Complete Summary

GUIDELINE TITLE

VA/DoD clinical practice guideline for management of ischemic heart disease.

BIBLIOGRAPHIC SOURCE(S)

Veterans Health Administration, Department of Defense. VA/DoD clinical practice guideline for the management of ischemic heart disease. Washington (DC): Veterans Health Administration, Department of Defense; 2003 Nov. Various p. [35 references]

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
CONTRAINDICATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY

SCOPE

DISEASE/CONDITION(S)

Ischemic heart disease

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Diagnosis
Management
Treatment

CLINICAL SPECIALTY

Cardiology
Emergency Medicine
Family Practice
Internal Medicine

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

- To describe the critical decision points in the management of ischemic heart disease
- To provide a clear and comprehensive guideline incorporating current information and practices for practitioners throughout the Department of Defense (DoD) and Veterans Health Administration system
- To improve local management of patients with ischemic heart disease and improve patient outcomes

TARGET POPULATION

Any person with ischemic heart disease who is eligible for care in the Veterans Administration (VA) or Department of Defense (DoD) health care delivery system

INTERVENTIONS AND PRACTICES CONSIDERED

Initial Evaluation/Triage

1. Brief history and physical examination
2. Assessment of signs and symptoms of myocardial ischemia
3. Assessment of emergency status based on vital signs and appearance
4. Emergency interventions (supplemental oxygen [O_2] therapy, aspirin, 12-lead electrocardiogram [ECG], intravenous access, nitroglycerin [NTG], cardiac monitoring, adequate analgesia, advanced cardiac life support, chest x-ray, and appropriate transportation to setting for appropriate level of monitoring)
5. Continuous monitoring of vital signs and ECG
6. Assessment of serum cardiac biomarkers
7. Hospital admission if applicable
8. Evaluation for acute coronary syndrome (ACS)
9. Non-invasive cardiac stress test
10. Referral for coronary angiography or revascularization
11. Evaluation for coronary artery disease (CAD)
12. Consideration of cardiac (non-ischemic) and non-cardiac reasons for chest pain discomfort

Suspected Acute Myocardial Infarction

1. Emergency interventions (continuous cardiac monitoring, supplemental O_2 therapy, aspirin, intravenous access, obtain cardiac enzymes/markers, sublingual NTG, ECG, adequate analgesia, chest x-ray, and transportation to setting for appropriate level of monitoring)
2. Focused history and physical examination
3. Assessment for alternative catastrophic diagnoses
4. Pharmacological therapy (non-coated aspirin, beta-blockers, intravenous unfractionated heparin, NTG, oral angiotensin-converting enzyme inhibitors [ACE inhibitors], and analgesics)
5. Percutaneous revascularization
6. Thrombolytic therapy
7. Salvage angioplasty
8. Anti-arrhythmic agents
9. Echocardiogram
10. Patient evaluation for cardiovascular risk prior to discharge
11. Discharge with appropriate follow-up

Suspected Acute Coronary Syndrome (Unstable Angina or Non-ST Segment Elevation Myocardial Infarction [MI])

1. Risk stratification
2. Emergency interventions (supplemental O_2 therapy, aspirin, 12-lead ECG, intravenous access, sublingual NTG, continuous cardiac monitoring, adequate analgesia, advanced cardiac life support, chest x-ray, and appropriate transportation to setting for appropriate level of monitoring)
3. Pharmacotherapy (non-coated aspirin, clopidogrel, intravenous unfractionated heparin [IV UFH], enoxaparin, beta-blockers, calcium antagonists, ACE inhibitors, NTG, and IV morphine)
4. Assessment of serial ECGs, cardiac-specific markers, and lipid profile
5. Treatment of conditions that may provoke angina symptoms
6. Antiplatelet and anticoagulant therapy
7. Glycoprotein (GP) IIb/IIIa receptor antagonists therapy
8. Coronary angiography
9. Contrast angiography, two-dimensional cardiac ultrasound, or radionuclide ventriculography to assess left ventricular function
10. Pharmacotherapy for congestive heart failure (CHF)/left ventricular (LV) dysfunction (beta-blockers and ACE-inhibitors)
11. Cardiac stress test
12. Referral to cardiologist
13. Discharge

