. A diagnosis of ACS may be made if at least *one major criterion* or at least *one minor criterion from each of columns I and II* is present.

**Table 5: Criteria Diagnosis of ACS**

<b>Major Criteria</b> <i>A diagnosis of an ACS can be made if one or more of the following major criteria is present</i>	<b>Minor Criteria</b> <i>In the absence of a major criterion, a diagnosis of ACS requires the presence of at least one item from both columns</i>	
	<b>I</b>	<b>II</b>
<ul style="list-style-type: none"> <li>• ST-elevation <sup>(a)</sup> or LBBB in the setting of recent (&lt;24 hours) or ongoing angina</li> <li>• New, or presumably new, ST-segment depression (<math>\geq 0.05</math> mV) or T-wave inversion (<math>\geq 0.2</math> mV) with rest symptoms</li> <li>• Elevated serum markers of myocardial damage (i.e., troponin I, troponin T, and CK-MB)</li> </ul>	<ul style="list-style-type: none"> <li>• Prolonged (i.e., &gt;20 minutes) chest, arm/shoulder, neck, or epigastric discomfort</li> <li>• New onset chest, arm/shoulder, neck, or epigastric discomfort during minimal exertion or ordinary activity (CCS class III or IV)</li> <li>• Previously documented chest, arm/shoulder, neck, or epigastric discomfort which has become distinctly more frequent, longer in duration, or lower in precipitating threshold (i.e., increased by <math>\geq 1</math> CCS class to at least CCS III severity)</li> </ul>	<ul style="list-style-type: none"> <li>• Typical or atypical angina <sup>(b)</sup></li> <li>• Male age &gt;40 or female age &gt;60 <sup>(c)</sup></li> <li>• Known CAD</li> <li>• Heart failure, hypotension or transient mitral regurgitation by examination</li> <li>• Diabetes</li> <li>• Documented extra-cardiac vascular disease</li> <li>• Pathologic Q-waves on ECG</li> <li>• Abnormal ST-segment or T-wave abnormalities not known to be new</li> </ul>

<sup>(a)</sup> ST elevation  $\geq 0.2$  mV at the J-point in two or more contiguous chest leads ( $V_1$  to  $V_6$ ) or  $\geq 0.1$  mV in all other leads. Contiguity in the limb leads (frontal plane) is defined by the lead sequence: I, aVL (lateral), and II, III, aVF (inferior).

<sup>(b)</sup> Use definitions in Table 6 to determine the likelihood that the presenting symptoms are angina

<sup>(c)</sup> These age and gender characteristics define a probability of CAD  $\geq 10\%$  in symptomatic patients (See Table 7).

**Table 6: Definitions of Angina Symptoms**

<i>Typical angina (definite)</i>	IF all three of the primary symptom characteristics are present
<i>Atypical angina (probable)</i>	IF any two of the primary three symptom characteristics are present
<i>Probably non-cardiac chest pain</i>	IF provocation by exertion or emotional distress or relief by rest or nitroglycerin are present and one or more symptom characteristics suggesting non-cardiac pain are present
<i>Definitely non-cardiac chest pain</i>	IF none of the primary symptom characteristics are present and one or more symptom characteristics suggesting non-cardiac pain are present
<p>The three primary symptom characteristics:</p> <ul style="list-style-type: none"> <li>• Substernal chest or arm discomfort with a <i>characteristic</i> quality and duration</li> <li>• Provoked by exertion or emotional stress</li> <li>• Relieved by rest or nitroglycerin</li> </ul> <p>Symptom <i>characteristics</i> that suggest non-cardiac pain, include the following: (but do not exclude a diagnosis of CAD)</p> <ul style="list-style-type: none"> <li>• Pleuritic pain (i.e., sharp or knife-like pain brought on by respiratory movements or cough)</li> <li>• Primary or sole location of discomfort in the middle or lower abdominal regions</li> <li>• Pain that may be localized at the tip of one finger, particularly over costochondral junctions or the left ventricular (LV) apex</li> <li>• Pain reproduced with movement or palpation of the chest wall or arms</li> <li>• Constant pain that lasts for many hours</li> <li>• Very brief episodes of pain that last a few seconds or less</li> <li>• Pain that radiates into the lower extremities</li> </ul>	

(Modified from the ACC/AHA Stable Angina Guideline [1999], Table 5 and ACC/AHA UA - NSTEMI guideline [2002], pages 11-12).

## **H. Is There ST-Segment Elevation Or New or Presumably New Left Bundle Branch Block (LBBB) With Ongoing/Recent Symptoms?**

### **OBJECTIVE**

Determine whether emergent reperfusion therapy may be appropriate.

### **ANNOTATION**

Patients with ST-segment elevation, true posterior MI, or a LBBB that is new or not known to be old, and with symptoms consistent with myocardial ischemia or infarction should be considered for emergent reperfusion therapy. These patients should receive urgent therapy for AMI as delineated in Module A. Patients with non-ST-elevation-acute coronary syndrome (NSTEMI/UA) that is covered in Module B.

## **I. Continue to Monitor Patients at Low-Risk for Death or MI**

### **OBJECTIVE**

Monitor low risk patients who may subsequently develop ACS

### **ANNOTATION**

### **Unstable Angina with Low Risk**

For patients with suspected ACS who, at initial presentation, do not have clinical features suggesting intermediate- or high-risk for death or MI, the following are recommended:

- Initial treatment with 160 mg to 325 mg of chewable aspirin
- Initial treatment with sublingual NTG for angina or suspected anginal equivalents
- Continuous ECG monitoring and continued surveillance of vital signs and for recurrent symptoms, for at least 6 to 12 hours, in an appropriate facility-specific unit
- A 12-lead ECG at the time of admission and at least 6 hours from the onset of symptoms, or as needed at change of symptoms or clinical status
- Assessment of serum cardiac biomarkers (troponin, CPK-MB) at the time of presentation. For patients with normal cardiac markers within 6 hours of symptom onset, another sample should be obtained over the subsequent 6-12 hours.

- Early stress testing for patients who do not develop clinical indicators of intermediate- or high-risk by the end of the monitoring period
- Hospital admission and intensification of medical therapy for patients who develop clinical indicators of intermediate- or high-risk by the end of the monitoring period

## **J. Are There Recurrent Symptoms Suggestive of Ischemia, or Diagnostic ECG and/or Elevated Cardiac Markers?**

### **OBJECTIVE**

Identify patients with ACS

### **ANNOTATION**

Patients with recurrent symptoms, positive cardiac specific markers, or evolutionary or dynamic ECG changes during the monitoring period are now demonstrated to have probable or definite ACS and considered at intermediate- or high-risk for death or MI. These patients should receive urgent therapy for ACS as delineated in Module A (STEMI) or B (NSTEMI/Unstable Angina), as appropriate.

Patients who do not develop these features, remain at low risk, and may proceed to stress testing, either immediately before discharge from the hospital or chest pain unit, or after discharge and within 72 hours.

## **K. Non-Invasive Cardiac Stress Test**

### **OBJECTIVE**

Determine the presence or absence of ischemia in patients with a low likelihood of CAD

### **ANNOTATION**

Patients who are pain-free, have a normal/unchanged ECG and a normal initial cardiac marker measurement should have a follow-up ECG and repeat cardiac marker measurement after 6 – 8 hours. Those patients, who remain pain-free with no ECG changes and negative cardiac marker measurements, should undergo a cardiac stress test either before discharge or within 72 hours to separate patients with nonischemic discomfort from those with low risk ACS. This information is key for the development of further diagnostic steps and therapeutic measures

Patients with NSTEMI-ACS who have been stabilized on medical therapy, but who are found to have LV dysfunction, may benefit from further risk stratification using coronary angiography to assess their hemodynamic status and to determine their likelihood of benefit from revascularization.

A detailed discussion of noninvasive stress testing in CAD is presented in Module F

## **L. Stress Test Results Indicate Diagnosis of CAD with High/Intermediate Risk Features**

### **OBJECTIVE**

Refer patients who may benefit from coronary angiography or revascularization.

### **ANNOTATION**

Patients with high or intermediate risk features on noninvasive stress testing may benefit from coronary angiography and subsequent coronary revascularization and should be referred to a specialist in cardiovascular diseases.

The following list includes examples of non-invasive test results that indicate high or intermediate risk, for which cardiology referral for coronary angiography should be considered (adapted from ACC/AHA Guidelines for Coronary Angiography: Executive Summary and Recommendations, 1999).

### **High-Risk:**

- Severe resting LV dysfunction (LVEF <0.35)
- High-risk Duke treadmill score (score  $\leq$ -11)
- Severe exercise LV dysfunction (exercise LVEF <0.35)
- Stress-induced large perfusion defect (particularly if anterior)
- Stress-induced moderate-size multiple perfusion defects
- Large, fixed perfusion defect with LV dilatation or increased lung uptake (thallium-201)
- Stress-induced moderate-size perfusion defect with LV dilatation or increased lung uptake (thallium-201)
- Echocardiographic wall motion abnormality (involving >2 segments) developing at low dose of dobutamine ( $\leq$ 10 mg/kg/min) or at a low heart rate (<120 bpm)
- Stress echocardiographic evidence of extensive ischemia

### **Intermediate-Risk:**

- Mild/moderate resting left ventricular dysfunction (LVEF = 0.35 to 0.49)
- Intermediate-risk treadmill score (greater than -11 and less than 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 two segments

Patients with high or intermediate risk features on stress testing may benefit from further risk stratification using coronary angiography to determine their likelihood of benefit from revascularization. The decision about coronary revascularization resides with a specialist in cardiovascular diseases, since this specialist is in the best position to discuss the relative risks and benefits of bypass surgery versus medical therapy or percutaneous coronary revascularization.

The survival benefits of myocardial revascularization are most pronounced among patients with LV dysfunction. Therefore, all patients with NSTEMI/UA who are found to have a reduced EF (<0.40) on non-invasive testing should be considered for referral to cardiology for possible coronary angiography and subsequent revascularization (AHA/ACC UA – NSTEMI, 2002). This recommendation applies even to patients who do not have clinical signs and symptoms of heart failure and to those whose ischemic symptoms have been stabilized.

## **M. Does The Patient Have Documented IHD Or A High Probability Of CAD?**

### **OBJECTIVE**

For patients who do not meet criteria for an ACS, identify those who have CAD or a high probability of CAD.

### **ANNOTATION**

#### **Known CAD**

For purposes of this guideline, a patient may be considered to have a “known” CAD if any of the following exist:

- Prior coronary revascularization procedure (PCI or CABG)

- Prior documented MI
- Prior coronary angiogram demonstrating an obstructive CAD (>50% left main stenosis and/or >70% stenosis of a major epicardial artery)
- Prior non-invasive test indicating a high probability of CAD (see also Module F):
  - Pathologic Q-waves (>0.04 seconds duration and >25% of the height of the R-wave) on a standard resting ECG (except leads III, aVR, and V<sub>1</sub>)
  - Greater than 1mm horizontal or down sloping ST-segment depression on exercise electrocardiography—Medium- or large-sized fixed or reversible defect on myocardial perfusion imaging (e.g., thallium)
  - Segmental wall motion abnormalities by cardiac ultrasound examination or LV angiography
  - Inducible, segmental wall motion abnormalities on stress echocardiography

- Silent ischemia, defined as reversible ST-segment depression by ambulatory ECG monitoring

### Probability of CAD

For patients who do not have documented CAD, the likelihood that a patient's symptoms are due to CAD is estimated using only age, gender and the character of the symptoms. For instance, typical angina in a male older than 50 years indicates high probability of CAD. The pretest likelihood of CAD is presented in Table 7. It should be reemphasized that Table 7 *applies only to patients who do not have ACS*. The table is based on data from the ACC/AHA Stable Angina (2003) guideline, (Table 9: Pretest Likelihood of CAD in Symptomatic Patients According to Age and Sex). The ECG and serum markers of myocardial necrosis are not considered.

**Table 7. Pretest Likelihood of CAD in Symptomatic Patients According to Age and Sex\* (Combined Diamond/Forrester [1979] and CASS Data)**

Age (Years) <sup>a</sup>	Non-anginal Chest Pain <sup>b</sup>		Atypical (Probable) Angina <sup>b</sup>		Typical (Definite) Angina <sup>b</sup>	
	Men	Women	Men	Women	Men	Women
30-39	4	2	34	12	76	26
40-49	13	3	51	22	87	55
50-59	20	7	65	31	93	73
60-69	27	14	72	51	94	86

\*Each value represents the percent with significant CAD on catheterization.

(a) No data exist for patients less than 30 years or greater than 69 years, but it can be assumed that prevalence of CAD increases with age. In a few cases, patients with ages at the extremes of the decades listed may have probabilities slightly outside the high or low range.

(b) Definitions Used In The Classification Of Symptoms Into Typical/Definite Angina, Atypical/Probable Angina, And Non-Anginal Chest Pain:

Typical angina (definite)	IF all three of the primary symptom characteristics are present
Atypical angina (probable)	IF any two of the primary three symptom characteristics are present
Probably non-cardiac chest pain	IF provocation by exertion or emotional distress or relief by rest or nitroglycerin are present and one or more symptom characteristics suggesting non-cardiac pain are present
Definitely non-cardiac chest pain	IF none of the primary symptom characteristics are present and one or more symptom characteristics suggesting non-cardiac pain are present

## N. Does The Patient Have Intermediate Probability Of CAD?

### OBJECTIVE

Identify patients who have symptoms with an intermediate likelihood of CAD.

### ANNOTATION

Patients who do not have a documented CAD, but the likelihood that the symptoms are due to CAD is intermediate (using age, gender and the character of the symptoms in Table 7), should be referred for non-invasive evaluation to rule out or confirm the diagnosis of CAD (see Module F).

### O. Does The Patient Have A Low Probability of CAD but Abnormal Cardiac Screening Tests?

#### OBJECTIVE

Consider evaluating specific asymptomatic patients who have abnormal cardiac screening tests.

#### ANNOTATION

In general, asymptomatic patients with normal ECGs do not warrant further evaluation for IHD. However, patients may seek guidance from their primary physician regarding abnormalities in cardiac tests performed elsewhere. Non-invasive testing for CAD is being performed with increasing regularity in asymptomatic individuals—both because of the concern of an association between subclinical (“silent”) CAD and an increased risk of coronary events, and of advances in techniques used to detect occult CAD. The testing may be done as part of a routine physical examination, an exercise program, a preoperative evaluation, an evaluation performed for peripheral or cerebral vascular disease, or by patient request. Patients with a low probability of CAD (e.g., asymptomatic or atypical/probably non-cardiac chest pain) but abnormal cardiac screening tests may warrant cardiology evaluation for need for further testing (Module D).

### P. Consider Other Causes For The Symptoms

#### OBJECTIVE

Consider both cardiac (non-ischemic) and non-cardiac causes of the patient’s chest discomfort.

#### ANNOTATION

Although the primary goal of the Core Module is to evaluate for ischemic sources of chest discomfort, the patient’s complaints deserve investigation even if ischemia is ruled out. In many instances, the source of non-cardiac chest discomfort will be obvious from the history (e.g., ascending midline pain associated with reflux of acid into the mouth and relieved entirely by antacids) or physical examination (e.g., the presence of dermatomal blisters in herpes zoster). Also, the physician must keep in mind that other cardiac diseases (such as pericarditis or valvular heart disease) can present with chest pain.

A thorough history, physical examination and review of symptoms, appropriate lab testing, and occasionally, an empiric trial of specific therapy may be necessary to confirm an alternative diagnosis. In many instances, no specific diagnosis will be made. The patient, however, will usually be reassured to know that the symptoms do not have a cardiac source. However, other risk factors for cardiovascular diseases should be addressed including screening for smoking, hypertension, diabetes, lipid profile and lifestyle modification.

**Table 8. Alternative Diagnoses to Angina for Patients with Chest Pain or Discomfort (adapted from ACC/AHA Stable Angina, 1999)**

Nonischemic Cardiovascular	Pulmonary	Gastrointestinal	Chest Wall	Psychiatric
<ul style="list-style-type: none"> <li>• Aortic dissection</li> <li>• Pericarditis</li> </ul>	<ul style="list-style-type: none"> <li>• Pulmonary embolus</li> <li>• Pneumothorax</li> <li>• Pneumonia</li> <li>• Pleuritis</li> </ul>	<ul style="list-style-type: none"> <li>• Esophageal               <ul style="list-style-type: none"> <li>—Esophagitis</li> <li>—Spasm</li> <li>—Reflux</li> </ul> </li> <li>• Biliary               <ul style="list-style-type: none"> <li>—Colic</li> <li>—Cholecystitis</li> <li>—Choledocholithiasis</li> <li>—Cholangitis</li> </ul> </li> <li>• Peptic ulcer</li> <li>• Pancreatitis</li> </ul>	<ul style="list-style-type: none"> <li>• Costochondritis</li> <li>• Fibrositis</li> <li>• Rib Fracture</li> <li>• Sternoclavicular arthritis</li> <li>• Herpes zoster (before the rash)</li> </ul>	<ul style="list-style-type: none"> <li>• Anxiety disorder               <ul style="list-style-type: none"> <li>—Hyperventilation</li> <li>—Panic disorder</li> <li>—Primary anxiety</li> </ul> </li> <li>• Affective disorders (e.g., depression)</li> <li>• Somatoform disorders</li> <li>• Thought disorders (e.g., fixed delusion)</li> </ul>

# VA/DOD CLINICAL PRACTICE GUIDELINE FOR THE MANAGEMENT OF ISCHEMIC HEART DISEASE MODULE A SUMMARY

## SUSPECTED ACUTE MYOCARDIAL INFARCTION ST-SEGMENT ELEVATION OR NEW OR PRESUMED NEW LBBB

### KEY ELEMENTS

For patients who meet criteria for **emergent reperfusion therapy**:

- Admit to an intensive care unit
- Initiate heparin or low-molecular weight heparin, if indicated
- Warfarin is recommended for patients at risk for systemic embolism (intraventricular clot or atrial fibrillations)
- Initiate IV beta-blocker followed by oral
- Initiate ACE inhibitor therapy in the absence of contraindications.

*If less than 12 hours from onset of symptoms:*

- *Refer to percutaneous coronary intervention (PCI) if intervention can be performed within 90 minutes of presentation in a high volume center by a high volume operator.*
- *Initiate thrombolytic therapy if not contraindicated and not referred for direct PCI.*
- *Refer to PCI if thrombolytic therapy is contraindicated or response to thrombolysis is unsatisfactory.*
- Consider non-invasive evaluation (cardiac stress test)
- Refer to cardiology if at high-risk for death or recurrent MI and/or left ventricular (LV) dysfunction.
- Ensure pharmacological therapy for ischemia, angina, and chronic heart failure (CHF)
- Discharge patient to home with appropriate follow-up.