Management of Stable Angina

1. History, physical examination, and routine laboratory tests
2. Assessment for conditions that may exacerbate angina symptoms
3. Antiplatelet therapy (aspirin)
4. Anti-anginal therapy (beta-blockers, NTG [as needed], long-acting nitrates, calcium channel-blockers, ACE-inhibitors, and lipid-lowering therapy)
5. Assessment for percutaneous intervention
6. Assessment of left ventricular function (contrast angiography, two-dimensional echocardiogram, radionuclide ventriculography)

7. Treatment for CHF/LV dysfunction (beta-blockers, ACE inhibitors, spironolactone, digoxin, and diuretics)
8. Cardiology referral
9. Assessment for stress test
10. Follow-up and secondary prevention

Follow-up and Secondary Prevention

1. Assessment of clinical predictors for ischemic heart disease (IHD) and identification of effective interventions
2. Assessment for changes in clinical status (Canadian Cardiovascular Society [CCS] classification)
3. Assessment of left ventricular function (contrast angiography, two-dimensional echocardiogram, radionuclide ventriculography)
4. Appropriate pharmacotherapy and adjustment
5. Assessment of risk for future cardiac events (stress testing)
6. Cardiology referral for patients who would benefit from revascularization or an electrophysiology (EP) study and/or therapy
7. Treatment and control of low- and high-density lipoproteins and blood pressure
8. Smoking cessation interventions
9. Glycemic control interventions
10. Treatment for depression
11. Patient and family education
12. Exercise rehabilitation program
13. Regular follow-ups

Outpatient Cardiac Rehabilitation

1. Exercise stress testing to determine risk stratification level
2. Contraindications for exercise
3. Exercise program based on risk for exercise-induced event
4. Secondary prevention of risk factors (i.e., hypertension, smoking cessation, weight management)
5. Education about safe activity levels

Non-invasive Evaluation for Diagnosis, Risk Stratification, and Guidance of Medical Therapy

1. Focused history and physical examination for contraindications to stress testing
2. Coronary angiography
3. Exercise imaging study (i.e., exercise-rest myocardial perfusion imaging or rest-exercise echocardiography)
4. Exercise stress test
5. Pharmacologic stress test with imaging modality
6. Identification and referral of patients who are candidates for revascularization procedure (percutaneous coronary intervention [PCI] or coronary artery bypass graft surgery [CABG]) or coronary arteriography
7. Cardiology referral

Evaluation and Management of the Asymptomatic Patient

Evaluation

1. Resting ECG
2. Exercise test
3. Myocardial perfusion study
4. Regional or global left ventricular wall motion using echocardiography, radionuclide ventriculography, or magnetic resonance imaging (MRI)
5. Coronary calcification (electron beam computed tomography)
6. Ankle/brachial index (ABI) or toe/brachial index (TBI)
7. Carotid duplex ultrasound

Diagnostic Follow-up

1. History, physical examination, chest radiograph, and ECG
2. Cardiology consultation
3. Further diagnostic testing for patients whose clinical findings suggests high probability of IHD (i.e., resting ST-segment depression >1mm)
4. Echocardiography
5. Risk-factor modification

MAJOR OUTCOMES CONSIDERED

- Functional status
- Symptoms
- Rate of progression of coronary disease
- Risk assessment
- Morbidity
- Mortality

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

A search was carried out using the National Library of Medicine's (NLM) MEDLINE database. Electronic searches of the Cochrane Controlled Trials Register (www.update-software.com) were undertaken. Papers selected for further review were those published in English-langue peer-reviewed journals between 1994 and 1999. Preference was given to papers based on randomized, controlled clinical trials, or nonrandomized case-control studies. Studies involving meta-analyses were also reviewed.

Selected articles were identified for inclusion in a table of information that was provided to each expert participant. The table of information contained title, author(s), publication type, abstract, and source. Copies of these tables were made available to all participants. In addition, the assembled experts suggested

numerous additional references. Copies of specific articles were provided to participants on an as-needed basis. This document includes references through the year 2003.

Note: The research on treatment for ischemic heart disease (IHD) is very intensive. During the final editing stages of this guideline, important relevant findings from early 2003 were incorporated into the modules and added to the reference list.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Quality of Evidence

I: Evidence is obtained from at least one properly randomized controlled trial (RCT)

II-1: Evidence is obtained from well-designed controlled trials without randomization

II-2: Evidence is obtained from well-designed cohort or case-control analytical studies, preferably from more than one center or research group

II-3: Evidence is obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence

III: Opinion of respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Evidence-based practice involves integrating clinical expertise with the best available clinical evidence derived from systematic research. The working group reviewed the articles for relevance and graded the evidence using the rating scheme published by the U.S. Preventive Services Task Force (U.S. PSTF) (See

Current methods of the US Preventive Services Task Force: a review of the process. Am J Prev Med. 2001 Apr;20(3 Suppl):21-35. (http://www.ahrq.gov/clinic/ajpmsuppl/harris1.htm).

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The specific language used to formulate each recommendation conveys panel opinion of both the clinical importance attributed to the topic and the strength of evidence available. When appropriate and necessary, expert opinion was formally derived from the working group panel to supplement or balance the conclusions reached after reviewing the scientific evidence.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Strength of Recommendation

The rating was influenced primarily by the significance of the scientific evidence. In addition, the risk of death or a cardiac event was taken into consideration. Several recommendations resulted in a strong "A" recommendation even though there were no trials or studies to provide evidence. Other factors that were taken into consideration when making the recommendation rating determination were standards of care, policy concerns, and cost of care.

A. A strong recommendation, based on evidence or general agreement, that a given procedure or treatment is useful/effective, always acceptable, and usually indicated
B. A recommendation, based on evidence or general agreement, that a given procedure or treatment may be considered useful/effective
C. A recommendation that is not well established, or for which there is conflicting evidence regarding usefulness or efficacy, but which may be made on other grounds
D. A recommendation, based on evidence or general agreement, that a given procedure or treatment may be considered not useful/effective
E. A strong recommendation, based on evidence or general agreement, that a given procedure or treatment is not useful/effective, always acceptable, and usually indicated

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The recommendations for the management of ischemic heart disease are organized into 8 major algorithms. The algorithm, the objectives and annotations that accompany it, and the evidence supporting the recommendations are presented below. The strength of recommendation grading (A, B, C, D, E) and quality of evidence grading (I, II-1, II-2, II-3, III) are defined at the end of the "Major Recommendations" field.

Note: A list of all abbreviations is provided at the end of the "Major Recommendations" field.

Core: Initial Evaluation/Triage
Module A: Suspected Acute Myocardial Infarction
Module B: Suspected Acute Coronary Syndrome (Unstable Angina or Non-ST Segment Elevation MI)
Module G: Follow-up and Secondary Prevention
Module E Outpatient Cardiac Rehabilitation
Module F Non-invasive Evaluation

Core: Initial Evaluation/Triage

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 acute coronary syndromes (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 myocardial infarction (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 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, 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 below). 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:

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 above). 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 in the original guideline document). 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) 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 include the following:

- Chest pain or epigastric pain, non-traumatic 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

The American College of Cardiology/American Heart Association (ACC/AHA) describes the different classes of the Canadian Cardiovascular Society (CCS) classifications as follows:

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

Class I:	Angina only with strenuous exertion 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.
Class II:	Angina with moderate exertion 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 than one flight of ordinary stairs at a normal pace and under normal conditions.
Class III:	Angina with minimal exertion or ordinary activity 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.
Class IV:	Angina at rest or with any physical activity Inability to carry on any physical activity without discomfort. --Anginal symptoms may be present at rest.

Evidence

Symptoms presenting as ischemia or myocardial ischemia: Quality of Evidence=III; Strength of Recommendation=A (National Heart, Lung, and Blood Institute [NHLBI], 1993; Braunwald et al., 2002)

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.

Evidence

Obtain 12-lead ECG, if not already done: Quality of Evidence = III; Strength of Recommendation = A (Braunwald et al, 2000; Ryan et al., 1996; Advanced Cardiac Life Support [ACLS], 1999)

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:

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

- Pulse >110 or <55 beats per minute
- Systolic blood pressure >200 or <90 mm Hg
- Diastolic blood pressure >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

Oxygen (O_2): 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. Carbon dioxide (CO_2) retention is not usually a concern with low flow nasal oxygen, even in patients with severe chronic obstructive pulmonary disease (COPD).

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 to 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.