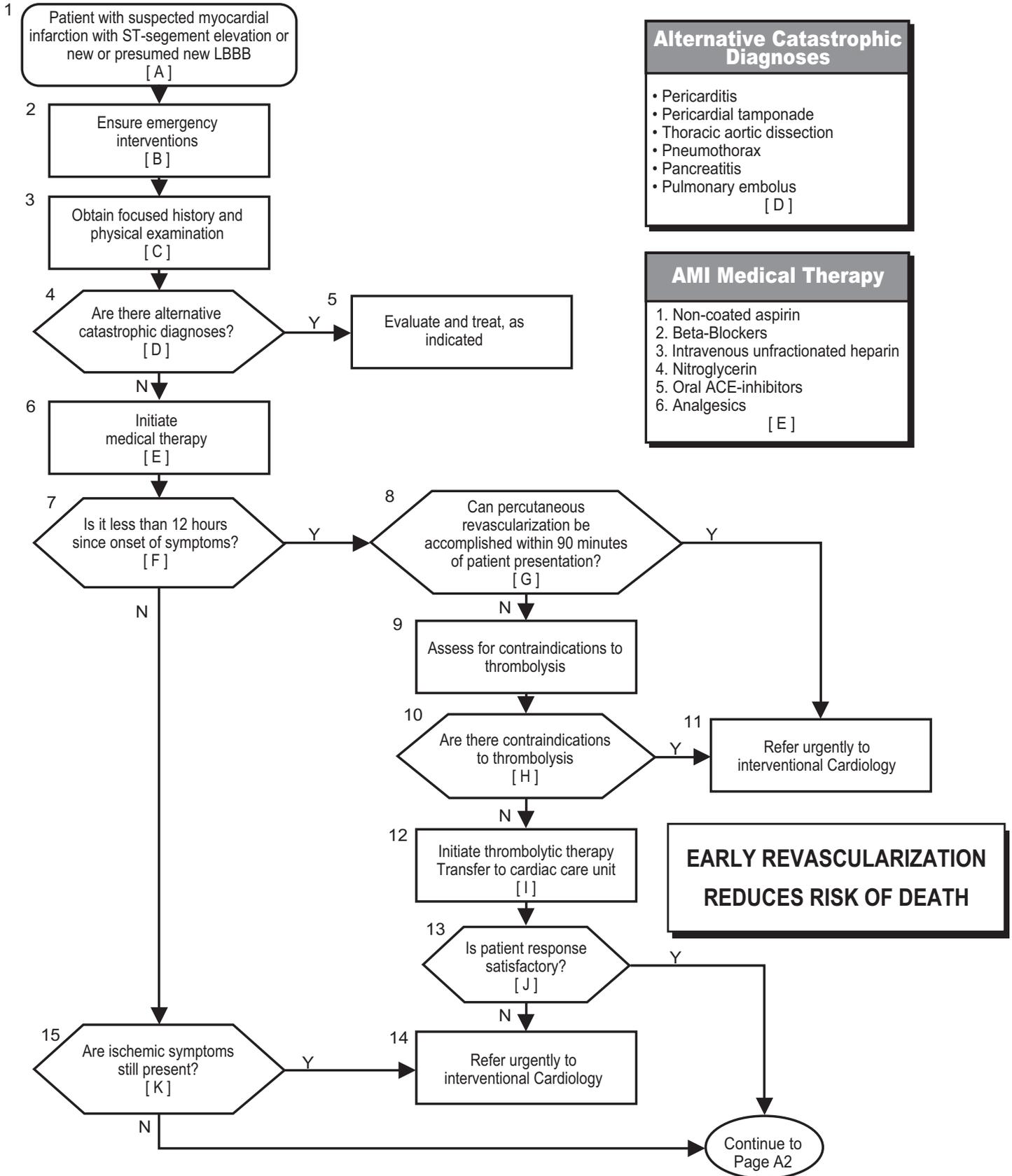
Patients with acute myocardial infarction (AMI), for which reperfusion therapies may be appropriate, are managed within this module. An AMI for which reperfusion therapies may be appropriate is defined by the following:

- Clinical history of ischemic- or infarction-type symptoms
- Diagnostic electrocardiogram (ECG) findings of new or presumed new left bundle branch block (LBBB) or ongoing ST-segment elevation in two or more contiguous leads (i.e., 0.2 mV or more in leads V<sub>1</sub>-V<sub>3</sub>, or 0.1 mV or more in other leads)

*Module A will be revised Spring 2004 following ACC/AHA revision of STEMI guideline.*

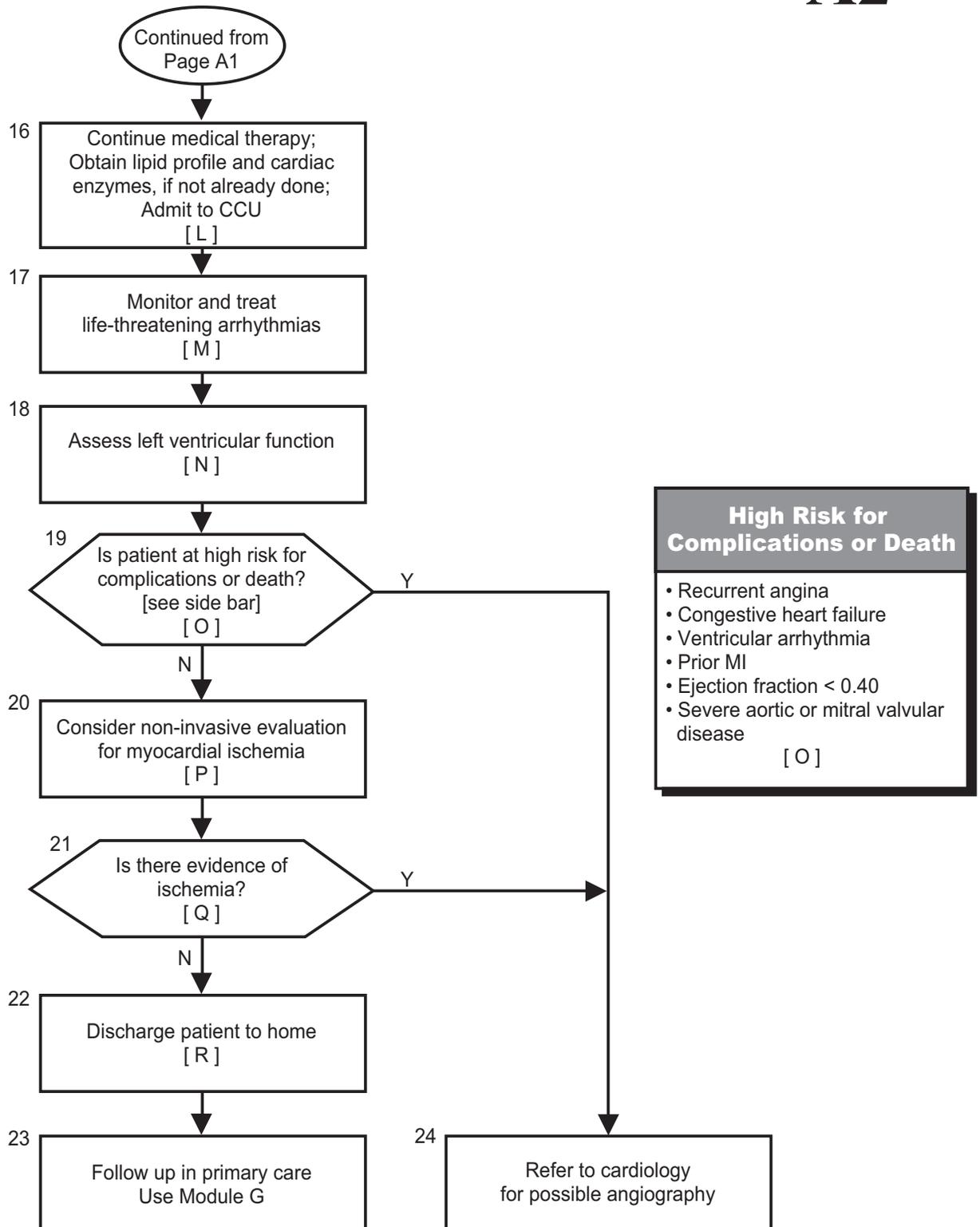
**MANAGEMENT OF ISCHEMIC HEART DISEASE**  
**Module A: Suspected Acute Myocardial Infarction**  
**(ST-Elevation or LBBB)**

**A1**



**MANAGEMENT OF ISCHEMIC HEART DISEASE**  
**Module A: Suspected Acute Myocardial Infarction**  
**(ST-Elevation or LBBB)**

**A2**



## EMERGENCY INTERVENTIONS

**Cardiac monitor:** Patients with acute coronary syndromes (ACS), especially with suspected myocardial infarction (MI), should be placed on continuous cardiac monitoring as soon as possible. Potentially lethal ventricular arrhythmias can occur within seconds to hours from the onset of coronary ischemia, and monitoring will allow their immediate detection and treatment.

**Oxygen (O<sub>2</sub>):** Supplemental oxygen should be administered on initial presentation, especially if congestive heart failure (CHF) or oxygen desaturation is present. For uncomplicated MIs, oxygen may be reassessed after six hours. CO<sub>2</sub> retention is not usually a concern with low flow nasal O<sub>2</sub>, even in patients with severe chronic obstructive pulmonary disease (COPD).

**Aspirin:** 160 mg to 325 mg should be chewed immediately to accelerate absorption and should be given even if the patient is on chronic aspirin therapy.

**Intravenous (IV) Access:** Intravenous access for the delivery of fluids and drugs should be obtained, with both antecubital veins used if possible for multiple infusions, especially if thrombolytic therapy is being considered. Unnecessary arterial and venous punctures should be avoided and experienced personnel should perform access. While the IV is being started, blood samples for cardiac enzymes/markers (i.e., troponin - preferred, CK, CK-MB acceptable), lipid profile, complete blood count (CBC), electrolytes, renal function, international normalized ratio (INR), and activated partial thromboplastin time (APTT) can be obtained, although immediate treatment of ACS should not be delayed by the results from these tests.

**Sublingual nitroglycerin** should be given, unless the patient is hypotensive or bradycardic, has taken sildenafil within the last 24 hours, or there is a strong suspicion of right ventricular infarction.

**ECG:** Obtain within 10 minutes of presentation and follow-up with a serial ECG. A right-sided ECG should be performed if a standard ECG suggests an inferior wall MI.

### **Adequate analgesia**

**Advanced cardiac life support (ACLS, 1999):** algorithm should be applied, as indicated.

**Chest X-ray:** A portable chest radiograph should be performed, particularly to evaluate for mediastinal widening (aortic dissection), cardiac silhouette, and evidence of CHF.

**Transportation:** In many settings within the DoD or the VA systems, the patient will need to be urgently transported to a setting where an adequate level of monitoring, evaluation, and treatment is available.

### **Obtain Focused History and Physical Examination**

Patients presenting with an acute ST-elevation myocardial infarction (STEMI) should have an expedited and focused history and physical examination and ECG within 10 minutes of presentation, to assess for eligibility of reperfusion therapy, complications from an AMI, and contraindications to reperfusion therapy.

### **Specific Clinical History Questions Should Include the Following:**

- Characteristics of MI symptoms
- Complications of MI
- Contraindications to Reperfusion Therapy

### **Focused Physical Examination Should Include:**

- Vitals Signs
- Limited examination of skin, lungs, heart, abdomen, peripheral pulse, and focal neurological signs (see full guideline for details)

### **Alternative Catastrophic Diagnoses**

Patients may present with chest pain syndromes that mimic AMI symptoms and signs, including ECG changes typical of an AMI. The focused history and physical examination should help make the appropriate diagnosis. It is important to diagnose such conditions rapidly, as most of them are life-threatening and may be worsened by standard AMI therapies.

## Clinical Findings for Alternative Catastrophic Diagnoses

Diagnoses	Clinical Findings
Pericarditis	<ul style="list-style-type: none"> <li>• Pain that is more severe in a supine position</li> <li>• Friction rub may be present</li> <li>• ECG with diffuse ST-elevation</li> </ul>
Pericardial tamponade	<ul style="list-style-type: none"> <li>• Jugular venous distension</li> <li>• Pulsus paradoxus</li> <li>• ECG with low voltage/electrical alternans</li> </ul>
Thoracic aortic dissection	<ul style="list-style-type: none"> <li>• Very severe midline pain, maximal at onset</li> <li>• Pain often radiates to the back</li> <li>• Unequal pulses or blood pressure difference in arms</li> </ul>
Pneumothorax	<ul style="list-style-type: none"> <li>• Associated with trauma, COPD, or mechanical ventilation</li> <li>• Unilateral diminished breath sounds</li> <li>• Normal or increased resonance to percussion</li> </ul>
Pulmonary embolus	<ul style="list-style-type: none"> <li>• Pleuritic chest pain</li> <li>• Shortness of breath, without evidence of CHF</li> </ul>
Pancreatitis	<ul style="list-style-type: none"> <li>• History of gall bladder disease or alcoholism</li> <li>• Abdominal tenderness</li> <li>• Nausea and vomiting</li> </ul>

## THERAPY

### Initial Medical Therapy

Medical therapy should be initiated while preparations are made for reperfusion therapy. Medications that may be given at this time include the following:

#### Non-Coated Aspirin

- All patients should chew 160 mg to 325 mg of aspirin within 10 minutes of presentation.
- Patients should be given aspirin, even if they are receiving anticoagulation (e.g., warfarin) or antiplatelet agents (e.g., aspirin or clopidogrel) at time of presentation.

- If a patient is unable to take aspirin by mouth because of nausea, vomiting, or other gastrointestinal disorders, 325 mg may be given as a suppository.
- Contraindications to aspirin include a documented allergy to salicylates, active bleeding, or active peptic ulcer disease.
- Patients who have an allergy to aspirin and no contraindication to antiplatelet therapy should be given clopidogrel, ticlopidine, or dipyridamole.

#### Beta-Blockers

- Metoprolol 5 mg IV up to 3 doses or atenolol 5 mg to 10 mg IV should be given within 12 hours of presentation.
- Oral beta-blockers should be started at the time the intravenous beta-blocker is given.
- Relative contraindications to beta-blockers, include: heart rate <60 beats per minute (bpm), systolic blood pressure <100 mm Hg, moderate or severe CHF, signs of peripheral hypoperfusion, PR interval >0.24 seconds on the ECG, second or third degree atrioventricular (AV) block, severe COPD, and history of asthma.
- Diabetes should not be considered a contraindication to beta-blocker therapy in the setting of an AMI.

#### Intravenous Unfractionated Heparin

- Unfractionated heparin should be initiated in all patients receiving alteplase, reteplase, or tenecteplase or referred for emergent revascularization. Heparin may be started at 60 U/kg (maximum 4000 U) IV bolus, followed by an infusion of 12 U/kg/hr infusion (maximum 1000 U/hr) with a goal APTT of 50 to 70 seconds. The use of heparin should be continued for 48 hours and then reassessed.
- Patients receiving streptokinase who are at high risk for systemic emboli (i.e., who have a large or anterior wall MI, previous embolus, or known left ventricular (LV) thrombus) should be started on intravenous heparin only if the APTT is <2 times control 6 hours from the initiation of streptokinase. Heparin may then be given with a goal APTT of 1.5 to 2.0 times control.

## Nitroglycerin

- Patients presenting with symptoms consistent with a MI and ECG changes suggestive of a STEMI, may be given nitroglycerin 0.3 mg to 0.4 mg sublingually during the initial evaluation. Vasospastic angina may respond to sublingual nitroglycerin. The administration of sublingual nitroglycerin should not delay reperfusion therapy.
- Intravenous nitroglycerin should be considered for 24 to 48 hours in patients with a large, anterior wall MI, persistent ischemia, CHF, or hypertension.
- Nitrates should be avoided in patients with evidence for a right ventricular infarction.
- Contraindications to nitrates include the use of sildenafil within 24 hours of presentation, hypotension (systolic blood pressure <90 mm Hg), or significant bradycardia (i.e., heart rate <50 bpm).

## Oral Angiotensin-Converting Enzyme Inhibitors (ACE-inhibitor)

- Oral ACE-inhibitor should be considered in all patients within 24 hours of a MI, but especially in those patients with an acute anterior wall MI, CHF from systolic dysfunction, or left ventricular ejection fraction (LVEF) <0.40.
- ACE-inhibitor should be avoided in patients with hypotension or known contraindication, including: history of ACE-inhibitor induced angioedema, hyperkalemia, acute renal failure, and bilateral renal artery stenosis.

## Analgesics

- Because of increased sympathetic stimulation associated with pain from an AMI, patients should be offered analgesics, such as morphine sulfate 2 mg to 4 mg IV as needed (PRN). Per ACC/AHA AMI (1996) recommendations, analgesia should not be withheld from patients to evaluate the efficacy of reperfusion therapy.
- Routine use of anxiolytics, such as diazepam, is usually not necessary.

## REPERFUSION THERAPY

Multiple studies have shown that patients who present within 12 hours of the onset of symptoms benefit the most from reperfusion strategies (i.e., percutaneous coronary intervention (PCI) or thrombolytic therapy).

While consideration for reperfusion should be given for up to 12 hours the risk:benefit ratio declines the first 6 hours. Thus, clinical judgment should be used in the decision to give reperfusion therapy, such as ongoing ischemia, size and location of the MI.

Onset of Symptoms	Intervention
<12 hours	If PCI can be accomplished within 90 minutes, refer to interventional Cardiology
<12 hours	Refer to interventional cardiology if thrombolytics are contraindicated or ineffective
<12 hours	If PCI not available/declined/inappropriate, administer thrombolytics, if not contraindicated. Transfer to CCU
>12 but <24 hours	If persistent symptoms or cardiogenic shock, refer to interventional Cardiology; consider PCI or thrombolytics
>24 hours	Continue Medical therapy

## Direct PCI

Direct percutaneous revascularization, performed within 90 minutes of presentation by an experienced center and operator, is the preferred mode of reperfusion. Patients should be evaluated for thrombolytic therapy if the center evaluating the patient cannot perform direct percutaneous revascularization within 90 minutes, or the patient cannot be transferred to a facility with direct percutaneous revascularization capability and an initial presentation to balloon inflation time no greater than 90 minutes.

Patients who present with ongoing ischemic symptoms or cardiogenic shock more than 12 hours from onset of symptoms should be referred for direct percutaneous revascularization. If direct percutaneous revascularization is not available at the receiving facility, patients should be transferred to a facility with percutaneous revascularization capability.

## CONTRAINDICATIONS TO THROMBOLYSIS

Patients with absolute contraindications to thrombolytic therapy should be considered for direct percutaneous revascularization. Relative contraindications are cautions only, where the relative risks and benefits must be weighted before administering the thrombolytic agent.

### Absolute Contraindications to Thrombolysis

- Previous hemorrhagic stroke at any time
- Other strokes or cerebrovascular events, within one year
- Known intracranial neoplasm
- Active internal bleeding (except menses)
- Suspected aortic dissection
- Acute pericarditis

### Relative Contraindications to Thrombolysis

- Severe, uncontrolled hypertension on presentation (i.e., blood pressure >180/110 mm Hg)
- Current use of anticoagulants in therapeutic doses
- Known bleeding problems
- Recent trauma (i.e., within 2 to 4 weeks) including head trauma or traumatic or prolonged (i.e., >10 minutes) cardiopulmonary resuscitation (CPR)
- Recent major surgery (i.e., within 3 weeks)
- Non-compressible vascular punctures
- Recent internal bleeding (i.e., within 2 to 4 weeks)
- Prior exposure to streptokinase, if that agent is to be administered (i.e., 5 days to 2 years)
- Pregnancy
- Active peptic ulcer
- History of chronic, severe hypertension
- Age >75 years
- Stroke Risk Score  $\geq 4$  risk factors:
  - Age  $\geq 75$  years
  - Female
  - African American descent
  - Prior stroke
  - Admission systolic blood pressure  $\geq 160$  mm Hg
  - Use of alteplase
  - Excessive anticoagulation (i.e., INR  $\geq 4$ ; APTT  $\geq 24$ )
  - Below median weight ( $\leq 65$  kg for women;  $\leq 80$  kg for men)

- Cardiogenic shock (i.e., sustained systolic blood pressure <90 mmHg and evidence for end-organ hypoperfusion, such as cool extremities and urine output <30 cc/hr) and CHF

## THROMBOLYTIC THERAPY

### Current Thrombolytic Agents

- Alteplase (tPA) (100 mg maximum): 15 mg IV bolus, then 0.75 mg/kg over 30 minutes, then 0.5 mg/kg over the next 60 minutes.
- Reteplase (rPA): 10 U over 2 minutes, followed by a second 10 U IV bolus 30 minutes later.
- Streptokinase: 1.5 million units (MU) IV over 60 minutes.
- Tenectaplastase: IV bolus weight adjusted (30 mg to patients who weigh <60 kg, 35 mg to patients who weigh 60 kg to 69.9 kg, 40 mg to patients who weigh 70 kg to 79.9 kg, 45 mg to patients who weigh 80 kg to 89.9 kg, and 50 mg to patients who weigh  $\geq 90$  kg).