12-Lead ECG: A 12-lead ECG is an essential component of the evaluation of a 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. ECG 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.

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 fibrinolytic therapy is being considered. While the IV is being started, blood samples for cardiac enzymes/markers (troponin, creatine kinase [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.

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.

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.

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.

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

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

Transportation: In some settings within the Department of Defense (DoD) or the Veterans Administration (VA) system, the patient will need to be urgently transported to a setting where an appropriate level of monitoring, evaluation, and treatment is available.

Evidence

Supplemental oxygen for patients with cyanosis or respiratory distress; finger pulse oximetry or arterial blood gas should be used to confirm adequate arterial oxygen saturation (>90%): Quality of Evidence = III; Strength of Recommendation = A (Braunwald et al., 2002; Ryan et al., 1999)

Aspirin: Quality of Evidence = I; Strength of Recommendation = A (Lewis et al., 1983; "Randomized trial of intravenous streptokinase," 1988; Antithrombotic Trialists' Collaboration, 2002)

Intravenous line(s) should be placed to ensure adequate venous access: Quality of Evidence = III; Strength of Recommendation = A (Ryan et al., 1999)

NTG, sublingual tablet or spray, followed by intravenous administration for the immediate relief of ischemia and associated symptoms: Quality of Evidence = III; Strength of Recommendation = A (Braunwald et al., 2002)

Bed rest with continuous ECG monitoring: Quality of Evidence = III; Strength of Recommendation = A (Braunwald et al., 2002; Ryan et al., 1999; ACLS, 1999)

Morphine sulfate intravenously when symptoms are not immediately relieved with NTG or when acute pulmonary congestion and/or severe agitation is present: Quality of Evidence = III; Strength of Recommendation = A (Braunwald et al., 2002; Ryan et al., 1999)

Consider chest radiograph: Quality of Evidence = III; Strength of Recommendation = B ("Clinical policy," 1995)

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 CK-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 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 (see Discussion).

Table 5. Criteria for Diagnosis of ACS

Major Criteria A diagnosis of an ACS can be made if one or more of the following major criteria are present	Minor Criteria In the absence of a major criterion, a diagnosis of ACS requires the presence of at least one item from both columns	
• ST-	I	II

elevation[a] or left bundle branch block (LBBB) in the setting of recent (<24 hours) or ongoing angina • New, or presumably new, ST-segment depression (≥0.05 mV) or T-wave inversion (≥0.2 mV) with rest symptoms • Elevated serum markers of myocardial damage (i.e., troponin I, troponin T, and CK-MB)	• Prolonged (i.e., >20 minutes) chest, arm/shoulder, neck, or epigastric discomfort • New onset chest, arm/shoulder, neck, or epigastric discomfort at rest, minimal exertion or ordinary activity (CCS class III or IV) • 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 ≥1 CCS class to at least CCS III severity)	• Typical or atypical angina[b] • Male age >40 or female age >60[c] • Known CAD • Heart failure, hypotension, or transient mitral regurgitation by examination • Diabetes • Documented extra-cardiac vascular disease • Pathologic Q-waves on ECG • Abnormal ST-segment or T-wave abnormalities not known to be new

[a] ST elevation ≥0.2 mV at the J-point in two or more contiguous precordial leads (V1-V6); or ≥0.1 mV in all other leads. Contiguity in the limb leads (frontal plane) is defined by the lead sequence:I, aVL,(lateral), or II, III, aVF (inferior).
[c] These age and gender characteristics define a probability of CAD >10% in symptomatic patients (See Table 7).
[b] Use the following definitions to determine the likelihood that the presenting symptoms are angina:

Typical (definite) angina	IF all three of the primary symptom characteristics are present
Atypical (probable) angina	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

The three primary symptom characteristics:

- Substernal chest or arm discomfort with a characteristic quality and duration
- Provoked by exertion or emotional stress
- Relieved by rest or nitroglycerin

Symptom characteristics that suggest non-cardiac pain, include the following:

- 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

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 new or presumably new LBBB, 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 NSTE-ACS should be admitted and receive urgent therapy for NSTEMI/UA that is covered in Module B.

Evidence

Patients with characteristic symptoms and ST-elevation or LBBB are candidates for reperfusion therapies: Quality of Evidence = I; Strength of Recommendation = A (Ryan et al., 1999; "Indications for fibrinolytic therapy," 1994)

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, CK-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 to 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 and 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 to 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 NSTE-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 non-invasive 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 non-invasive 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.

High-Risk

- Severe resting LV dysfunction (left ventricle ejection fraction [LVEF] <0.35)
- High-risk Duke treadmill score (score <-11) (estimated annual mortality rate >3%)
- 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 (<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 = 35 to 49%)
- Intermediate-risk treadmill score (greater than –11 and less than 5) (1 to 3% annual mortality rate)
- 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. 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 1)
    - 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 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*

	Non-anginal Chest Pain		Atypical (probable) Angina		Typical (Definite) Angina	
Age (Years)	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

Nonischemic Cardiovascular	Pulmonary	Gastrointestinal	

• Aortic dissection
• Pericarditis
	• Pulmonary embolus
	• Pneumothorax
	• Pneumonia
	• Pleuritis
		• Esophageal
		  • Esophagitis
		  • Spasm
		  • Reflux
		• Biliary
		  • Colic
		  • Cholecystitis
		  • Choledo-cholithiasis
		  • Cholangitis
		• Peptic ulcer
		• Pancreatitis	

Module A: Suspected Acute Myocardial Infarction

A. Patient With Suspected Myocardial Infarction (MI), With ST-Segment Elevation Or New Or Old Left Bundle Branch Block (LBBB)

Patients with acute myocardial infarction (AMI), for which reperfusion therapies may be appropriate, are managed within this module.

Annotation

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 old LBBB or ongoing ST-segment elevation in two or more contiguous leads (i.e., 0.2 mV or more in leads V1-V3, or 0.1 mV or more in other leads)

Evidence

Patients with characteristic symptoms and ST elevation, or new or presumed new LBBB, are candidates for reperfusion therapies: Quality of Evidence = I; Strength of Recommendation = A (Ryan et al., 1996; Newby et al., 1996)

Patients with characteristic symptoms and old LBBB are candidates for reperfusion therapies: Quality of Evidence = II; Strength of Recommendation = B ("Indications for fibrinolytic therapy," 1994)

B. Ensure Emergency Interventions

Objective

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

Annotation

No matter how patients enter the guideline, a logical and timely evaluation for IHD is required, especially for an acute or unstable coronary syndrome, which can be fatal.

1. Cardiac monitor: Patients with acute coronary syndromes (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.
2. Oxygen (O_2): Supplemental oxygen should be administered on initial presentation, especially if CHF or oxygen desaturation is present. For uncomplicated MIs, oxygen may be reassessed after six hours. CO_2 retention is not usually a concern with low flow nasal O_2, even in patients with severe chronic obstructive pulmonary disease (COPD).
3. 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.
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. 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., CK, CK-MB, and troponin), 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.

5. 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.
6. 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.
7. Adequate analgesia
8. Advanced cardiac life support: algorithm should be applied, as indicated.
9. Chest x-ray: A portable chest radiograph should be performed, particularly to evaluate for mediastinal widening (aortic dissection), cardiac silhouette, and evidence of CHF.
10. 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.

Evidence

Supplemental oxygen: pulse oximetry or arterial blood gas should be used to confirm adequate arterial oxygen saturation: Quality of Evidence = III; Strength of Recommendation = A (Braunwald et al., 2000; Ryan et al., 1996)

Intravenous line(s) should be placed to ensure adequate venous access: Quality of Evidence = III; Strength of Recommendation = A (Braunwald et al., 2000; Ryan et al., 1996)

Consider chest radiograph: Quality of Evidence = III; Strength of Recommendation = B (Braunwald et al., 2000; Ryan et al., 1996)

Provide continuous ECG monitoring: Quality of Evidence = III; Strength of Recommendation = A (Braunwald et al., 2000; Ryan et al., 1996)

C. Obtain Focused History And Physical Examination

Objective

Perform expedited and focused history and physical examination to elicit characteristics of MI, evidence for complications, and contraindications to reperfusion therapy.