Thrombolytic agents should be started in the emergency room as mortality is directly related to time to reperfusion. Once thrombolytic agents are initiated, patients may be transferred to an intensive care unit/cardiac care unit (ICC/CCU).

### Clinical Signs of Reperfusion Following Thrombolytic Administration

- Resolution of chest discomfort, within 90 minutes
- At least 50% resolution of ECG changes, within 90 minutes
- Early CK washout
- Reperfusion arrhythmias (i.e., bradyarrhythmias or accelerated idioventricular rhythm)

If a patient's symptoms and/or ECG changes do not resolve within 90 minutes, the patient should be referred to cardiology and considered for salvage angioplasty, especially if an anterior wall MI exists.

## CONTINUED MEDICAL THERAPY

### Recommendations Following Successful Reperfusion

- Admit patient to CCU/ICU with continuous ECG monitoring for dysrhythmic events with nurse staffing appropriate to level of care.

- Draw serial cardiac markers (e.g., CK-MB t.i.d. and/or cardiac troponins b.i.d.) until peak is reached; CBC; lipid panel, if within 24 hours of onset of symptoms; electrolytes, including renal function; upright CXR, if not yet obtained.
- Administer supplemental O<sub>2</sub>, especially for overt pulmonary congestion or arterial oxygen desaturation; O<sub>2</sub> may be discontinued in 2 to 6 hours following presentation for an uncomplicated MI; the use of O<sub>2</sub> needs to be reassessed every 24 hours for all patients.
- For electrolyte management, keep K<sup>+</sup> greater than 4.0 mEq/L and Mg<sup>++</sup> greater than 2.0 mEq/L.
- Give aspirin, 160 mg to 325 mg P.O. qd, indefinitely (clopidogrel or ticlopidine should be administered to patients who are unable to take aspirin because of hypersensitivity or major GI intolerance).
- Intravenous heparin should be given to patients who receive alteplase, reteplase, or tenecteplase to maintain an APTT 50 to 75 seconds for 48 hours. Patients should be given intravenous heparin—especially those patients at high risk of systemic emboli—unless given a nonselective thrombolytic agent (e.g., streptokinase) and they are at low risk for systemic embolus. These latter patients can be considered for subcutaneous heparin (7,500 U to 12,500 U b.i.d., until ambulatory).
- Give intravenous nitroglycerin for the first 24 to 48 hours, if not hypotensive or bradycardic (i.e., heart rate <50 bpm) for patients with CHF, large anterior wall MI, hypertension, or recurrent ischemic symptoms. The use of nitroglycerin should be reassessed beyond 48 hours from presentation, unless the patient has recurrent angina or CHF.
- Continue oral beta-blockers or initiate, if not started. Beta-blockers should be started within 12 hours of presentation.
- Continue oral ACE-inhibitor or initiate, if not started. ACE-inhibitor should be started within 24 hours of presentation.
- Initiate dietary counseling and smoking cessation.

### **PATIENTS AT HIGH RISK FOR COMPLICATIONS OR DEATH**

Patients at increased risk for complications or death following MI should be referred to cardiology for possible intervention. Findings that place patients at increased risk for complications or death following a MI, include the following:

- Recurrent angina (i.e., spontaneous or inducible)
- CHF
- Polymorphic ventricular tachycardia, ventricular fibrillation, or sustained monomorphic ventricular tachycardia more than 48 hours from presentation
- Prior MI
- Ejection fraction (EF) <0.40
- Associated severe mitral or aortic valvular disease (e.g., aortic stenosis, aortic regurgitation, or mitral regurgitation)

## **LIFE-THREATENING ARRHYTHMIAS**

### **Bradyarrhythmias That May Require Treatment with Atropine**

- Symptomatic sinus bradycardia
- Ventricular asystole
- Symptomatic, suprahisian atrioventricular (AV) block (i.e., second-degree or third-degree AV block, with a narrow-QRS-complex escape rhythm)

### **Bradyarrhythmias That May Require Treatment with Temporary Transvenous Pacing**

- Symptomatic bradycardia that is unresponsive to medical therapy
- Asystole
- Bilateral BBB (i.e., alternating BBB or right bundle branch block (RBBB) with alternating left anterior fascicular block/left posterior fascicular block (LAFB/LPFB))
- Newly acquired trifascicular block (i.e., RBBB with LAFB/LPFB or LBBB and first-degree AV block)
- Mobitz Type-II second-degree AV block
- Complete heart block with a wide ventricular escape

### **Supraventricular Tachycardias That May Require Treatment**

- Atrial fibrillation (AF) with rapid ventricular response should be rate-controlled with nodal blocking agents, such as a beta-blocker.
- Unstable AF (i.e., angina, hypotension, or CHF) should be considered for cardioversion.
- Paroxysmal supraventricular tachycardias (PSVT) may be cardioverted, if unstable, or treated medically with nodal blocking agents, such as a beta-blocker.

## Ventricular Tachycardias That Require Treatment

- Pulseless, monomorphic ventricular tachycardia, polymorphic ventricular tachycardias, and ventricular fibrillation, all of which require defibrillation and treatment according to ACLS guidelines.
- Unstable (i.e., angina, hypotension, or CHF) monomorphic ventricular tachycardia requires synchronized cardioversion
- Stable, sustained monomorphic ventricular tachycardia may be treated initially with antiarrhythmics (i.e., lidocaine or intravenous amiodarone), followed by synchronized cardioversion, if medical therapy is unsuccessful

## Ventricular Events That Do Not Require Treatment

- Accelerated idioventricular rhythm (AIVR)
- Asymptomatic premature ventricular contractions (PVCs) or asymptomatic nonsustained ventricular tachycardia (NSVT)

Antiarrhythmic agents, started at any point, may be continued 24 to 48 hours after initiation, then reassessed and stopped as soon as possible. Episodes of polymorphic ventricular tachycardia, ventricular fibrillation, or monomorphic ventricular tachycardia sustained for more than 30 seconds, more than 48 hours after presentation, should be referred to a cardiologist or electrophysiologist for further evaluation. ACLS protocols should be observed during episodes of sustained polymorphic or monomorphic ventricular tachycardia or ventricular fibrillation, until the restoration of a stable rhythm.

## NON-INVASIVE EVALUATION

### Obtain an Echocardiogram, if Available, to Assess for the Following:

- Reduced LV function
- Associated wall motion abnormalities
- Associated valvular disease
- Ventricular thrombus

### Non-Invasive Evaluation For Myocardial Ischemia

- Patients with an uncomplicated MI should be referred for a non-invasive evaluation for ischemia at 4 to 6 days from presentation.
- Patients undergoing early coronary catheterization, or are planned for catheterization may not need a stress test.

- The yield of performing the test should be evaluated for patients with major comorbidity that severely shorten their life expectancy.
- Patients should undergo a symptom-limited treadmill at 3 to 6 weeks for functional capacity and prognosis, if early stress was submaximal.
- Patients with evidence of ischemia during non-invasive evaluation should be considered for further cardiac evaluation, such as cardiac catheterization.
  - Hypotensive response (i.e., sustained decrease in systolic blood pressure >10 mmHg or a flat systolic blood pressure response <130 mmHg) and/or chest pain and/or ST-segment depression of  $\geq 1$  mm during a submaximal (low level) EST
  - Reversible perfusion defect on sestamibi or thallium myocardial imaging
  - Inducible wall motion abnormality during stress echocardiogram

## DISCHARGE PATIENT TO HOME

Patients can begin regular walking programs immediately following discharge. Sexual activity may be resumed within 7 to 10 days of discharge. Patients may resume driving a week from discharge, following an uncomplicated MI, if permitted by state laws.

Patients with uncomplicated MI may be discharged to home 3 to 7 days following the acute presentation. Discharge medications should include the following, unless contraindicated:

- Aspirin
- Beta-blocker
- ACE-inhibitor
- Sublingual nitroglycerin
- Lipid-lowering therapy
- Consider Warfarin, in patients with larger, anterior wall MI

Discharge planning should include the following:

- Activity prescription
- Dietary habits
- Medical therapy
- Smoking cessation
- 4 to 6 weeks symptom-limited EST

Management of the patient's follow-up is described in Summary for Medical Follow-Up and Secondary Prevention.

# VA/DOD CLINICAL PRACTICE GUIDELINE FOR THE MANAGEMENT OF ISCHEMIC HEART DISEASE MODULE B SUMMARY

## DEFINITE/PROBABLE NON-ST-SEGMENT ELEVATION ACUTE CORONARY SYNDROME (ACS) (UNSTABLE ANGINA/NON-ST-SEGMENT ELEVATION MI [NSTEMI])

### KEY ELEMENTS

Patients with ACS (UA/NSTEMI) are at high risk for MI or death and are candidates for further aggressive diagnostic and therapeutic interventions that should include:

- Ensure emergency intervention
- Admission to an intensive- or intermediate-care unit
- Immediate cardiac rhythm monitoring
- Therapy directed at stabilizing ischemia (beta-blocker, NTG)
- Risk-stratification to determine prognosis and guide treatment. Assessment for risk of death or MI based on symptoms, level of biomarker (troponin, CK) and ECG
- Antithrombotic therapy tailored to individual risk that should include:
  - ASA
  - Heparin (UFH) or low molecular weight heparin (LMWH)
  - Clopidogrel if intervention is not planned

\* UA/NSTEMI patients should *not* receive reperfusion fibrinolytic therapy

High-risk patients are candidates for further aggressive diagnostic and therapeutic interventions including

- Early (i.e., <48 hour) coronary angiography with subsequent revascularization if indicated.
- GP IIb/IIIa antagonist in addition to aspirin, heparin and clopidogrel in patients with continuing ischemia or with other high-risk features.
- GP IIb/IIIa antagonist may also be used in patients in whom an early invasive strategy is planned. GP IIb/IIIa can be administered just prior to PCI.

In patients not undergoing angiography:

Perform non-invasive evaluation (cardiac stress test and left ventricular [LV] function), and:

If LV function is compromised:

- Ensure pharmacologic therapy for ischemia, angina, and congestive heart failure
- Initiate ACE inhibitor therapy
- Consider referral to cardiology

All patients with suspected, but unproven, unstable angina should have further diagnostic testing to determine the accuracy of the diagnosis.

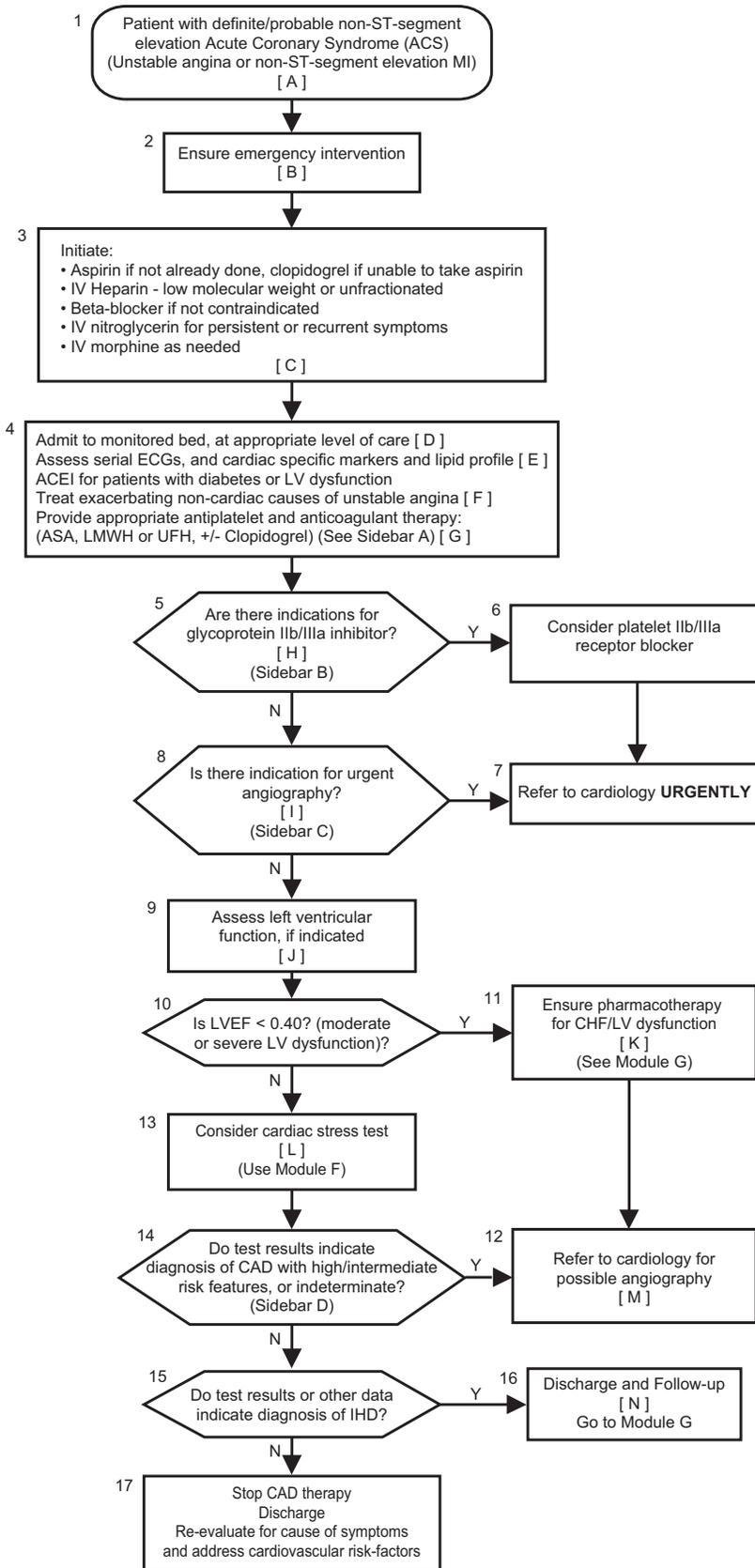
Discharge patient to home with appropriate follow-up.

## EXECUTIVE SUMMARY

Unstable angina (UA) and non-ST-segment elevation myocardial infarction (NSTEMI) are related clinical conditions that share a common pathophysiological basis. Both, acute myocardial infarction (AMI) with ST-segment elevation or bundle branch block (BBB) and UA and NSTEMI are referred to as acute coronary syndromes (ACS). The initial management of patients presenting with non-ST-segment elevation-ACS (NSTEMI-ACS) is identical to the approach for myocardial infarction (MI) with ST-segment elevation or left BBB. Patients with ACS are at high risk for MI or death and should be admitted to an intensive- or intermediate-care unit and receive immediate cardiac rhythm monitoring and medical therapy directed at stabilizing ischemia. However, UA/NSTEMI patients should not receive reperfusion fibrinolytic therapy. Patients whose clinical presentation suggests a high-risk for death and/or MI are candidates for further aggressive diagnostic and therapeutic interventions including glycoprotein IIb/IIIa receptor inhibitors and early (i.e., <48 hour) coronary angiography with subsequent revascularization if indicated. If left ventricular function (LV) is compromised, congestive heart failure/left ventricular dysfunction therapy should be initiated.

All patients with suspected UA/NSTEMI should be risk-stratified to determine their prognosis and guide their treatment. Patients, who do not have clinical findings that suggest either intermediate or high short-term risk of death or MI, should also be monitored. Monitoring of these patients can be performed either in an inpatient setting or in a specialized chest pain evaluation center, where they do not require initial medical treatment other than aspirin and sublingual nitroglycerin (NTG). All patients with suspected, but unproven, unstable angina should have further diagnostic testing to determine the accuracy of the diagnosis.

**MANAGEMENT OF ISCHEMIC HEART DISEASE**  
**Module B: Definite/Probable Acute Coronary Syndrome**  
**(Unstable Angina or Non-ST-Segment Elevation MI)**



**B**

**Sidebar A (Box 4) - Antiplatelet and Anticoagulant Therapy**

High Risk (Recurrent ischemia or other high risk features)	Moderate Risk (Likely/definite ACS)
Aspirin Clopidogrel* LMWH or UFH GP IIb/IIIa inhibitor	Aspirin Clopidogrel* LMWH or UFH

\* Unless angiography is planned

**Sidebar B (Box 5) - Indications for IIb/IIIa and Early Invasive Therapy in High Risk Patients**

- Recurrent angina/ischemia despite therapy
- Elevated troponin (TnT or TnI)
- New or presumably new ST-segment depression

**Sidebar C (Box 8) - Indications for Angiography in Intermediate Risk Patients**

- New/recurrent angina/ischemia
- High risk findings on non-invasive testing
- Depressed left ventricular LV systolic function (e.g., ejection fraction (EF) <0.40)
- Hemodynamic instability (e.g., hypotension)
- Sustained ventricular tachycardia
- Previous PCI within 6 months
- Prior CABG

**Consider Referral to Cardiology**

- Prior myocardial infarction
- New T-wave inversion (>0.2 mV)
- Indeterminate troponin

**Sidebar D (Box 14) - Cardiac Stress Test**

**High-Risk Findings**

- Duke treadmill score less than or equal to -11 (estimated annual mortality >3%)
- Large stress-induced perfusion defect
- 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 >2 segments at ≤10 mg/kg/min dobutamine or HR <120/min

**Intermediate-Risk Findings**

- Duke treadmill score (greater than -11 and less than 5) (estimated annual mortality 1-3%)
- Moderate stress-induced perfusion defect without LV dilation or increased lung uptake
- Limited stress echocardiographic ischemia with wall motion abnormality involving ≤2 segments at higher doses of dobutamine (>10 mg/kg/min dobutamine)

## MODULE B: DEFINITE/PROBABLE NON-ST ELEVATION ACUTE CORONARY SYNDROME (ACS) UNSTABLE ANGINA/NON-ST-SEGMENT ELEVATION MI

### ANNOTATIONS

#### **A. Patient with Definite/Probable Non-ST Elevation Acute Coronary Syndrome (Unstable Angina Or Non-ST-Segment Elevation MI )**

Module B presents guidelines for the diagnosis and management of UA and the closely related condition, NSTEMI. UA/NSTEMI, together with ST-segment elevation myocardial infarction (STEMI), make up the acute coronary syndromes (ACS). Patients presenting with UA/NSTEMI are considered to have non-ST elevation ACS (NSTEMI-ACS)

UA is commonly considered to have three presentations: (1) rest angina; (2) new onset of severe angina, defined as at least Class III severity by the Canadian Cardiovascular Society (CCS) classification; and (3) increasing angina to at least CCS Class III severity. The hallmark of NSTEMI is an elevation of markers of myocardial injury in the blood stream (e.g., troponin I, troponin T, or CK-MB). Because the pathogenesis and responses to therapy of UA and NSTEMI are similar, they are considered together here, as well as in the American College of Cardiology and the American Heart Association (ACC/AHA) Guidelines for the Management of Patients with Unstable Angina and Non-ST-Segment Elevation Myocardial Infarction (ACC/AHA UA - NSTEMI, 2002).