Annotation

Patients presenting with an acute 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
  - Character of symptoms
  - Time of onset
  - Duration of symptoms
  - Prior cardiac symptoms and evaluation
  - Current medical therapy including sildenafil
- Complications of MI
  - Syncope
  - Shortness of breath
  - Orthopnea
  - Weakness or other symptoms suggestive of a neurologic event
- Contraindications to Reperfusion Therapy
  - Medication allergies
  - Prior use of thrombolytic agents
  - Contraindications to thrombolytic therapy (see Annotation H below)

A focused physical examination should include the following:

- Vitals Signs
  - Heart rate greater than 60 and less than 100
  - Systolic blood pressure greater than 90 mmHg and less than 160 mmHg
- Skin
  - Pallor
  - Cool extremities
- Lungs
  - Character of breath sounds (e.g., vesicular or diminished)
  - Rales
  - Wheezes
- Heart
  - Point of maximal impact (PMI)
  - Jugular vein distention/abdominal jugular reflux (JVD/AJR)
  - S3
  - Murmurs
  - Rubs
- Abdomen
  - Presence or absence of bowel sounds (PMI)
  - Abdominal tenderness
  - Murphy's sign
  - Rebound
  - Guarding
- Peripheral Vascular
  - Character of radial, femoral, dorsalis pedis, and posterior tibial pulses
- Neurological

- Limited evaluation for focal neurological findings (e.g., cranial nerves, motor, and reflexes)

Evidence

Focused evaluation of patient's clinical history (character of symptoms, prior coronary events, contraindications to therapy, complications of MI): Quality of Evidence = III; Strength of Recommendation = A (Ryan et al., 1996)

Focused physical examination and a 12-lead ECG, within 10 minutes of presentation: Quality of Evidence = III; Strength of Recommendation = A (Ryan et al., 1996)

D. Are There Alternative Catastrophic Diagnoses?

Objective

Identify patients with life-threatening conditions that may mimic an AMI and may also require immediate medical attention.

Annotation

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. Potential catastrophic mimics include pericarditis, pericardial tamponade, thoracic aortic dissection, pneumothorax, pulmonary embolus, and pancreatitis.

Table 4. Clinical Findings for Alternative Catastrophic Diagnoses

Diagnoses	Clinical Findings
Pericarditis	• Pain that is more severe in a supine position • Friction rub may be present • ECG with diffuse ST-elevation
Pericardial tamponade	• Jugular venous distension • Pulsus paradoxus • ECG with low voltage/electrical alternans
Thoracic aortic dissection	• Very severe midline pain, maximal at onset • Pain often radiates to the back • Unequal pulses or blood pressure difference in arms
Pneumothorax	• Associated with trauma, COPD, or

Diagnoses	Clinical Findings
	mechanical ventilation • Unilateral diminished breath sounds • Normal or increased resonance to percussion
Pulmonary embolus	• Pleuritic chest pain • Shortness of breath, without evidence of CHF
Pancreatitis	• History of gall bladder disease or alcoholism • Abdominal tenderness • Nausea and vomiting

Evidence

Assess for pericarditis: Quality of Evidence = III; Strength of Recommendation = A (Ryan et al., 1996)

Assess for pericardial tamponade: Quality of Evidence = III; Strength of Recommendation = A (Ryan et al., 1996)

Assess for thoracic aortic dissection: Quality of Evidence = III; Strength of Recommendation = A (Ryan et al., 1996)

Assess for pneumothorax: Quality of Evidence = III; Strength of Recommendation = A (Ryan et al., 1996)

Assess for pulmonary embolus: Quality of Evidence = III; Strength of Recommendation = A (Ryan et al., 1996)

Assess for pancreatitis: Quality of Evidence = III; Strength of Recommendation = A (Khoury et al., 1996; Cohen et al., 1971)

E. Initiate Medical Therapy

Objective

Initiate medical therapy that may improve cardiac symptoms and reduce cardiovascular mortality, while preparations are made for reperfusion therapy.

Annotation

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

1. 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, active peptic ulcer disease, or gastrointestinal intolerance.
    - Patients who have an allergy to aspirin and no contraindication to antiplatelet therapy should be given clopidogrel, ticlopidine, or dipyridamole.
2. Beta-blockers:
    - Metoprolol 5 mg IV for up to 3 doses or atenolol 5 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.
3. 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 4,000 U) IV bolus, followed by an infusion of 12 U/kg/hr infusion (maximum 1,000 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.
4. Nitroglycerin:
    - Patients presenting with symptoms consistent with a MI and ECG changes suggestive of an STEMI may be given nitroglycerin 0.3 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).

5. Oral angiotensin-converting enzyme inhibitors (ACE-inhibitor):
    - Oral ACE-inhibitor should be considered in all patients within 24 hours of an 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.
6. Analgesics:
    - Because of increased sympathetic stimulation associated with pain from an AMI, patients should be offered analgesics, such as morphine sulfate 2 to 4 mg IV as needed (PRN). Per ACC/AHA AMI 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.

Evidence

Aspirin: Quality of Evidence = I; Strength of Recommendation = A ("Randomized trial of intravenous streptokinase," 1988)

Heparin: Quality of Evidence = II; Strength of Recommendation = B (Granger et al., 1996)

Beta-blockers: Quality of Evidence = I; Strength of Recommendation = A ("A randomized trial of propranolol," 1982; "Randomised trial of intravenous atenolol," 1986; Roberts et al., 1991)

ACE-inhibitor: Quality of Evidence = I; Strength of Recommendation = A ("ISIS-4," 1995; "GISSI-3," 1994; Ambrosioni, Borghi, & Magnani, 1995; "Oral captopril versus placebo," 1995; "Indications for ACE inhibitors," 1998)

Intravenous nitroglycerin: Quality of Evidence = II; Strength of Recommendation = B (Jugdutt, 1993; Come & Pitt, 1976)

F. Is It Less Than 12 Hours Since Onset Of Symptoms?

Objective

Identify those patients who are likely to benefit most from reperfusion strategies.

Annotation

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 after the first 6 hours. Thus, clinical judgment should be used in the decision to give reperfusion therapy, such as ongoing ischemia and size and location of the MI.

Evidence

Provide reperfusion therapy within 12 hours of onset of symptoms: Quality of Evidence = I; Strength of Recommendation = A ("Indications for fibrinolytic therapy," 1994)

G. Can Percutaneous Revascularization Be Accomplished Within 90 Minutes of Patient Presentation?

Objective

Identify those patients who are eligible for direct (primary) percutaneous revascularization.

Annotation

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.

Evidence

Perform direct percutaneous revascularization, in eligible patients: Quality of Evidence = I; Strength of Recommendation = B (Grines et al., 1993; Weaver et al., 1997; Schomig et al., 2000)

Direct percutaneous revascularization to be performed by experienced physicians (with more than 75 cases per year) at high volume centers (with more than 200 interventions per year): Quality of Evidence = III; Strength of Recommendation = A (Ryan et al., 1999)

Perform balloon inflation, no more than 90 minutes from presentation: Quality of Evidence = I; Strength of Recommendation = A (Berger et al., 1999)

H. Are There Contraindications To Thrombolysis?

Objective

Identify patients who have contraindications to thrombolytic therapy.

Annotation

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, include the following:

1. Previous hemorrhagic stroke at any time
2. Other strokes or cerebrovascular events, within one year
3. Known intracranial neoplasm
4. Active internal bleeding (except menses)
5. Suspected aortic dissection
6. Acute pericarditis

Relative contraindications to thrombolysis, include the following:

1. Severe, uncontrolled hypertension on presentation (i.e., blood pressure >180/110 mm Hg)
2. Current use of anticoagulants in therapeutic doses
3. Known bleeding problems
4. Recent trauma (i.e., within 2 to 4 weeks) including head trauma or traumatic or prolonged (i.e., >10 minutes) cardiopulmonary resuscitation (CPR)
5. Recent major surgery (i.e., within 3 weeks)
6. Non-compressible vascular punctures
7. Recent internal bleeding (i.e., within 2 to 4 weeks)
8. Prior exposure to streptokinase, if that agent is to be administered (i.e., 5 days to 2 years)
9. Pregnancy
10. Active peptic ulcer
11. History of chronic, severe hypertension
12. Age >75 years
13. 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)

14. 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

Evidence

Absolute contraindications to thrombolysis: Quality of Evidence = III; Strength of Recommendation = E (Ryan et al., 1996)

Relative contraindications to thrombolysis: Quality of Evidence = III; Strength of Recommendation = E (Ryan et al., 1996)

Relative contraindication: age >75 years: Quality of Evidence = II; Strength of Recommendation = D (Thiemann et al., 2000)

Relative contraindication: stroke risk score >4: Quality of Evidence = II; Strength of Recommendation = D (Brass et al., 2000)

Relative contraindication: cardiogenic shock: Quality of Evidence = I; Strength of Recommendation = E (Bates & Topol, 1991; Hochman et al., 1999)

I. Initiate Thrombolytic Therapy
Transfer To Cardiac Care Unit (CCU)

Objective

Initiate thrombolytic therapy for patients not referred to direct percutaneous revascularization.