Patients presenting with ST-segment elevation myocardial infarction (STEMI) or MI with left bundle branch block (LBBB) should be managed using Module A of this guideline. The distinction between ST-segment

elevation myocardial infarction and non-ST elevation ACS is important, because immediate reperfusion, with either primary angioplasty or thrombolytic agents, has been shown to reduce mortality in patients with STEMI or LBBB MI, whereas the use of fibrinolytic agents may be potentially harmful in UA and NSTEMI.

Patients with Ischemic Heart Disease (IHD) who do not meet the criteria for ACS (as defined in the CORE Module) can be managed using Module C: Management of Stable Angina or Module G: Follow-up and Secondary Prevention.

#### **Risk stratification of patients with NSTEMI-ACS**

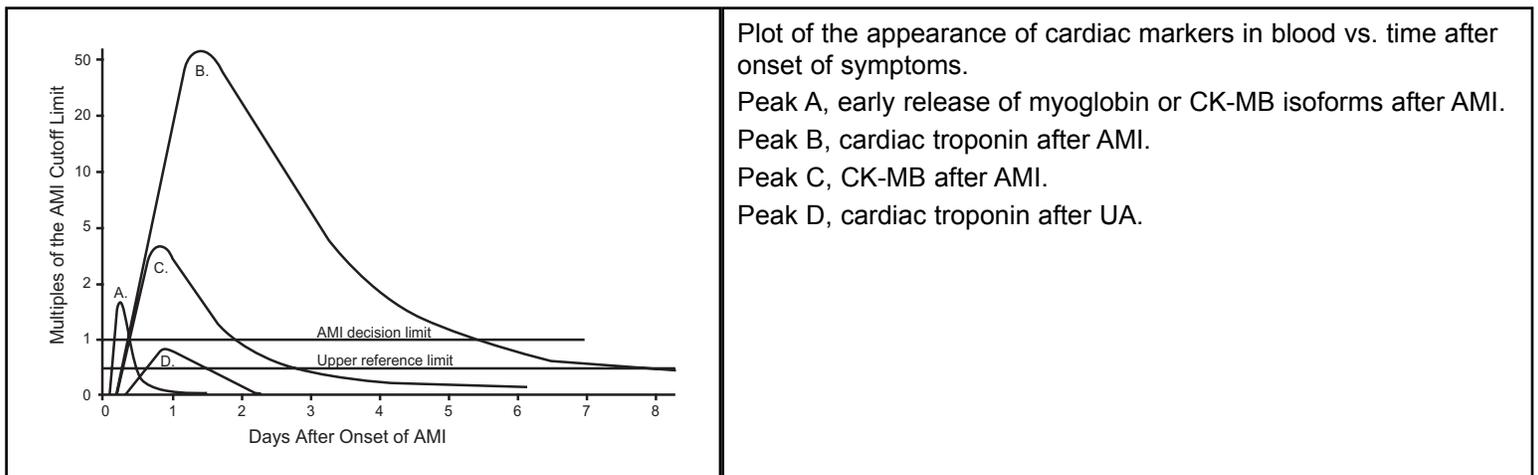
The initial management of patients with NSTEMI-ACS is determined by the predicted risk for adverse outcomes (e.g., death or MI). The degree of risk for a subsequent adverse cardiac event in patients with UA or NSTEMI can, in a large part, be assessed by determining presenting clinical features, including frequency and duration of symptoms, age, signs of hemodynamic instability or heart failure, elevated serum markers, and electrocardiogram (ECG) findings. Table 1 can be used to identify patients at high- or intermediate-risk for early adverse outcomes.

Table 1 is meant to offer general guidance and illustration, rather than rigid algorithm. Estimation of the short-term risks of death and nonfatal cardiac ischemic events in UA is a complex multivariable problem that cannot be fully specified in a table.

## Short-Term Risk of Death or Nonfatal MI in Patients With UA (ACC/AHA UA - NSTEMI, 2000)

	High Risk	Intermediate Risk	Low Risk
<b>Feature</b>	At least 1 of the following features must be present.	No high-risk feature, but one of the following features must be present.	No high- or intermediate- risk feature, but any of the following features may be present.
<b>History</b>	<ul style="list-style-type: none"> <li>Accelerating tempo of ischemic symptoms in the preceding 48 hours</li> </ul>	<ul style="list-style-type: none"> <li>Prior MI, peripheral or cerebrovascular disease, or coronary artery bypass graft (CABG)</li> <li>Prior aspirin use</li> </ul>	
<b>Character of Pain</b>	<ul style="list-style-type: none"> <li>Prolonged ongoing rest pain (&gt;20 minutes)</li> </ul>	<ul style="list-style-type: none"> <li>Prolonged rest angina (&gt;20 minutes), now resolved, with moderate or high likelihood of coronary artery disease (CAD) (see Table 6, Core Module)</li> <li>Rest angina (&lt;20 minutes or relieved with rest or sublingual NTG)</li> </ul>	<ul style="list-style-type: none"> <li>New-onset CCS Class III or IV angina in the past 2 weeks without prolonged rest pain (&gt;20 minutes), but with moderate or high likelihood of CAD (see Table 6, Core Module)</li> </ul>
<b>Clinical Findings</b>	<ul style="list-style-type: none"> <li>Pulmonary edema, most likely related to ischemia</li> <li>New or worsening mitral regurgitation (MR) murmur</li> <li>S3 or new/worsening rales</li> <li>Hypotension, bradycardia, or tachycardia</li> <li>Age &gt;75 years</li> </ul>	<ul style="list-style-type: none"> <li>Age &gt;70 years</li> </ul>	
<b>ECG Findings</b>	<ul style="list-style-type: none"> <li>Transient ST-segment changes &gt;0.05 mV in association with rest angina</li> <li>BBB, new or presumed new</li> <li>Sustained ventricular tachycardia</li> </ul>	<ul style="list-style-type: none"> <li>T-wave inversions &gt;0.2 mV</li> <li>Pathological Q-waves</li> </ul>	<ul style="list-style-type: none"> <li>Normal or unchanged ECG during an episode of chest discomfort</li> </ul>
<b>Cardiac Markers</b>	<ul style="list-style-type: none"> <li>Elevated (e.g., TnT or TnI &gt;0.1 ng/mL)</li> </ul>	<ul style="list-style-type: none"> <li>Slightly elevated (e.g., TnT &gt;0.01, but &lt;0.1 ng/mL)</li> </ul>	<ul style="list-style-type: none"> <li>Normal</li> </ul>

**FIGURE 1: CARDIAC MARKERS IN BLOOD VS. TIME AFTER ONSET OF SYMPTOMS\***



\*Data are plotted on a relative scale, where 1.0 is set at the AMI cutoff concentration. (Adapted from ACC/AHA 2002)

The optimal management strategy for patients with ACS is the topic of very active ongoing investigation. The recommendations contained within this module closely correspond to the published guidelines of the American College of Cardiology and the American Heart Association (ACC/AHA UA - NSTEMI, 2002).

## **B. ENSURE EMERGENCY INTERVENTIONS**

Institute specific interventions that are necessary early in the evaluation and treatment of AMI and UA.

### **1. Oxygen (O<sub>2</sub>)**

Supplemental oxygen should be administered to all patients with respiratory distress, those with cyanosis or those with documented desaturation. Oxygen should start on initial presentation and during the first 2 to 3 hours and continued if necessary to maintain oxygen saturations of at least 90%. Oxygen may be considered for all patients with suspected ACS. Because oxygen can actually cause systemic vasoconstriction, continued administration should be reassessed for uncomplicated patients. CO<sub>2</sub> retention is not usually a concern with low flow nasal O<sub>2</sub>, even in patients with severe chronic obstructive pulmonary disease (COPD).

### **2. Aspirin:**

- All patients should chew non-coated aspirin, 160 mg to 325 mg, within 10 minutes of presentation to accelerate absorption.
- If a patient is unable to take aspirin by mouth because of nausea, vomiting, or other gastrointestinal disorders, 325 mg may be given as a suppository.
- Patients should be given aspirin, even if they are receiving anticoagulation (e.g., warfarin) or antiplatelet (e.g., aspirin or clopidogrel) at the time of presentation.
- Contraindications to aspirin include a documented allergy to salicylates, active bleeding, or active peptic ulcer disease.
- Subsequent aspirin dose of 81-325 mg per day should be given for chronic therapy. Chronic therapy with doses above 81 mg/day is associated with increased bleeding risk without incremental benefit.
- Patients who have an allergy to aspirin and no contraindication to antiplatelet therapy should be given clopidogrel 300 mg loading dose followed by 75 mg daily for at least a month.

### **3. 12-Lead ECG**

A 12-lead ECG is an essential component of the evaluation of the patient with known or suspected ACS. For patients with ongoing symptoms, an urgent ECG should be obtained and interpreted within the first 10 minutes of the initial evaluation and followed up with 2 to 3 serial ECGs in the first 24 hours. A right-sided ECG should be performed if a standard ECG suggests an inferior wall MI.

### **4. Intravenous (IV) Access:**

Intravenous access for the delivery of fluids and drugs should be obtained. While the IV is being started, blood samples for cardiac enzymes/markers (i.e., troponin, CK, and CK-MB), lipid profile, complete blood count (CBC), electrolytes, renal function, international normalized ratio (INR), and activated partial thromboplastin time (APTT) can be obtained. Immediate treatment of ACS should not be delayed by the results from these tests.

### **5. Sublingual nitroglycerin:**

NTG should be given for ongoing chest pain or other ischemic symptoms, unless the patient is hypotensive or bradycardic, has taken sildenafil within the last 24 hours, or there is a strong suspicion of right ventricular infarction.

### **6. Cardiac monitor:**

Patients with ACS, especially with suspected MI, should be placed on continuous cardiac monitoring as soon as possible. Potentially lethal ventricular arrhythmias can occur within seconds to hours from the onset of coronary ischemia, and monitoring will allow their immediate detection and treatment.

### **7. Adequate analgesia:**

Adequate analgesia should be given promptly; morphine sulfate (IV) is effective, decreases the often excess sympathetic tone, and is a pulmonary vasodilator. Some patients may require a large dose. The patient should be monitored for hypotension and respiratory depression, but these are less likely in the anxious, hyperadrenergic patient who is kept supine.

## 8. Advanced cardiac life support (ACLS, 2000):

ACLS algorithm should be applied, as indicated.

## 9. Chest X-ray:

A chest x-ray should be obtained in the ED, particularly if there is concern about aortic dissection; however, treatment of hypotension, low cardiac output, arrhythmias, etc., usually has higher priority.

## 10. Transportation:

In some settings within the DoD or the VA systems, the patient will need to be urgently transported to a setting where an appropriate level of monitoring, evaluation, and treatment is available.

## C. INITIATE:

- **Aspirin 162 mg to 325 mg, If Not Already Given (See Annotation B and Core Module)**
- **Clopidogrel 75 mg if hypersensitivity to aspirin or major GI intolerance**
- **IV Unfractionated Heparin (UFH) Or Subcutaneous Low Molecular Weight Heparin (LMWH)**
- **Beta-blocker if not contraindicated**
- **IV nitroglycerin for persistent or recurrent symptoms**
- **IV morphine as needed**

The goals of initial therapy include symptom relief and the prevention of subsequent MI or death. Antiplatelet therapy is a cornerstone in the management of UA/NSTEMI. Aspirin therapy should be initiated as soon as possible after presentation and continued indefinitely; Clopidogrel should be administered to patients who are unable to take aspirin because of hypersensitivity or major gastrointestinal intolerance.

For patients with NSTEMI-ACS in whom an interventional approach has been precluded, clopidogrel should be added to aspirin as soon as possible and administered for at least 1 month and for up to 9 months.

Fibrinolytic therapy should not be given unless ST-segment elevation or LBBB MI are present. (See module A: Acute MI, ST-segment elevation MI).

Beta-blockers should be used in all patients with UA/NSTEMI unless contraindicated, with initial IV route, followed by oral dosing.

## Aspirin (ASA)

Randomized trials have demonstrated that ASA reduces the risk of MI and vascular death in patients with unstable coronary disease

A dose as low as 75 mg has been shown to be effective in UA, and the ACC/AHA consensus suggests 75 mg to 325 mg daily after an initial dose of 162-325 mg. (Gibbons 2002).

## Clopidogrel

There is strong evidence to support the addition of clopidogrel to ASA in the management of patients with UA and NSTEMI. Clopidogrel appears to be especially useful on admission in hospitals that do not have a routine policy of early invasive procedures and in patients who are not candidates or who do not wish to be considered for revascularization. In patients who undergo revascularization, clopidogrel should be started in conjunction with the procedure. Clopidogrel should be withheld in patients whom elective CABG is planned, for 5 to 7 days. The optimal duration of therapy with clopidogrel has not been determined. The major benefits were observed at 30 days, with small additional benefits observed over the subsequent treatment period out to one year.

## IV Unfractionated Heparin

Several small randomized placebo controlled trials suggest that intravenous unfractionated heparin (UFH), in combination with aspirin, reduces the short-term likelihood (i.e., 2 to 7 days) of adverse clinical events in unstable coronary disease. The addition of UFH to ASA increases major bleeding from 0.4% (ASA alone) to 1.5% (ASA plus UFH). The optimal duration of therapy is unclear, but 2 to 5 days of treatment after stabilization is reasonable.

## Enoxaparin

Enoxaparin is preferable to UFH as an anticoagulant in patients with UA/NSTEMI, in the absence of renal failure and unless CABG is planned within 24 hours.

Enoxaparin should not be used in patients with known creatinine clearance of less than approximately 30 cc/minute. Other low molecular weight heparin preparations have not yet demonstrated the degree of benefit observed with enoxaparin in the treatment of UA/NSTEMI.

### **Beta Blockers**

Unless contraindicated, beta-blockers should be used in all patients with UA/NSTEMI, with initial IV route, followed by oral dosing, being preferable in patients with ongoing symptoms.

Beta-blockers should be continued indefinitely unless a contraindication arises. Contraindications to the use of beta-adrenergic blocking agents include: patients with second- or third- degree heart block (without a pacemaker), severe heart failure, severe reactive airway disease, hypotension (i.e., <90 mm Hg), and bradycardia (i.e., <50 bpm).

Reactive Airway Disease or COPD should not preclude the use of beta-blockers; however, when there is concern, an ultra short acting or short acting agent could be used.

Patients with diabetes, once considered a relative contraindication to beta-blockers, appear to derive as much, or more, mortality benefit from treatment with a beta-blocker following myocardial infarction as non-diabetics and without increased risk of hospitalization for diabetic complications.

### **Calcium Antagonists**

In patients with ACS, for whom beta-blockers and nitrates are either unsuccessfully controlling ischemia or are contraindicated, calcium channel blockers may be considered in the absence of evidence of heart failure. The calcium antagonists verapamil and diltiazem have proven efficacy for symptomatic relief in patients with ACS and more limited evidence for a reduction in re-infarction. Cautions for the use of diltiazem and verapamil are similar to those listed for beta-blockers, with the exception that calcium antagonists may be safely used in patients with asthma.

### **ACE Inhibitors**

ACE inhibitors should be given to all patients with LV systolic dysfunction, CHF or diabetes once the patient is hemodynamically stable and in the absence of recognized contraindications. ACE inhibitors may be considered in other patients with ACS especially if hypertension persists despite treatment with NTG and beta-blockers.

### **Nitroglycerin**

Nitroglycerin (NTG) as a sublingual tablet or buccal spray should be given to the patient on presentation, as recommended in the Core Module, unless the patient has used sildenafil (Viagra) within the preceding 24 hours. If ischemic symptoms persist following three doses of NTG tablets or spray given five minutes apart and the initiation of an intravenous beta-adrenergic blocking agent, IV NTG should be initiated.

### **Morphine Sulphate**

Intravenous morphine sulphate (1 mg to 5 mg) is commonly used for pain and anxiety relief in patients with ACS who do not achieve adequate symptomatic relief with antianginal medications. The rationale for its use is based on the perception that ongoing pain and/or anxiety provokes increases in blood pressure and heart rate, which in turn, increase myocardial oxygen demands in the setting of reduced supply. The principal precautions for its use in this setting are a known history of intolerance and hypotension.

**Fibrinolytic therapy should *not* be given to patient with UA/NSTEMI unless ST-segment elevation/LBBB MI or a true posterior MI develops**

## **D. ADMIT TO MONITORED BED, AT APPROPRIATE LEVEL OF CARE**

Patients with intermediate- or high-risk of death and/or MI (see Table 1) should be admitted to an inpatient unit with cardiac monitoring capabilities to ensure for monitoring of the ECG and rapid availability of emergency medical care (e.g., ACLS) as well as, personnel trained in the recognition and management of cardiac arrhythmias..

## E. ASSESS SERIAL ECGs, CARDIAC-SPECIFIC MARKERS AND LIPID PROFILE

- **Serial ECGs** are vital to diagnosis and prognosis of patient with ACS. This has implications for the length of unit and hospital stay, and further adds to risk assessment. Two to three serial ECGs should be performed within the first 24 hours. Serial ECGs should be performed for any clinical change, probably after any transfer and subsequently at least daily and especially on the day of discharge.

- **Cardiac biomarkers** should be performed in all patients with suspected ACS. A cardiac-specific troponin is preferred and should be measured in all patients. CK-MB by mass assay may have added value for early diagnosis. For patients with normal cardiac markers within 6 hours of symptom onset, another sample should be obtained over the subsequent 6-12 hours. In patients with elevated cardiac markers, repeat testing should be performed every 8 hours until they have peaked.
- **A lipid profile** should be performed as soon as possible after admission, within the first 24 hours.

### Biochemical Cardiac-Markers for the Evaluation and Management of Patients Suspected of Having an ACS, but Without ST-Segment Elevation on 12-Lead ECG (ACC/AHA UA - NSTEMI, 2000)

Marker	Advantages	Disadvantages	Clinical Recommendations
CK-MB	<ul style="list-style-type: none"> <li>• Rapid, cost-efficient, accurate assays</li> <li>• Detection of early reinfarction</li> </ul>	<ul style="list-style-type: none"> <li>• Loss of specificity in the setting of skeletal muscle disease or injury, including surgery</li> <li>• Low sensitivity during very early MI (i.e., &lt;6 hours after onset of symptoms) or later after onset of symptoms (i.e., &gt;36 hours) and for minor myocardial damage (detectable by troponins)</li> </ul>	<ul style="list-style-type: none"> <li>• Prior standard and still acceptable diagnostic test in most clinical circumstances</li> </ul>
CK-MB Isoforms	<ul style="list-style-type: none"> <li>• Early detection of MI</li> </ul>	<ul style="list-style-type: none"> <li>• Specificity profile is similar to CK-MB</li> <li>• Current assays require special expertise</li> </ul>	<ul style="list-style-type: none"> <li>• Useful for extremely early (i.e., 3 to 6 hours after onset of symptoms) detection of MI in centers with demonstrated familiarity with the assay technique</li> </ul>
Myoglobin	<ul style="list-style-type: none"> <li>• High sensitivity</li> <li>• Early detection of MI</li> <li>• Detection of reperfusion</li> <li>• Most useful in ruling out MI</li> </ul>	<ul style="list-style-type: none"> <li>• Very low specificity in the setting of skeletal muscle injury or disease</li> <li>• Rapid return to normal range limits sensitivity, for later presentations</li> </ul>	<ul style="list-style-type: none"> <li>• Should not be used as the only diagnostic marker, because of a lack of cardiac specificity</li> <li>• A more convenient early marker than CK-MB isoforms because of greater availability of assays for myoglobin. Rapid-release kinetics make myoglobin useful for the non-invasive monitoring of reperfusion in patients with established MI.</li> </ul>
Cardiac Troponins	<ul style="list-style-type: none"> <li>• Powerful tool for risk stratification</li> <li>• Greater sensitivity and specificity than CK-MB</li> <li>• Detection of recent MI up to 2 weeks after onset</li> <li>• Useful for the selection of therapy</li> <li>• Detection of reperfusion</li> </ul>	<ul style="list-style-type: none"> <li>• Low sensitivity in very early phase of MI (i.e., &lt;6 hours after onset of symptoms) and requires a repeat measurement at 8 to 12 hours, if negative</li> <li>• Limited ability to detect the late minor reinfarction</li> </ul>	<ul style="list-style-type: none"> <li>• 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</li> <li>• Data on diagnostic performance and potential therapeutic implications are increasingly available from clinical trials</li> </ul>

## F. TREAT EXACERBATING NON-CARDIAC CAUSES OF UNSTABLE ANGINA

Several conditions may provoke or exacerbate angina and ischemia even though the existing coronary disease is not otherwise significant. In particular, conditions that increase oxygen demand or decrease oxygen supply may provoke ischemic symptoms in patients who otherwise would not have symptoms, if based exclusively on atherosclerotic lesions.

**Table 3. Conditions and Medications Provoking or Exacerbating Ischemia  
(adapted from the ACC/AHA Stable Angina guidelines, 2003)**

INCREASED OXYGEN DEMAND	DECREASED OXYGEN SUPPLY
<p><b>Noncardiac</b></p> <ul style="list-style-type: none"> <li>• Hyperthermia</li> <li>• Hyperthyroidism</li> <li>• Sympathomimetic toxicity (e.g., cocaine use)</li> <li>• Hypertension</li> <li>• Anxiety</li> <li>• Arteriovenous fistulae</li> </ul> <p><b>Cardiac</b></p> <ul style="list-style-type: none"> <li>• Hypertrophic cardiomyopathy</li> <li>• Aortic stenosis</li> <li>• Dilated cardiomyopathy</li> <li>• Tachycardia               <ul style="list-style-type: none"> <li>- Ventricular</li> <li>- Supraventricular</li> </ul> </li> </ul> <p><b>Medications</b></p> <ul style="list-style-type: none"> <li>• Vasodilators</li> <li>• Excessive thyroid replacement</li> </ul>	<p><b>Noncardiac</b></p> <ul style="list-style-type: none"> <li>• Anemia</li> <li>• Hypoxemia               <ul style="list-style-type: none"> <li>- Pneumonia</li> <li>- Asthma</li> <li>- Chronic obstructive pulmonary disease</li> <li>- Pulmonary hypertension</li> <li>- Interstitial pulmonary fibrosis</li> <li>- Obstructive sleep apnea</li> </ul> </li> <li>• Sickle cell disease</li> <li>• Sympathomimetic toxicity (e.g., cocaine use)</li> <li>• Hyperviscosity               <ul style="list-style-type: none"> <li>- Polycythemia</li> <li>- Leukemia</li> <li>- Thrombocytosis</li> <li>- Hypergammaglobulinemia</li> </ul> </li> </ul> <p><b>Cardiac</b></p> <ul style="list-style-type: none"> <li>• Aortic stenosis</li> <li>• Hypertrophic cardiomyopathy</li> </ul> <p><b>Medications</b></p> <ul style="list-style-type: none"> <li>• Vasoconstrictors</li> </ul>

## G. PROVIDE APPROPRIATE ANTIPLATELET AND ANTICOAGULANT THERAPY

Provide antithrombotic therapy to modify the disease process and its progression to death, MI, or recurrent MI

Patients with NSTEMI-ACS who are at short-term intermediate- or high-risk of death or MI should be given appropriate antiplatelet therapy. The specific antiplatelet therapy recommended depends on whether the patient is to undergo prompt revascularization and whether the revascularization is via percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG).

A combination of ASA, heparin, and a platelet GP IIb/IIIa receptor antagonist represents the most comprehensive therapy. The intensity of treatment should be tailored to individual risk. Triple antithrombotic treatment (a GP IIb/IIIa inhibitor, in addition to aspirin and heparin or low molecular weight heparin) should be used in patients with continuing ischemia or with other high-risk features and in patients in whom an early invasive strategy is planned. (see Table 4) The GP IIb/IIIa antagonist may also be administered just prior to PCI. If intervention is not planned, clopidogrel should be added to aspirin, heparin and GP IIb/IIIa.

**Table 4: Antiplatelet and Anticoagulant Therapy**

HIGH RISK ACS Continuing Ischemia or Other High-Risk Features			MODERATE RISK Likely/definite ACS	LOW RISK Possible ACS
No Planned Intervention	Planned Intervention			
		PCI□	CABG□	
Aspirin	Aspirin	Aspirin	Aspirin	Aspirin
Clopidogrel	—	—	Clopidogrel	Clopidogrel
LMWH or UFH	LMWH or UFH	UFH	LMWH or UFH	—
Platelet GP IIb/IIIa antagonist: Eptifibatide Tirofiban	Platelet GP IIb/IIIa antagonist: Abciximab Eptifibatide	Platelet GP IIb/IIIa antagonist: Eptifibatide Tirofiban	—	—

If LMWH is used during the period of initial stabilization, the dose can be withheld on the morning of the procedure; and if an intervention is required and more than 8 hours has elapsed since the last dose of LMWH, UFH can be used for PCI according to usual practice patterns. Because the anticoagulant effect of UFH can be more readily reversed than that of LMWH, UFH is preferred in patients likely to undergo CABG within 24 h. **Table 5** shows the recommended doses of the various agents.

**Table 5: Antiplatelet and Anticoagulant Agents**

<b>Aspirin</b>	160 mg to 325 mg. No trial has directly compared the efficacy of different doses of ASA in patients who present with UA/NSTEMI. However, trials in secondary prevention of stroke, MI, death, and graft occlusion have not shown an added benefit for ASA doses of greater than 80 and 160 mg per day but have shown a higher risk of bleeding.
<b>Clopidogrel</b>	Loading dose of 300 mg followed by 75 mg daily. In patients in whom an early noninterventional approach is planned, clopidogrel should be added to ASA as soon as possible on admission and administered for at least 1 month and for up to 9 months
<b>Enoxaparin</b>	Enoxaparin is given as 1 mg/kg sq bid. A bolus of enoxaparin 30 mg IV may be given initially. Enoxaparin is preferable to UFH as an anticoagulant in patients with UA/NSTEMI, in the absence of renal failure and unless CABG is planned within 24 hours.
<b>UFH</b>	Because the anticoagulant effect of UFH can be more readily reversed than that of LMWH, UFH is preferred in patients likely to undergo CABG within 24 h. UFH is also preferred in patients with renal failure.
<b>Abciximab</b>	Abciximab is bolused at 0.25 mg/kg, then infused at 0.125 mcg/kg/min (maximum of 10 mcg/min) for 18 to 24 hours, or 12 hours post-PCI.
<b>Eptifibatide</b>	Eptifibatide is bolused at 180 mcg/kg (maximum 22.6 mg) and then infused at 2 mcg/kg/min (maximum of 15mg/hr) for up to 72 hours. If a PCI is performed, the infusion is decreased to 0.5 mcg/kg/min and continued for 20 to 24 hours post-procedure. If serum creatinine is $\geq 2.0$ , but $< 4.0$ mg/dL, the bolus should be reduced to 135 mcg/kg and the infusion to 0.5 mcg/kg/min. If the serum creatinine is $\geq 4.0$ , this agent should not be used.
<b>Tirofiban</b>	Tirofiban is given at 0.4 mcg/kg/min for 30 minutes, then 0.1 mcg/kg/min for 48 to 96 hours, or 12 to 24 hours post-PCI.

## H. ARE THERE INDICATIONS FOR GLYCOPROTEIN IIb/IIIa RECEPTOR ANTAGONISTS ?

GP IIb/IIIa receptor antagonists are indicated in all patients in whom an invasive management strategy is followed as well as patients being managed non-invasively with one or more high-risk features. ACS patients with one or more of the following high-risk features may benefit from the addition of a Glycoprotein IIb/IIIa receptor antagonist:

- 1) Patients with elevated serum troponin
- 2) New or presumably new ST-segment depression  $\geq 1.0$  mm in two or more contiguous leads.
- 3) Patients with recurrent angina or other ischemic symptoms despite initial medical therapy
- 4) Other high risk features (see table 1).

## I. IS THERE INDICATION FOR URGENT ANGIOGRAPHY?

An early invasive strategy is recommended in patients with UA/NSTEMI who present with any of the following high-risk indicators:

- Patients with recurrent angina/ischemia at rest or with low-level activities, despite intensive anti-ischemic therapy
- Patient with elevated cardiac markers (TnI or TnT) and no contraindications to revascularization
- Patients who present with new or presumably new ST-segment depression
- Recurrent angina/ischemia with CHF symptoms, an S3 gallop, pulmonary edema, worsening rales, or new or worsening MR
- High risk findings on non-invasive stress testing
- Depressed LV systolic function (e.g., EF <0.40 on a non-invasive study)
- Hemodynamic instability
- Sustained ventricular tachycardia
- Previous PCI within 6 months
- Prior CABG

Many cardiologists also recommend an early invasive strategy for the following subgroups of patients

- Patients having repeated presentations with UA/NSTEMI despite therapy even in the absence of evidence of ongoing ischemia or high risk
- Patients with prior MI
- Patient with indeterminate biomarkers elevation
- New or presumed new ischemic T wave inversion (>0.2 mV)
- Ongoing ischemic symptoms or signs refractory to appropriate medical therapy.

Invasive strategy should be *avoided* if:

- Risks of the procedure are not likely to outweigh the benefits (life expectancy)
- Patients would not consent to revascularization regardless of the findings
- Precluded by other comorbidity (e.g., active GI bleeding)

In the absence of above findings, most cardiologists prefer an invasive strategy. RCT data suggest that medical therapy be continued until invasive therapy is available. It appears that a modern invasive strategy, preceded by modern antiischemic and antithrombotic medication, in high-risk patients with unstable coronary artery disease reduces death, myocardial infarction, symptoms, and readmissions compared to a conservative strategy.

In the early conservative strategy, coronary angiography is reserved for patients with evidence of recurrent ischemia (angina at rest or with minimal activity or dynamic ST-segment changes) or a strongly positive stress test despite vigorous medical therapy. In the *early invasive strategy*, patients without clinically obvious contraindications to coronary revascularization are routinely recommended for coronary angiography and angiographically directed revascularization, if possible

Coronary arteriography *should not* be performed in patients with extensive comorbidities (e.g., liver or pulmonary failure or cancer) that are likely to make the risks of revascularization outweigh the benefits (unless clarification of the correct diagnosis by cardiac catheterization is believed to be necessary). Similarly, coronary arteriography *should not* be performed in patients who will not consent to revascularization, regardless of the findings.

If patients are stable, risk stratification can continue electively with assessment of systolic function. If, at any time, previously stabilized patients in this module become unstable again, they will return to this box in the algorithm.

## J. ASSESS LEFT VENTRICULAR FUNCTION, IF INDICATED

LV systolic function may be assessed by contrast angiography at cardiac catheterization, two-dimensional cardiac ultrasound or radionuclide ventriculography. The relative advantages and disadvantages of cardiac ultrasound versus radionuclide ventriculography are presented in Table 6.

Test	Advantages	Disadvantages
Echocardiogram	<ul style="list-style-type: none"><li>• Permits concomitant assessment of valvular disease, ventricular hypertrophy and left atrial size</li><li>• Can detect pericardial effusion and LV thrombus</li><li>• Usually less expensive and more widely available than radionuclide studies</li></ul>	<ul style="list-style-type: none"><li>• Provides only semi-quantitative estimate of EF</li><li>• Technically inadequate study in as many as 18% of patients and particularly difficult in patients with emphysema</li></ul>
Radionuclide ventriculography	<ul style="list-style-type: none"><li>• More precise, reliable, and quantitative measurement of ejection fraction, compared to echocardiography</li><li>• Better assessment of right ventricular function</li></ul>	<ul style="list-style-type: none"><li>• Limited assessment of valvular function and ventricular hypertrophy</li><li>• Requires venipuncture and radiation exposure</li><li>• Should generally not be used with patients with irregular heart rhythm</li></ul>

*Adapted from AHCPR Heart Failure Clinical Practice Guideline, 1995*

If the patient, otherwise, does not have an indication for prompt left heart catheterization and LVEF assessment is not available in the hospital, this test can also be performed as an outpatient. Of note, Silver et al., (1994) developed a clinical rule to predict LVEF  $\geq 0.40$ , with a positive predictive value of 98% in those patients who have ALL of the following characteristics:

- Interpretive ECG (without LBBB, ventricular pacing, or LV with strain pattern)
- No prior Q-wave MI
- No history of CHF
- Index MI which is not a Q-wave anterior infarction

## **K. ENSURE PHARMACOTHERAPY FOR CONGESTIVE HEART FAILURE (CHF)/LV DYSFUNCTION**

### **Beta-Blockers**

In patients with moderate to severe CHF symptoms, beta-blockers have been shown to improve symptoms, New York Heart Association (NYHA) class and overall morbidity and mortality. Thus far, studies support use of carvedilol, metoprolol, and bisoprolol for this indication. Before using beta-blockers, all patients should be on optimal doses of an ACE-inhibitor, as in the clinical trials. Beta-blockers should not be used in uncompensated CHF and should be used with great caution in patients with Class IV CHF. Early termination of the COPERNICUS trial, which studied carvedilol in the setting of severe CHF, may alter this practice in the near future.

### **ACE-Inhibitors**

ACE-inhibitors should be given to all patients, in the absence of recognized contraindications, with LV systolic dysfunction (EF <0.40), and all attempts should be made to have patients on at least 20 mg of enalapril, or its equivalent, a day. ACE Inhibitors should be strongly considered for all patients with diabetes and/or hypertension, and can be considered for all IHD patients based on the HOPE study.

## **L. CONSIDER CARDIAC STRESS TEST**

All patients with suspected UA/NSTEMI should be risk-stratified to determine their prognosis and guide their treatment. Patients, who do not have clinical findings that suggest either intermediate or high short-term risk of death or MI (i.e. troponin elevations, ECG changes), should receive a stress imaging study prior to discharge as final confirmation of the absence of high risk. All patients with suspected, but unproven, unstable angina should have further diagnostic testing to determine the accuracy of the diagnosis.

## **Indications for Non-Invasive Evaluation:**

- Establish or confirm a diagnosis of ischemic heart disease
- Estimate prognosis in patients with known or suspected ischemic heart disease (IHD)
- Assess the effects of therapy.

Patients with contraindications to exercise testing should undergo pharmacologic stress testing with an imaging modality.

## **Establishing diagnoses:**

- Is most useful if the pre-test probability of coronary artery disease (CAD) is Intermediate (10% to 90%)
- Should generally not be done in patients with very high or very low probabilities of CAD.

## **Variables useful in estimating prognosis include:**

- Maximum workload achieved
- Heart rate and blood pressure responses to exercise
- Occurrence and degree of ST-segment deviation
- Occurrence and duration of ischemic symptoms
- Size and number of stress-induced myocardial perfusion or wall motion abnormalities.

For detailed discussion of Non-Invasive evaluation see Module F – Non Invasive Evaluation

## **M. REFER TO CARDIOLOGY FOR POSSIBLE ANGIOGRAPHY**

The survival benefits of myocardial revascularization are most pronounced among patients with LV dysfunction. Therefore, all patients with NSTEMI/UA who are found to have a reduced EF (<0.40) on non-invasive testing or found to have high- or intermediate-risk for death or MI on a stress test should be considered for referral to cardiology for possible coronary angiography and subsequent revascularization. This recommendation applies even to patients who do not have clinical signs and symptoms of heart failure and to those whose ischemic symptoms have been stabilized.

Patients with UA/NSTEMI who have been stabilized on medical therapy, but who are found to have LV dysfunction, may benefit from further risk stratification using coronary angiography to determine their likelihood of benefit from revascularization. This decision most properly resides with a specialist in cardiovascular diseases, since this specialist is in the best position to discuss the relative risks and benefits of bypass surgery versus medical therapy or percutaneous revascularization.

Patients with the following coronary anatomic findings should be considered for bypass surgery:

- Significant left main coronary artery stenosis
- Left main equivalent: significant stenosis (70%) of proximal LAD and proximal left circumflex artery
- Three-vessel disease (survival benefit is greater in patients with abnormal LV function; e.g., with an EF <0.50.)
- Proximal LAD stenosis where PCI is technically difficult

The following list includes examples of non-invasive test results that indicate intermediate- or high-risk, for which cardiology referral for coronary angiography should be considered.

**High-Risk (greater than 3% annual mortality rate):**

- Severe resting LV dysfunction (LVEF<0.35)
- High-risk Duke treadmill score (score  $\leq$ -11)
- Severe exercise LV dysfunction (exercise LVEF<0.35)
- Stress-induced large perfusion defect (particularly if anterior)
- Stress-induced moderate-size multiple perfusion defects
- Large, fixed perfusion defect with LV dilatation or increased lung uptake (thallium-201)
- Stress-induced moderate-size perfusion defect with LV dilatation or increased lung uptake (thallium-201)
- Echocardiographic wall motion abnormality (involving >2 segments) developing at low dose of dobutamine ( $\leq$ 10 mg/ kg/min) or at a low heart rate (<120 bpm)
- Stress echocardiographic evidence of extensive ischemia

**Intermediate-Risk (1%-3% annual mortality rate):**

- Mild/moderate resting left ventricular dysfunction (LVEF = 0.35 to 0.49)
- Intermediate-risk Duke treadmill score (greater than -11 and less than 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 two segments

**N. DISCHARGE**

The acute phase of UA/NSTEMI is usually over within 2 months. The risk of progression to MI or the development of recurrent MI or death is highest during that period. At 1 to 3 months after the acute phase, most patients resume a clinical course similar to that in patients with chronic stable coronary

**Disease**

Many patients with UA/NSTEMI have chronic stable angina at hospital discharge. The management of the patient with stable CAD is detailed in Module C of this guideline.

The selection of a medical regimen is individualized to the specific needs of each patient based on the in-hospital findings and events, the risk factors for CAD, drug tolerability, or the type of recent procedure. The mnemonic ABCDE (Aspirin and antianginals; Beta-blockers and blood pressure; Cholesterol and cigarettes; Diet and diabetes; Education and exercise) has been found to be useful in guiding treatment.

For follow-up and secondary prevention see Module G of this guideline

# VA/DOD CLINICAL PRACTICE GUIDELINE FOR THE MANAGEMENT OF ISCHEMIC HEART DISEASE MODULE C SUMMARY

## STABLE ANGINA

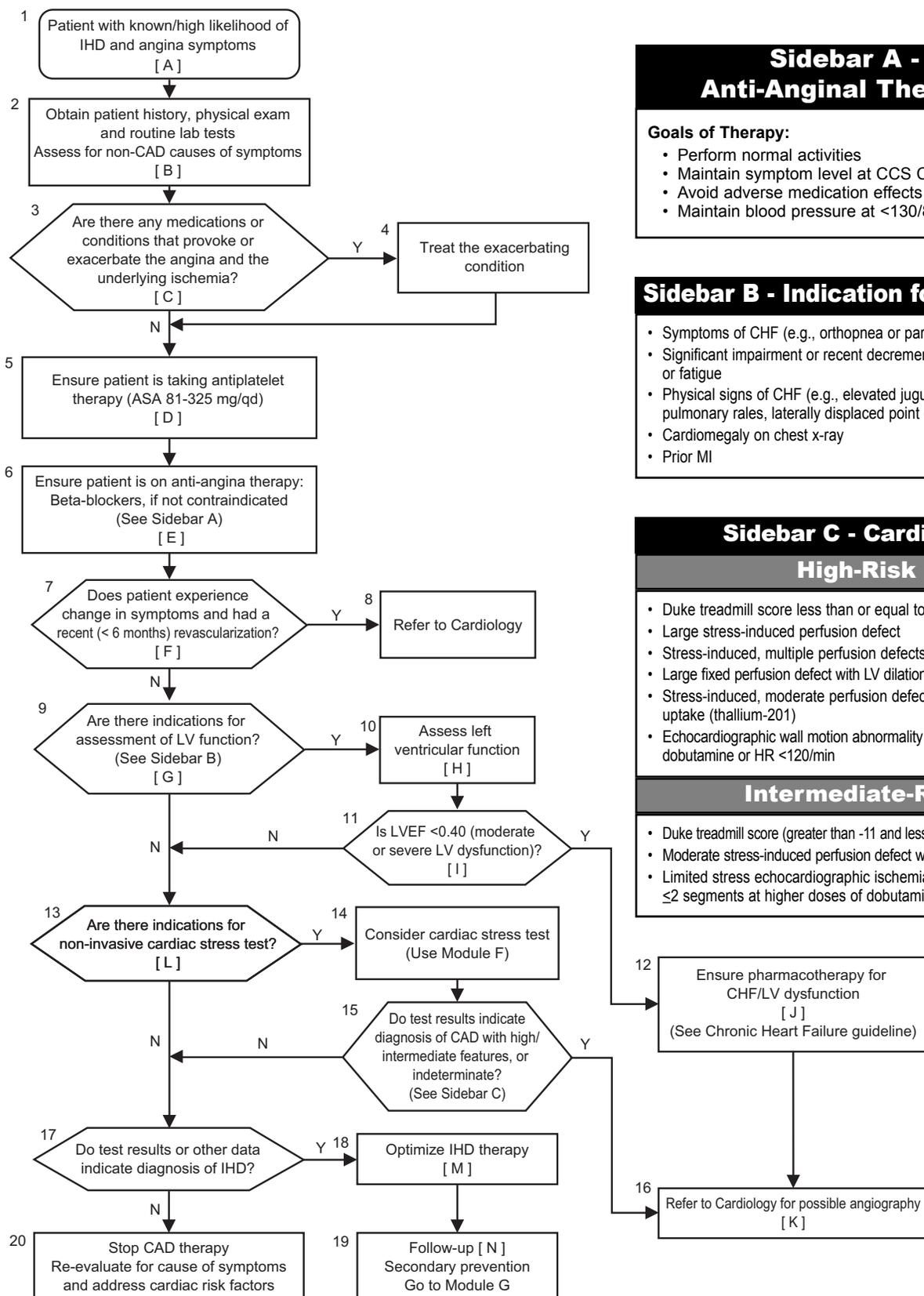
Patients with known ischemic heart disease (IHD), or with a high likelihood of IHD based on clinical factors, who have stable symptoms (referred to as angina) that suggest transient myocardial ischemia are managed within this module. Most commonly, angina is described as a squeezing, heavy, or aching substernal discomfort that is provoked by physical or emotional stress and is relieved by rest and/or sublingual nitroglycerin. Symptoms may also radiate to or be felt exclusively in the jaw, shoulders, arms, or back. Patients may also experience concurrent dyspnea, diaphoresis, or nausea. Occasionally, transient myocardial ischemia may manifest solely as one of these latter symptoms, especially as dyspnea on exertion; in such cases, the symptoms are described as "anginal equivalents" (AHCPR USA, 1994; ACC/AHA Stable Angina, 1999).

This module is not intended for the management of patients with unstable angina. Unstable angina should be suspected when patients have either prolonged angina (i.e., >20 minutes) or new onset or increasing angina, which occurs either at rest or with minimal exertion. These patients should be managed in Module B (Suspected Acute Coronary Syndrome: Unstable Angina/Non-ST-Segment Elevation MI).

# MANAGEMENT OF ISCHEMIC HEART DISEASE

## MODULE C: MANAGEMENT OF STABLE ANGINA

# C



### Sidebar A - Anti-Anginal Therapy

**Goals of Therapy:**

- Perform normal activities
- Maintain symptom level at CCS Class I
- Avoid adverse medication effects
- Maintain blood pressure at <130/85 & pulse <70

### Sidebar B - Indication for Assessment of LVF

- Symptoms of CHF (e.g., orthopnea or paroxysmal nocturnal dyspnea)
- Significant impairment or recent decrement in exercise tolerance, due to dyspnea or fatigue
- Physical signs of CHF (e.g., elevated jugular venous pressure, unexplained pulmonary rales, laterally displaced point of maximal impulse, and S3 gallop)
- Cardiomegaly on chest x-ray
- Prior MI

### Sidebar C - Cardiac Stress Test

#### High-Risk Findings

- Duke treadmill score less than or equal to -11 (estimated annual mortality >3%)
- Large stress-induced perfusion defect
- 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 >2 segments at ≤10 mg/kg/min dobutamine or HR <120/min

#### Intermediate-Risk Findings

- Duke treadmill score (greater than -11 and less than 5) (estimated annual mortality 1-3%)
- Moderate stress-induced perfusion defect without LV dilation or increased lung uptake
- Limited stress echocardiographic ischemia with wall motion abnormality involving ≤2 segments at higher doses of dobutamine (>10 mg/kg/min dobutamine)

## ASSESSMENT

### **Patient History, Physical Exam, And Routine Laboratory Tests; Assess For Non-Coronary Artery Disease (CAD) Causes Of Symptoms**

Patients with IHD may also experience symptoms unrelated to transient myocardial ischemia, but which nonetheless raise concern regarding the possibility of angina and therefore pose diagnostic difficulties. Many conditions other than coronary disease present with chest pain or discomfort that mimic angina symptoms. The history and physical examination should be used to develop a differential diagnosis of the patient's symptoms.

#### **Obtain the following history for all patients with suspected angina:**

- A detailed chest pain history, to include character, frequency, location, duration, radiation of pain, and provoking and relieving factors (i.e., exercise, emotion, and response to sublingual nitroglycerin)
- History of prior myocardial infarction
- History of prior myocardial revascularization
- History of prior diagnostic testing for IHD
- Assessment for coronary risk factors (e.g., hyperlipidemia, diabetes, smoking, hypertension, and family history of premature coronary disease)
- History of symptoms suggestive of heart failure
- History of cerebral or peripheral vascular disease

#### **History that may be helpful for the evaluation of potential non-cardiac causes for symptoms in some patients includes the following:**

- Medications, over-the-counter drugs, and substance use
- Anemia (fatigue, weakness, bleeding disorders, menstrual flow, hematuria, hematochezia, and nutrition)
- Thyroid disease (diaphoresis, nervousness, insomnia, weight loss, and neck pain)
- Pulmonary disease (smoking, wheezing, coughing, pleuritic chest pain, exposure to tuberculosis, and hemoptysis)

- Gastrointestinal disorders (relationship between pain or discomfort and meals, melena, hematochezia, and heartburn)
- Other possible non-cardiac sources of chest pain or discomfort

#### **Physical examination components include the following:**

- Blood pressure, pulse rate and regularity, and respiratory rate
- Complete cardiac exam for the presence of cardiac enlargement, murmurs, extra heart sounds, etc.
- Evaluation of the carotid and jugular vessels for the presence of jugular venous distention, carotid bruits, and abnormal carotid pulsations
- Peripheral vascular evaluation, including assessment of pulse quality and presence of bruits
- Evaluation for peripheral edema
- Thyroid examination (e.g., tenderness and enlargement)
- Abdominal examination (e.g., bruits, tenderness, and masses)
- Pulmonary/thoracic examination (e.g., pulmonary congestion rubs, chest wall tenderness, and skin lesions)

#### **Obtain the following laboratory tests, if not previously done:**

- Complete blood count
- Fasting glucose
- Fasting lipid profile including triglycerides
- 12-lead electrocardiogram (ECG)
- Chest x-ray in patients with signs of heart failure, valvular heart disease, pericardial disease, or aortic dissection/aneurysm

#### **Obtain additional laboratory tests, as clinically indicated, to include the following:**

- Renal panel including electrolytes
- Liver Function Tests
- Thyroid Function Tests
- Drug screening
- Amylase/lipase

**Features that are not characteristic of myocardial ischemia include the following:**

- Pleuritic pain (i.e., sharp or knife-like pain brought on by respiratory movements or a cough)
- Primary or sole location of discomfort in the middle or lower abdominal regions
- Pain that may be localized at the tip of one finger, particularly over the left ventricular apex
- Pain reproduced with movement or palpation of the chest wall or arms
- Constant pain that lasts for many hours
- Very brief episodes of pain that last a few seconds or less
- Pain that radiates into the lower extremities

**Table 1. Alternative Diagnoses to Angina for Patients with Chest Pain or Discomfort (adapted from ACC/AHA Stable Angina, 1999)**

Non-ischemic Cardiovascular	Pulmonary	Gastrointestinal	Chest Wall	Psychiatric
<ul style="list-style-type: none"> <li>• Aortic dissection</li> <li>• Pericarditis</li> </ul>	<ul style="list-style-type: none"> <li>• Pulmonary embolus</li> <li>• Pneumothorax</li> <li>• Pneumonia</li> <li>• Pleuritis</li> </ul>	<ul style="list-style-type: none"> <li>• Esophageal                             <ul style="list-style-type: none"> <li>-Esophagitis</li> <li>-Spasm</li> <li>-Reflux</li> </ul> </li> <li>• Biliary                             <ul style="list-style-type: none"> <li>-Colic</li> <li>-Cholecystitis</li> <li>-Cholecholithiasis</li> <li>-Cholangitis</li> </ul> </li> <li>• Peptic ulcer</li> <li>• Pancreatitis</li> </ul>	<ul style="list-style-type: none"> <li>• Costochondritis</li> <li>• Fibrositis</li> <li>• Rib fracture</li> <li>• Sternoclavicular arthritis</li> <li>• Herpes zoster (before the rash)</li> </ul>	<ul style="list-style-type: none"> <li>• Anxiety disorder                             <ul style="list-style-type: none"> <li>- Hyperventilation</li> <li>- Panic disorder</li> <li>- Primary anxiety</li> </ul> </li> <li>• Affective disorders (e.g., depression)</li> <li>• Somatoform disorders</li> <li>• Thought disorders (e.g., fixed delusion)</li> </ul>

**Medications Or Conditions That Provoke Or Exacerbate The Angina And The Underlying Ischemia**

In addition to non-CAD conditions, whose symptoms mimic the symptoms of angina, there are many conditions that may provoke or exacerbate angina and the underlying

ischemia, even though the existing coronary disease is not otherwise significant. In particular, conditions that increase oxygen demand or decrease oxygen supply may provoke ischemic symptoms in patients who otherwise would not have symptoms, if based exclusively on atherosclerotic lesions.

**Table 2. Conditions and Medications Provoking or Exacerbating Ischemia (adapted from the ACC/AHA Stable Angina Guidelines, 1999)**

INCREASED OXYGEN DEMAND	DECREASED OXYGEN SUPPLY
<p><b>Noncardiac</b></p> <ul style="list-style-type: none"> <li>• Hyperthermia</li> <li>• Hyperthyroidism</li> <li>• Sympathomimetic toxicity (e.g., cocaine use)</li> <li>• Hypertension</li> <li>• Anxiety</li> <li>• Arteriovenous fistulae</li> </ul> <p><b>Cardiac</b></p> <ul style="list-style-type: none"> <li>• Hypertrophic cardiomyopathy</li> <li>• Aortic stenosis</li> <li>• Dilated cardiomyopathy</li> <li>• Tachycardia               <ul style="list-style-type: none"> <li>- Ventricular</li> <li>- Supraventricular</li> </ul> </li> </ul> <p><b>Medications</b></p> <ul style="list-style-type: none"> <li>• Vasodilators</li> <li>• Excessive thyroid replacement</li> </ul>	<p><b>Noncardiac</b></p> <ul style="list-style-type: none"> <li>• Anemia</li> <li>• Hypoxemia               <ul style="list-style-type: none"> <li>- Pneumonia</li> <li>- Asthma</li> <li>- Chronic obstructive pulmonary disease</li> <li>- Pulmonary hypertension</li> <li>- Interstitial pulmonary fibrosis</li> <li>- Obstructive sleep apnea</li> </ul> </li> <li>• Sickle cell disease</li> <li>• Sympathomimetic toxicity (e.g., cocaine use)</li> <li>• Hyperviscosity               <ul style="list-style-type: none"> <li>- Polycythemia</li> <li>- Leukemia</li> <li>- Thrombocytosis</li> <li>- Hypergammaglobulinemia</li> </ul> </li> </ul> <p><b>Cardiac</b></p> <ul style="list-style-type: none"> <li>• Aortic stenosis</li> <li>• Hypertrophic cardiomyopathy</li> </ul> <p><b>Medications</b></p> <ul style="list-style-type: none"> <li>• Vasoconstrictors</li> </ul>

## TREATMENT

### ENSURE PATIENT IS TAKING ANTIPLATELET THERAPY

#### Aspirin (ASA) 81 to 325 mg qd

Aspirin is known to be effective for reducing mortality in patients with CAD. Use of aspirin has been associated with a decrease in nonfatal MI, nonfatal stroke, and vascular death. The doses used ranged from 81 mg to 325 mg per day and doses throughout this range appeared to have similar effect .

For patients who require warfarin therapy, aspirin may be safely used at a dose of 80 mg/day .

If use of aspirin is contraindicated, **clopidogrel** may be used. Although it has not been studied in stable angina patients, in a large randomized controlled study of more than 19,000 patients with a history of ischemic stroke, MI, or atherosclerotic peripheral arterial disease, clopidogrel (75 mg daily) demonstrated a relative-risk reduction of 8.7% when compared with aspirin (325 mg daily).

### ENSURE PATIENT IS TAKING ADEQUATE ANTI-ANGINAL THERAPY

Treatment should be individualized. In general, the goal of adequate therapy is to allow the patient to perform normal activity and to be maintained at a symptom level of Canadian Cardiovascular Society (CCS) class I, with minimum adverse effects, BP >130/85 and pulse <70.

#### Beta-Blockers

Beta-blockers should be prescribed in all patients (with or without prior MI), in the absence of known contraindications. Beta-blockers are effective in controlling exercise-induced angina. In addition, they have been shown to decrease mortality in post-MI patients. In patients with chronic obstructive pulmonary disease, including those with a reactive airway component, beta-blockers with selective beta-1 antagonist properties may be used judiciously.

#### Nitroglycerin As Needed (PRN)

Short-acting nitroglycerin in sublingual, buccal, or spray form is known to be effective in the treatment of symptoms of acute angina, on an as-needed basis.

#### Long-Acting Nitrates

If optimal doses of beta-blockers fail to adequately control symptoms or adverse drug events, long-acting nitrates should be added. Long-acting nitrates have no proven affect on long-term survival, however; therefore emphasis should be placed on optimized beta-blockers as much as possible.

#### Calcium Channel-Blockers

If optimal doses of beta-blockers or long-acting nitrates fail to adequately control symptoms or are not tolerated, calcium channel-blocking agents may be used as adjunctive therapy. Long-acting non-dihydropyridine calcium antagonists are preferred over dihydropyridine calcium antagonists. Short-acting dihydropyridine calcium antagonists should be avoided.

#### ACE-Inhibitors

Angiotensin-converting enzyme (ACE)-inhibitors should be used for all patients with CAD who also have diabetes and/or left ventricular systolic dysfunction. ACE-inhibitors should also be considered in patients with CAD and other vascular disease in the absence of left ventricular dysfunction. ACE-inhibitors have been shown to improve outcomes in these patients, although ACE-inhibitors should not be considered anti-anginal drugs.

#### Lipid-Lowering Therapy

In patients with established coronary disease, including chronic stable angina pectoris, dietary intervention and treatment with lipid-lowering medications should not be limited to those with extreme values. The clinical trial data establish the benefits of aggressive lipid-lowering treatment for most coronary disease patients, even when LDL-cholesterol is within a range considered acceptable for patients in a primary prevention setting. For patients with established coronary disease, nonpharmaceutical

treatment should be initiated when LDL-cholesterol is >100 mg/dL, and drug treatment is warranted when LDL-cholesterol is >130 mg/dL and may be considered for LDL-C 100 to 129 mg/dL.

### **HAS THE PATIENT EXPERIENCED AN INCREASE IN SYMPTOM SEVERITY OR FREQUENCY?**

Patients who have had a recent increase in symptom severity or frequency may have an acute coronary syndrome or progression of CAD. Patients who have had a significant increase in symptoms within the preceding two weeks should be evaluated in Module B. Patients who have had a gradual worsening of symptoms >2 weeks warrant further evaluation.

### **DID PATIENT HAVE A RECENT (<6 MONTHS) REVASCULARIZATION?**

Patients who have had a recent revascularization procedure and have recurrent angina are a special subset of patients with stable angina. Recurrent angina following a revascularization procedure may represent either restenosis, following percutaneous coronary intervention, or graft failure, following a coronary artery bypass graft. Therefore, patients who present with recurrent typical angina within 6 months of revascularization should be referred to a cardiologist for further evaluation and possible coronary angiography.

### **Assessment of Left Ventricular Function (LVF) (e.g., Signs or Symptoms of CHF)**

Left ventricular systolic dysfunction is one of the strongest predictors of both increased mortality and increased morbidity, including Congestive Heart Failure (CHF) and malignant arrhythmias. Pharmacologic therapy and/or revascularization can favorably affect this clinical course.

Accepted criteria for at least one assessment of LVF in patients with known CAD include the following:

- Symptoms of CHF (e.g., orthopnea or paroxysmal nocturnal dyspnea)
- Significant impairment or recent decrement in exercise tolerance, due to dyspnea or fatigue
- Physical signs of CHF (e.g., elevated jugular venous pressure, unexplained pulmonary rales, laterally displaced point of maximal impulse, and S3 gallop)

- Cardiomegaly on chest x-ray
- History of prior MI or pathologic Q-waves on the ECG

Repeat assessment is indicated if there has been an unexplained worsening of CHF symptoms or signs or a significant decrement in exercise tolerance, due to fatigue or dyspnea. Routine reassessment of LVF in stable patients is not indicated.

It is also important to recognize that patients with normal or near-normal LVF (ejection fraction [EF] >0.40) may experience symptoms of heart failure due to diastolic LV dysfunction. Such patients may also experience symptomatic benefit from diuretics, beta-blockers or nitrates, but there is little or no evidence of benefit from calcium channel-blockers or ACE-inhibitors. For specific recommendations for the treatment of diastolic heart failure, the provider is referred to the ACC/AHA Task Force on Practice Guidelines, Guidelines for the Evaluation and Management of Heart Failure (2001).

Select the most appropriate method for the assessment of LV systolic function. LV systolic function may be assessed by contrast angiography at cardiac catheterization, two-dimensional cardiac ultrasound, and radionuclide ventriculography.

Of note, Silver et al. (1994) developed a clinical rule to identify patients with prior MI who had LVEF >0.40. They found a positive predictive value of 98 percent in those patients who have ALL of the following characteristics:

- An interpretable ECG (no left bundle branch block, ventricular pacing, or left ventricular hypertrophy with strain pattern)
- No prior Q-wave MI
- No history of CHF
- Index MI which is not a Q-wave anterior infarction

### **NON-INVASIVE RISK STRATIFICATION**

Patients with known IHD and angina who have not experienced any recent changes in symptom severity or frequency should undergo non-invasive risk stratification.

A stress test is not required if:

- The patient has had a prior stress test (or recent angiography).
- The patient has been free of angina symptoms since the most recent stress test or angiography.

Risk-stratification generally includes both cardiac stress testing and an assessment of resting left ventricular function. *Routine periodic stress testing (e.g., yearly treadmill) is not indicated in patients with stable angina.*

Stress tests will not be of benefit to the following patients for whom the results of stress testing are unlikely to change the treatment regimen:

- Patients with limited life expectancy from other conditions
- Patients with comorbidities that limit therapy or magnify the risk of procedures
- Patients with an established diagnosis of CAD, who are unwilling to consider alternatives to medical therapy

Patients with intermediate- or high-risk features (see Table) found on non-invasive risk testing should be referred to Cardiology for further evaluation and possible coronary angiography. Patients without intermediate- or high-risk features and normal non-invasive test results should be evaluated for non-cardiac causes of chest pain. Patients with evidence of CAD on non-invasive testing but without intermediate- or high-risk features should be treated according to Module G.

## IS THE RESPONSE TO THERAPY UNSATISFACTORY?

Even after optimizing anti-anginal medications, a patient may require revascularization if the symptoms are not resolved or if the patient is dissatisfied with his or her functional status or symptoms.

In addition to reducing mortality, the goal of IHD therapy should be to return the patient to as nearly a normal quality of life as possible. Patients who do not meet this goal of medical therapy and are willing to accept the risks of revascularization, in the hope of meeting this goal, may be offered invasive evaluation.

The patient for whom medical therapy results in satisfactory control of symptoms should be followed periodically. The follow-up of the IHD patient, focusing on interventions for secondary prevention, is included in Module G.

<b>Cardiac Stress Test</b>
<b>High-Risk Findings</b>
<ul style="list-style-type: none"> <li>• Duke treadmill score less than or equal to -11 (estimated annual mortality &gt;3%)</li> <li>• Large stress-induced perfusion defect</li> <li>• Stress-induced, multiple perfusion defects of moderate size</li> <li>• Large fixed perfusion defect with LV dilation or increased lung uptake (thallium-201)</li> <li>• Stress-induced, moderate perfusion defect with LV dilation or increased lung uptake (thallium-201)</li> <li>• Echocardiographic wall motion abnormality involving &gt;2 segments at <math>\leq 10</math> mg/kg/min dobutamine or HR &lt;120/min</li> </ul>
<b>Intermediate-Risk Findings</b>
<ul style="list-style-type: none"> <li>• Duke treadmill score (greater than -11 and less than 5) (estimated annual mortality 1-3%)</li> <li>• Moderate stress induced perfusion defect without LV dilation or increased lung uptake</li> <li>• Limited stress echocardiographic ischemia with wall motion abnormality involving <math>\leq 2</math> segments at higher doses of dobutamine (&gt;10 mg/kg/min dobutamine)</li> </ul>

# VA/DOD CLINICAL PRACTICE GUIDELINE FOR THE MANAGEMENT OF ISCHEMIC HEART DISEASE MODULE G SUMMARY

## MEDICAL FOLLOW-UP AND SECONDARY PREVENTION

Patients who have a history of ischemic heart disease (IHD) are candidates for secondary prevention of further coronary events. These include patients with prior myocardial infarction (MI), ischemic cardiomyopathy, silent ischemia, segmental wall motion abnormality by left ventricular (LV) angiography or cardiac ultrasound, positive stress test, prior coronary revascularization, pathologic Q-waves on the resting electrocardiogram (ECG), and males older than age 50 with typical angina.

This module provides guidelines for clinical predictors for progression of IHD and identifies areas for which there are effective interventions. It also emphasizes that all patients are on optimal doses of pharmacological therapies with proven morbidity and mortality benefits, and that patients are assessed for possible benefits from a revascularization procedure.

This module also emphasizes the assessment for coronary artery disease (CAD) risk factors, where interventions are known to reduce the likelihood of future coronary events (particularly smoking, diabetes mellitus [DM], dyslipidemia, and hypertension). Although the evidence of benefit is less strong, the diagnosis and treatment of depression and promotion of cardiac rehabilitation are also discussed.

### KEY ELEMENTS

#### Management of Medical Follow-Up

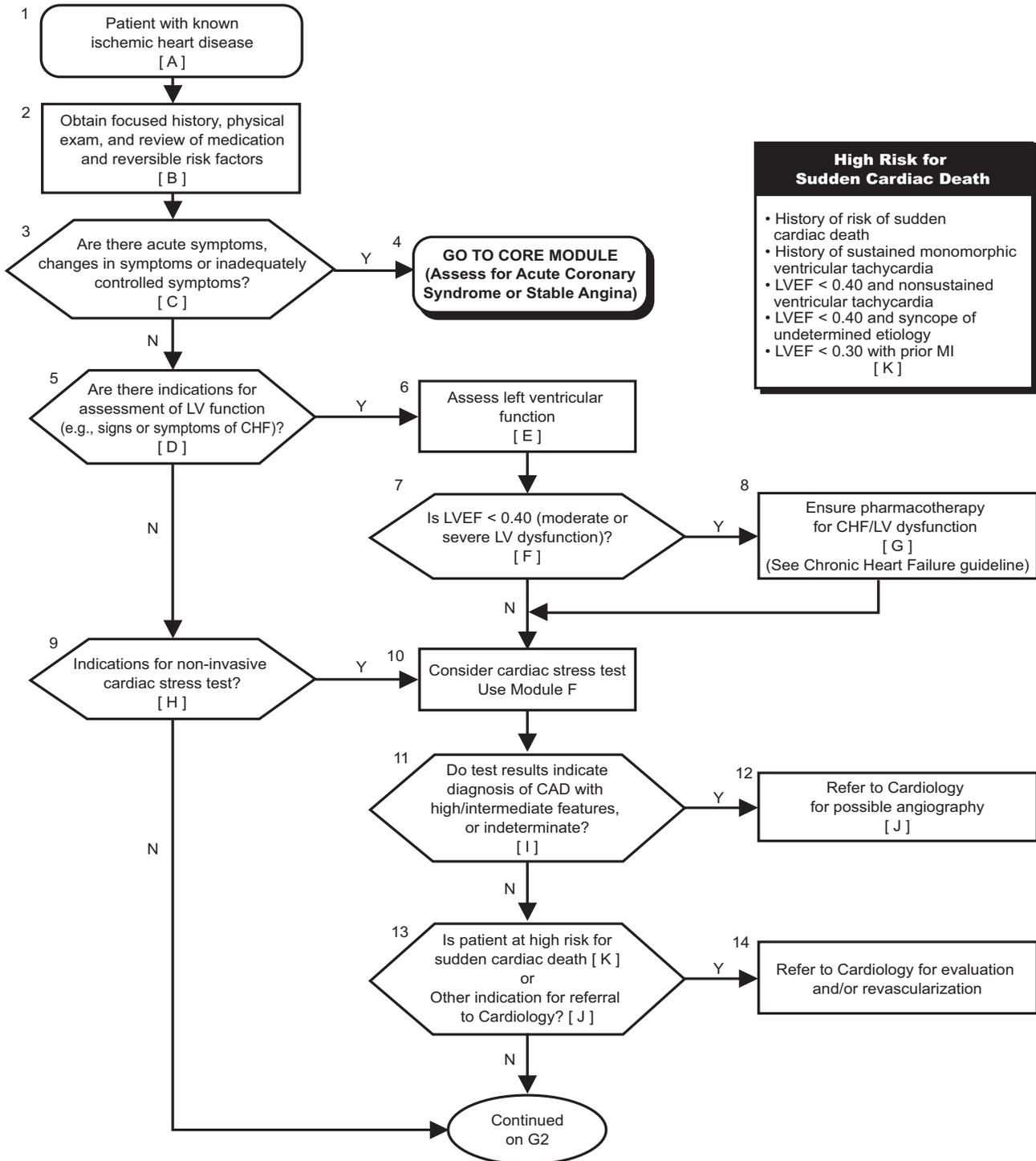
- Identify and triage IHD patients with a possible acute coronary syndrome (i.e., ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), or unstable angina).
- Assess if stable symptoms are due to noncardiac conditions.
- Identify and treat other medical conditions that may exacerbate IHD symptoms.
- Ensure all patients receive aspirin (or other antiplatelet therapy, as appropriate).
- Titrate pharmacological therapy for ischemia, angina, and congestive heart failure (CHF) to physiologic end-points, therapeutic doses, or patient tolerance.
- Administer a cardiac stress test to assess the risk of future cardiac events, if not previously performed, or if there has been worsening of ischemic symptoms.
- Initiate angiotension-converting-enzyme (ACE) inhibitor therapy for patients with significant DM and/or left ventricular (LV) dysfunction (ejection fraction [EF] <0.40). Consider in patients without LV dysfunction.
- Identify and provide therapy for patients with heart failure.
- Identify patients at high risk for sudden cardiac death or complications for whom a cardiology referral is appropriate.

#### Secondary Prevention

- Assure appropriate treatment with beta-adrenergic blocking agents (beta-blockers) in patients with prior MI.
- Identify and treat patients with high low-density-lipoprotein cholesterol (LDL-C).
- Assess and treat high blood pressure.
- Reduce cardiac risk with smoking cessation.
- Promote cardiac rehabilitation as secondary prevention.
- Achieve tight glycemic control in diabetics.
- Screen for depression and initiate therapy or refer.
- Provide patient education and arrange follow-up.

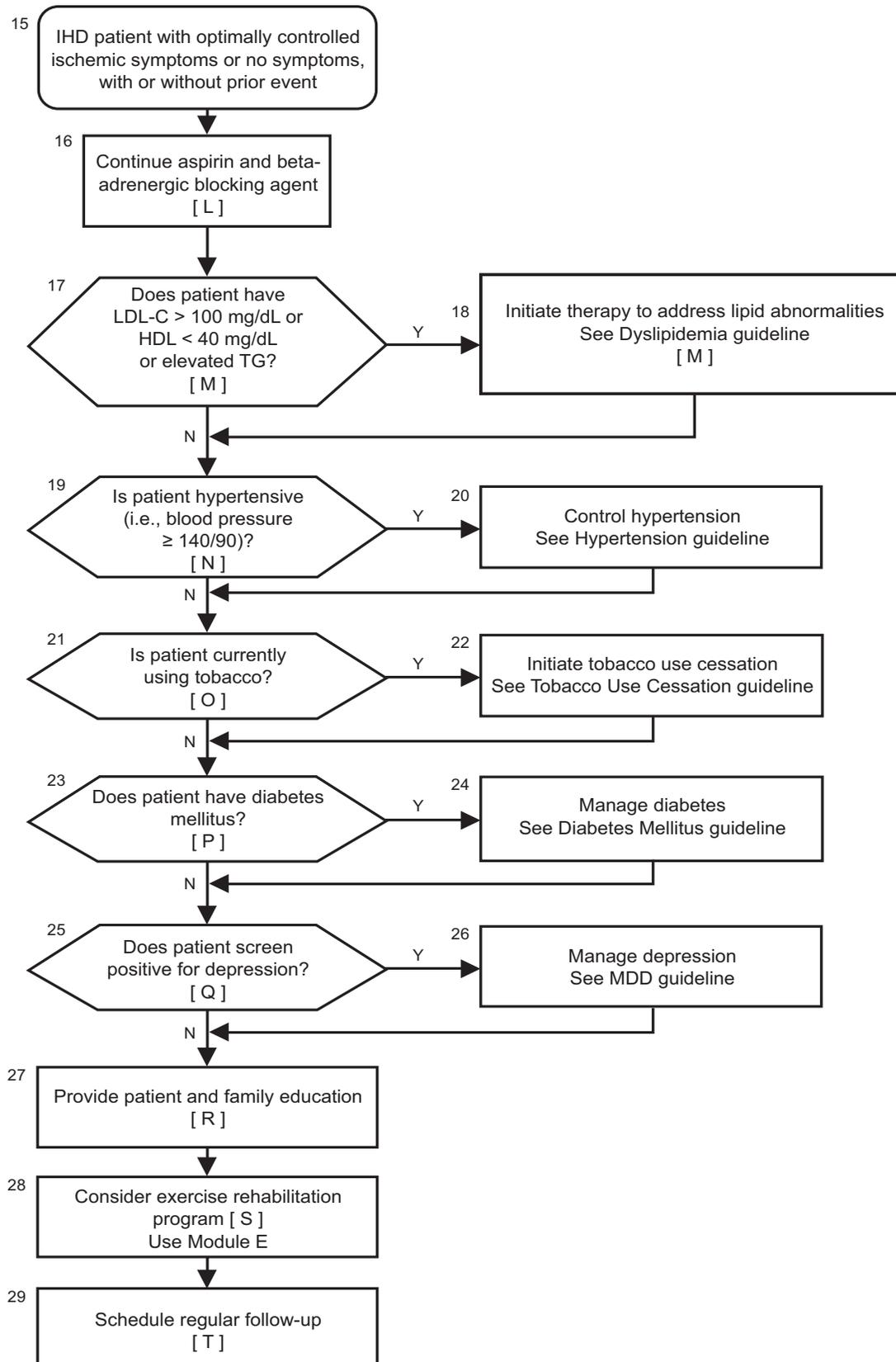
**MANAGEMENT OF ISCHEMIC HEART DISEASE**  
**Module G: IHD Follow-Up and Secondary Prevention**

**G1**



**MANAGEMENT OF ISCHEMIC HEART DISEASE**  
**Module G: IHD Follow-Up and Secondary Prevention**

**G2**



## MEDICAL FOLLOW-UP AND SECONDARY PREVENTION

Candidates for secondary prevention of IHD are patients who have a history of clinical coronary disease.

Generally accepted criteria for a diagnosis of CAD include the following:

- Prior MI and/or pathologic Q-waves on the resting ECG
- Typical stable angina in males older than 50 years or females older than 60 years of age
- Cardiac stress test showing evidence of myocardial ischemia or infarction
- LV segmental wall motion abnormality by angiography or cardiac ultrasound
- Silent ischemia, defined as reversible ST-segment depression by ambulatory ECG monitoring
- Definite evidence of CAD by angiography
- Prior coronary revascularization (percutaneous coronary intervention or coronary artery bypass graft (CABG) surgery)

### ASSESS AND DETECT CHANGES IN CLINICAL STATUS

A focused history should include assessment of risk factors for which interventions can improve outcome. Life-extending therapies, such as beta-blockers after MI, aspirin, ACE inhibitors and lipid-lowering therapy, are under-prescribed in patients with known IHD.

Stable patients with IHD may experience sudden or acute changes in their clinical status (e.g., STEMI, NSTEMI, or unstable angina). The diagnosis of acute coronary syndrome (ACS) may be suspected on the basis of a compelling clinical history, specific ECG findings, and/or elevations in serum markers of cardiac necrosis. Patients with symptoms that are new, acute, changed or inadequately controlled should be evaluated according to the CORE Module

#### Symptoms That May Represent Ischemia or MI

The following may be symptoms of myocardial ischemia. If they are new or are occurring in an accelerating fashion, they should prompt consideration of a possible ACS.

- New onset or worsening chest pain, discomfort, pressure, tightness, or heaviness
  - “New onset” is defined as chest pain or discomfort being evaluated for the first time or the patient with a complaint of chest pain is new to the clinic.
  - “Worsening” is defined as at least a one-class increase (Canadian Cardiovascular Society [CCS] angina classification) in a patient with known previous symptoms attributed to myocardial ischemia.

- Radiating pain to the neck, jaw, arms, shoulders, or upper back
- Unexplained or persistent shortness of breath
- Unexplained epigastric pain
- Unexplained indigestion, nausea, or vomiting
- Unexplained diaphoresis
- Unexplained weakness, dizziness, or loss of consciousness

Patients with evidence of acute changes in symptoms should be evaluated using the core module.

#### Symptom Characteristics That Suggest Noncardiac Pain But Do Not Exclude a Diagnosis of CAD

- Pleuritic pain (i.e., sharp or knife-like pain brought on by respiratory movements or cough)
- Primary or sole location of discomfort in the middle or lower abdominal regions
- Pain that may be localized at the tip of one finger, particularly over costochondral junctions or the LV apex
- Pain reproduced with movement or palpation of the chest wall or arms
- Constant pain that lasts for many hours
- Very brief episodes of pain that last a few seconds or less
- Pain that radiates into the lower extremities

#### Adequate Control of Symptoms

The level of symptoms that constitute “adequate control” is highly dependent on the following:

- Stage of the CAD
- Whether or not revascularization is feasible at an acceptable risk
- Patient’s tolerance or intolerance of anti-anginal drugs
- Patient’s preference

Changes in exercise tolerance and symptoms, over time, are particularly useful in assessing the adequacy of control of myocardial ischemia symptoms. The CCS classification of angina is useful for the serial assessment of exercise tolerance and anginal symptoms. Indications for altering therapy and the therapeutic details are presented in Module C, Stable Angina.

#### Canadian Cardiovascular Society Classification of Angina

Class I	Angina only with <i>strenuous</i> exertion
Class II	Angina with <i>moderate</i> exertion
Class III	Angina with <i>minimal</i> exertion or ordinary activity
Class IV	Angina <i>at rest</i> or with <i>any</i> physical activity

## MAINTENANCE/MEDICAL THERAPY OF CHRONIC IHD

### Recommended Medications for Patients with IHD

Aspirin (or clopidogrel) reduces cardiovascular (CV) events in patients with acute MI, previous MI, and unstable angina
Aspirin reduces risk of MI in patients with chronic stable angina
Beta-blockers improve symptoms in patients with IHD
Beta blockers improve CV outcomes in patients with IHD, previous MI and ischemic LV dysfunction
Beta-blockers reduce CV events in patients with silent ischemia
Nitroglycerin (prn)
ACE inhibitors improve CV outcomes in patients with IHD, and are especially recommended in patients with diabetes or low LV ejection fraction
Lipid-lowering therapy improves CV outcomes in patients with IHD and elevated lipids
Lipid-lowering therapy improves CV outcomes in patients with IHD and average cholesterol
Gemfibrozil improves outcomes in patients with IHD and low high-density lipoproteins – cholesterol (HDL-C)

### Recommended Medications for Patients with IHD and LV Dysfunction

ACE inhibitors improve morbidity and mortality in patients with CHF or low EF
Asymptomatic patients, but with low EF, experience survival benefit from ACE inhibitors
Doses of ACE inhibitors should be titrated to target or maximum tolerable dose
Beta-blockers should be considered for all patients with NYHA class II or III CHF, and EF<0.40, after stabilization on ACE inhibitors
Addition of spironolactone to ACE inhibitors and diuretics in patients with severe heart failure improves morbidity and mortality
Digoxin use in heart failure (EF<0.45) does not affect mortality, but decreases hospitalization due to heart failure
Diuretics improve symptoms of volume overload

### Adjust Angina Management, if Indicated

Ensure the patient is on optimal anti-anginal therapies.

Three classes of drugs are available for the control of symptoms in patients with chronic stable angina: beta-adrenergic blocking agents, calcium channel blocking agents, and nitrates.

Beta-adrenergic blocking agents are generally considered the first drug of choice because of: (1) the documented survival benefit in patients with prior MI, and (2) the survival benefit in patients with hypertension. Beta-blockers also reduce morbidity from stroke and heart failure in patients with hypertension. Beta-adrenergic blocking agents probably achieve their anti-anginal effect primarily through slowing of the heart rate and to a lesser extent from reduction in systolic pressure and contractility. Therefore, a commonly used “rule of thumb” is to titrate the beta-blocker to angina relief or to a resting heart rate of 55 to 60.

Patients with prior MI, treated with adequate doses of beta-blockers, have reduction in recurrent events and mortality. Every effort should be made to use this class of drugs in these patients in particular but also in all

patients with documented IHD. Physicians may overrate contraindications to using beta-blockers in post-MI patients (i.e., diabetes, lower EF, depression, and chronic obstructive pulmonary disease (COPD)). In fact, patients with diabetes and lower EF have proven benefits from beta-blockers post-MI and patients with COPD can often tolerate beta-blockers. The association between depression and beta-blockers has been questioned. In general, the decision to avoid beta-blockers, based on theoretical concerns, should be carefully weighed against the overwhelming evidence supporting their use in patients with CAD.

Overviews of multiple randomized trials indicate that beta-adrenergic blocking agents and calcium channel-blocking agents are equally effective in providing angina relief and in enhancing exercise duration to 1 mm ST-segment depression (Figures 9 and 10, ACC/AHA Stable Angina Guidelines, 1999). Therefore, in patients without prior MI or hypertension, a long-acting calcium channel agent would be acceptable. However, there is ongoing controversy about whether the short-acting calcium channel drugs are associated with increased morbidity and mortality.

Sublingual nitroglycerin has been used in the treatment of angina for more than two hundred years. It is still the mainstay therapy for the immediate relief of angina that has been provoked by exertion or emotion. Furthermore, sublingual nitroglycerin, when taken prior to an activity that commonly causes angina (e.g., walking up stairs or up hill) will often prevent the development of symptoms. Several forms of longer acting nitrates (e.g., isosorbide dinitrate, isosorbide mononitrate, and topical nitroglycerin patches) are also commonly used for prophylaxis of angina. However, care must be taken to ensure a nitrate-free interval of 8 to 12 hours out of every 24, to prevent the development of tolerance. Suggest combining NTG with beta-blockers to prevent reflex tachycardia. The use of a nitrate preparation within 24 hours of the use of sildenafil (Viagra) may cause dangerous hypotension.

The following mnemonic may aid in remembering treatment elements that should be considered:

- A = Aspirin and anti-anginal therapy
- B = Beta-blocker and blood pressure
- C = Cigarette smoking and cholesterol
- D = Diet and diabetes
- E = Education and exercise

## NON-INVASIVE RISK EVALUATION

### Assess the Risk of Future Cardiac Events

Among patients with known IHD, the risk of future fatal and nonfatal coronary events ranges from no detectable increase compared to individuals without known IHD to >50 percent per year. Knowledge of such risk is essential to planning diagnostic and treatment strategies. The incidence of complications from non-invasive risk stratification in appropriately selected candidates is extremely low. Thus, the main arguments for not performing non-invasive risk stratification include the following:

- Major morbidity limiting functional status (e.g., bed-ridden from multiple strokes)
- Major morbidity limiting life expectancy (e.g., metastatic cancer)
- Patient refusal

Non-invasive risk assessment has two components: (1) assessment of LV function (LVF), and (2) cardiac stress testing to identify patients likely to have ischemic myocardium at risk.

### Assessment of LVF (e.g., Signs or Symptoms of CHF)

Left ventricular ejection function (LVEF) less than 0.40 is one of the strongest predictors of both increased mortality and increased morbidity, including CHF and malignant arrhythmias. Pharmacologic therapy and/or revascularization can favorably affect this clinical course.

Accepted criteria for at least one assessment of LVF in patients with known CAD include the following:

- Symptoms of CHF (e.g., orthopnea or paroxysmal nocturnal dyspnea)
- Significant impairment or recent decrement in exercise tolerance, due to dyspnea or fatigue
- Physical signs of CHF (e.g., elevated jugular venous pressure, unexplained pulmonary rales, laterally displaced point of maximal impulse, and S3 gallop)
- Cardiomegaly on chest x-ray
- Prior MI

Repeat assessment is indicated if there has been an unexplained worsening of CHF symptoms or signs or a significant decrement in exercise tolerance, due to fatigue or dyspnea. Routine reassessment of LVF in stable patients is not indicated.

It is also important to recognize that patients with normal or near-normal LVF (EF >0.40) may experience symptoms of heart failure due to diastolic LV dysfunction. Such patients may also experience symptomatic benefit from diuretics, beta-blockers or nitrates. For specific recommendations for the treatment of diastolic heart failure, the provider is referred to the ACC/AHA Task Force on Practice Guidelines, Guidelines for the Evaluation and Management of Heart Failure (2001).

LV systolic function may be assessed by contrast angiography at cardiac catheterization, two-dimensional echocardiogram, and radionuclide ventriculography. An echocardiogram is preferable in evaluation of patients who also have physical findings suggestive of valvular heart disease in order to assess the severity of mitral regurgitation or aortic stenosis along with assessment of LV systolic function.

Of note, Silver et al. (1994) developed a clinical rule to identify patients with prior MI who had LVEF  $\geq 0.40$ . They found a positive predictive value of 98 percent in those patients who have ALL of the following characteristics:

- Interpretive ECG (without left bundle branch block [LBBB], ventricular pacing, or LV with strain pattern)
- No prior Q-wave MI
- No history of CHF
- Index MI which is not a Q-wave anterior infarction

### Cardiac Stress Test

The risk of exercise testing in appropriately selected candidates is extremely low, and thus the main argument for not performing an exercise test is that the extra information provided would not be worth the extra cost of obtaining that information or the test might provide misinformation that could lead to inappropriate testing or therapy.

- Unless cardiac catheterization is indicated, completed or planned symptomatic patients with suspected or known CAD should usually undergo exercise testing to assess the risk of future cardiac events, unless they have confounding features on the rest ECG.
- Patients undergoing only a submaximal exercise stress test (EST) prior to discharge for an acute coronary syndrome (ACS) should receive a symptom-limited EST at 3 to 6 weeks from discharge.

Cardiac stress testing is indicated in the initial evaluation of all patients with known or suspected IHD (with the exceptions noted above), unless there are criteria for proceeding directly to cardiac catheterization and coronary arteriography (see Referral to Cardiology below). Patients with evidence of inducible ischemia during risk stratification should be considered for further cardiac evaluation, such as coronary arteriography. Repeat cardiac stress testing is indicated if there has been a significant change in symptoms or decrement in exercise tolerance; however, routine periodic stress testing is not indicated.

## REFERRAL TO CARDIOLOGY

With only a few exceptions, coronary angiography is generally not indicated in asymptomatic or mildly symptomatic patients with either known or suspected CAD, unless non-invasive testing reveals findings that suggest a high risk for adverse outcomes. Also, some patients with extenuating circumstances should *not* be routinely referred to cardiology. These general circumstances include the following:

- Review of prior coronary angiogram by current clinician showing disease not amenable to revascularization by current standards
- Patient refusal of catheterization and/or revascularization and/or patient and physician prefer medical therapy alone, without further evaluation
- Noncardiac disease with projected life expectancy  $< 6$  months or quality of life unlikely to be improved by revascularization.

The following indications for referral to a cardiologist apply only to patients with stable IHD, and not to those with a current or recent ACS, in whom different criteria apply.

- Patients with CCS class 3 to 4 symptoms of ischemia or heart failure on medical therapy.
- Patients dissatisfied with symptoms despite maximal medical therapy.
- Patients with recurrent symptoms following recent ( $< 6$  months) revascularization.
- Patients at increased risk for sudden cardiac death
- Patients with high-risk findings on non-invasive testing
- Patients with non-invasive test results that are inadequate for management.

### Increased Risk for Sudden Cardiac Death:

Patients with increased risk for sudden cardiac death would benefit from evaluation by an electrophysiologist for consideration of an implantable cardioverter defibrillator device, including:

- History of risk of sudden cardiac death
- History of sustained monomorphic ventricular tachycardia
- Reduced LVEF (EF  $< 0.40$ ) and nonsustained ventricular tachycardia
- Reduced LVEF (EF  $< 0.40$ ) and syncope of undetermined etiology
- Reduced LVEF (EF  $< 0.30$ ) and prior history of MI

## Non-Invasive Cardiac Testing:

The following list includes examples of non-invasive test results that indicate high and intermediate risk, for which cardiology referral for coronary angiography should be considered (adapted from ACC/AHA Guidelines for Coronary Angiography: Executive Summary and Recommendations, 1999).

### High-Risk Findings:

- Severe resting LV dysfunction (LVEF<0.35)
- High-risk Duke treadmill score (score  $\leq$  -11)
- Severe exercise LV dysfunction (exercise LVEF<0.35)
- Stress-induced large perfusion defect (particularly if anterior)
- Stress-induced moderate-size multiple perfusion defects
- Large, fixed perfusion defect with LV dilatation or increased lung uptake (thallium-201)
- Stress-induced moderate-size perfusion defect with LV dilatation or increased lung uptake (thallium-201)
- Echocardiographic wall motion abnormality (involving >2 segments) developing at low dose of dobutamine ( $\leq$  10 mg/kg/min) or at a low heart rate (<120 bpm)
- Stress echocardiographic evidence of extensive ischemia

### Intermediate-Risk Findings:

- Mild/moderate resting left ventricular dysfunction (LVEF = 0.35 to 0.49)
- Intermediate-risk treadmill score (greater than -11 and less than 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 two segments

## Consideration for bypass surgery:

Patients with results from coronary angiography that suggest the need for coronary bypass surgery, but which have not been addressed to the satisfaction of the patient or provider. Patients with the following coronary anatomic findings warrant consideration for bypass surgery:

- Significant left main coronary artery stenosis
- Left main equivalent: significant (70 percent) stenosis of proximal left anterior descending coronary artery (LAD) and proximal left circumflex artery
- Three-vessel disease (survival benefit is greater in patients with abnormal LVF; e.g., with an EF <0.50)
- Proximal LAD stenosis with 1- or 2-vessel disease

## SECONDARY PREVENTION FOR IHD

### Patient with Prior MI

Patients with prior MI, treated with adequate doses of beta-blockers, have reduction in recurrent coronary events and mortality. Every effort should be made to use beta-blockers in patients with MI in particular but also in all patients with documented IHD. Physicians may overrate contraindications to using beta-blockers in post-MI patients (i.e., diabetes, lower EF, depression, and chronic obstructive pulmonary disease [COPD]). In fact, observational data analyses suggest that patients with DM and lower EF may have a survival benefit from beta-blockers post-MI, and patients with COPD can often tolerate beta-blockers. The association between depression and beta-blockers has been questioned. In general, the decision to avoid beta-blockers, based on theoretical concerns, should be carefully weighed against the overwhelming evidence supporting their use in patients with CAD.

LDL-C THRESHOLDS FOR INITIAL DYSLIPIDEMIA TREATMENT IN PATIENTS WITH IHD		
	Baseline LDL-C [mg/dL]	
	$\geq 100$	$\geq 130$
Patient with known IHD	Diet/exercise Consider drug therapy	Diet/exercise Initiate drug therapy

### Treatment of Dyslipidemia

- **Initial Therapy:** Evidence clearly supports initiation of pharmacotherapy when LDL-C is >130 mg/dL in patients with CHD (Scandinavian Simvastatin Survival Study Group [4S], 1994). For CHD and CHD equivalents (i.e., type 2 DM) and patients with HDL-C >40 mg/dL and LDL-C <130 mg/dL, there is insufficient evidence on which to base a recommendation for pharmacotherapy. Individual clinicians may choose to initiate drug therapy

for LDL-C >100mg/dL for secondary CHD prevention, based on consensus opinion. However, the CARE study, a prospective secondary prevention trial, found no outcomes benefit when high-dose pravastatin was initiated at a baseline LDL-C <125mg/dL (Sacks, 1996).

- **Choice of Drug:** Statins are the best studied and show most benefit, in terms of absolute LDL-C reduction and patient outcome. Older trials with niacin and bile acid resins have shown modest reduction in LDL-C (10 to 20 percent) and CHD event rates, with some evidence of small mortality benefit. Fibrates, which have minimal effect on LDL-C, have shown reduced CHD event rates but not mortality (Frick et al., 1987; Rubins et al., 1999). Statin-based outcome trials have included lovastatin, pravastatin, and simvastatin. There is no convincing evidence that one statin is better than another. Choice and starting dose should be dictated by the required LDL-C reduction, as statins differ in their potency. The dose should be adjusted at 6- to 8-week intervals until the LDL-C reduction goal is achieved.

- **Aggressiveness of LDL-C Reduction:**

There is no direct evidence from randomized clinical trials (RCTs) that demonstrates a net benefit (in terms of clinically relevant endpoints) of treating to an LDL-C goal of less than 130 mg/dL. Indirect evidence from the 4S Trial (1994) demonstrated that in patients with previous CHD, treated with simvastatin to an average LDL-C of 118 mg/dL, the benefits clearly outweighed the harms. NCEP III recommends lowering LDL-C to <100 mg/dL in the secondary CHD and CHD equivalents (i.e., type 2 DM) prevention setting. Trials are now underway to determine whether even more aggressive treatment produces additional benefit. An angiographic trial in CABG patients showed that patients treated to a target LDL-C <140mg/dL had worse outcomes than those treated more aggressively to a target LDL-C <85mg/dL (Post CABG Trial, 1997). After four years, angiographic progression for the aggressive and moderate groups was 27 percent and 39 percent, respectively. Revascularization was reduced by 29 percent in the lower LDL-C group. Some experts argue that it is the percentage drop in LDL-C, not the absolute LDL-C achieved, that is important in achieving benefit. Treating to New Targets (TNT) is a 5 year RCT currently underway looking at lowering

LDL-C to very low target levels in patients with CHD, who are randomizing to atorvastatin 10 mg versus 80 mg/day. The results of the 4S Trial suggest that there may be additional benefits of lowering LDL-C to less than 130 mg/dL. The VA/DoD Working Group for the management of dyslipidemia recommends a treatment goal of <120 mg/dL, while waiting for a more definitive answer.

- **HDL-C <40 mg/dL with LDL-C <130 mg/dL:**

Large epidemiologic trials have shown that a low HDL-C is associated with an increased risk for cardiovascular events (Gordon, 1989). In the VA-HIT trial (1999), patients with established cardiovascular disease, an HDL-C <40 mg/dL and an LDL-C <140 mg/dL were randomized to treatment with gemfibrozil versus placebo. The mean entry HDL-C of the treatment arm was 32 mg/dL, and the mean entry LDL-C level was 111 mg/dL. After a mean follow-up of 5 years, the gemfibrozil treatment arm saw a 22 percent relative risk reduction in the combined end-point of nonfatal MI or death due to cardiovascular disease, and a 25-percent reduction in stroke (Rubins et al., 1999). Subgroup analysis of VA-HIT strongly suggests that CHD patients with low HDL-C, triglycerides >200 mg/dL, hypertension, or impaired fasting glucose were particularly likely to benefit from gemfibrozil therapy. The study was not powered to detect an overall mortality benefit.

### **Assessment and Treatment of High Blood Pressure**

Hypertension is a risk factor for developing cardiovascular disease, the risk increasing in proportion to the severity of the hypertension, as demonstrated in multiple observational studies. Treatment of hypertension results in reduction in coronary events, even in patients with mild hypertension or in older populations. There is evidence from hypertension trials that both diuretics and beta-blockers reduce coronary events. In patients with hypertension and IHD, beta-blockers are the preferred first-line agents as they provide additional therapeutic benefit – particularly in patients with prior MI and/or angina. See the VA/DoD Clinical Practice Guideline for the Diagnosis and Management of Hypertension in the Primary Care Setting.

### **Promote Tobacco Use Cessation**

Tobacco use is a strong risk factor for IHD. Smoking cessation is associated with significant reduction in acute cardiac syndromes. Evidence supports the effectiveness of several smoking cessation interventions, including physician recommendation, multidisciplinary clinics, and pharmacological interventions. However, in general, the better smoking cessation rates have been achieved with combinations of interventions, as compared with a single intervention alone.

Primary care providers should advise every patient who smokes about the potential adverse medical consequences associated with tobacco use and counsel them to quit. Detailed recommendations can be found in the VA/DoD Clinical Practice Guideline Management of Tobacco Use in Primary Care.

### **Management of Diabetes Mellitus (DM)**

Achieve tight glycemic control to reduce macrovascular events and achieve microvascular benefits. Patients with DM are at increased risk for adverse cardiovascular events, with rates of MI similar to that of patients with known IHD. Microvascular complications, such as retinopathy and nephropathy, are decreased with improving glycemic control. There is conflicting evidence on whether tight glycemic control reduces macrovascular events, such as MI and stroke. Tight control of glucose in both type 1 and type 2 DM is recommended because of potential reduction of macrovascular events and proven microvascular benefits.

### **Screen for Depression**

Identify patients who also have depression and initiate therapy or referral for therapy. Depression is prevalent in patients with IHD and is independently associated with a worse prognosis. There is efficacious treatment available for depression. It is not known whether the treatment of depression improves CV outcomes, though it is known that such treatment improves compliance with efficacious therapies. There are several available tools to screen for depression in the primary care setting. See the VA/DoD Clinical Practice Guideline for the Management of Major Depressive Disorder in Adults for a discussion of depression screening. As an example, the PRIME MD efficiently screens for criteria-based DSM IV diagnosis of depressive disorders.

### **Exercise Rehabilitation Program**

Consider cardiac rehabilitation as secondary prevention. The benefits of a multi-factorial approach to CV risk-factor management, such as found in a cardiac rehabilitation program, include the following:

- Improvement in exercise tolerance and anginal symptoms
- A more favorable blood lipid profile
- Reduced stress and improved psychosocial well-being
- Reduction in cigarette smoking

### **Nutrition Therapy**

Consider Medical Nutrition Therapy (MNT) by a registered dietician or nutrition professional for clinical nutrition assessment and provision of appropriate nutrition therapy. There are other sources for “heart-healthy” diets, including the American Heart Association (see <http://www.deliciousdecisions.org>).

### **Regular Follow-Up**

Appropriate follow-up of the patient with IHD will vary for the individual patient. Many patients on a stable medical regimen can be followed on a 6- to 12-month basis. Other patients, however, will need more frequent follow-up to encourage risk-factor modification, assess efficacy of medical regimen, and follow appropriate laboratory tests (e.g., lipids, electrolytes, renal function, and drug levels).

### **Patient Education**

High-quality care requires education to encourage and motivate the patient to participate in therapeutic and preventive efforts. Education should be individualized depending on the patient’s resources and needs. Patient and family education may include the following:

- Assess the patient’s baseline understanding
- Elicit the patient’s desire for information
- Use epidemiologic and clinical evidence
- Use ancillary personnel and professional patient educators when appropriate
- Develop a plan with the patient on what to do when symptoms occur
- Involve family members in educational efforts.
- Remind, repeat, and reinforce