Annotation

Four current thrombolytic agents, include:

1. 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
2. Reteplase (rPA): 10 U over 2 minutes, followed by a second 10 U IV bolus 30 minutes later
3. Streptokinase: 1.5 million units (MU) IV over 60 minutes
4. Tenecteplase: IV bolus weight adjusted (30 mg to patients who weigh <60 kg, 35 mg to patients who weigh 60 to 69.9 kg, 40 mg to patients who weigh 70 to 79.9 kg, 45 mg to patients who weigh 80 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).

Evidence

Initiate thrombolytic therapy for eligible patients: Quality of Evidence = I; Strength of Recommendation = A ("Randomized trial of intravenous streptokinase," 1988; "An international randomized trial," 1993; "The effects of tissue plasminogen," 1993; "A comparison of reteplase," 1997)

J. Is Patient Response Satisfactory?

Objective

Identify patients who have not achieved the desired objective of an open artery following thrombolytic administration.

Annotation

Clinical signs of reperfusion following thrombolytic administration, include the following:

- 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.

Evidence

Look for clinical markers of reperfusion: Quality of Evidence = II; Strength of Recommendation = B (Ryan et al., 1996)

Refer patient for emergency percutaneous revascularization, if failed thrombolysis: Quality of Evidence = II; Strength of Recommendation = B (Vermeer et al., 1999; Ross et al., 1998)

K. Are Ischemic Symptoms Still Present?

Objective

Identify patients who should be referred to direct percutaneous revascularization, who present late into a STEMI.

Annotation

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.

Evidence

Refer patients for direct percutaneous revascularization, if ischemic symptoms present beyond 12 hours: Quality of Evidence = I; Strength of Recommendation = A (Ryan et al., 1999; Hochman et al., 1999)

L. Continue Medical Therapy
Obtain Lipid Profile And Cardiac Enzymes, If Not Already Done
Admit To CCU

Objective

Initiate therapy that may decrease infarct size, improve overall mortality, and determine future therapies.

Annotation (see Annotation E for the Discussion and Evidence)

After the patient has undergone successful reperfusion, the following 10 actions are recommended:

1. Admit patient to CCU/ICU with continuous ECG monitoring for dysrhythmic events with nurse staffing appropriate to level of care.
2. Draw serial cardiac markers (e.g., cardiac troponins twice daily [b.i.d] and/or CK-MB three times daily [t.i.d.]) until peak is reached; CBC; lipid panel, if within 24 hours of onset of symptoms; electrolytes, including renal function; upright chest x-ray, if not yet obtained.
3. Administer supplemental O_2, especially for overt pulmonary congestion or arterial oxygen desaturation; O_2 may be discontinued in 2 to 6 hours following presentation for an uncomplicated MI; the use of O_2 needs to be reassessed every 24 hours for all patients.
4. For electrolyte management, keep K+ greater than 4.0 mEq/L and Mg++ greater than 2.0 mEq/L.
5. Give aspirin, 160 to 325 mg by mouth daily (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).
6. 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 to 12,500 U b.i.d., until ambulatory).
7. 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.
8. Continue oral beta-blockers or initiate, if not started. Beta-blockers should be started within 12 hours of presentation.
9. Continue oral ACE-inhibitor or initiate, if not started. ACE-inhibitor should be started within 24 hours of presentation.
10. Initiate dietary counseling and smoking cessation.

M. Monitor And Treat Life-Threatening Arrhythmias

Objective

Identify those patients at risk for life-threatening arrhythmias that can complicate an AMI.

Annotation

1. Bradyarrhythmias that may require treatment with atropine include the following:
    - 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)
2. Bradyarrhythmias that may require treatment with temporary transvenous pacing include the following:
    - 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
3. Supraventricular tachycardias that may require treatment include the following:
    - 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.
4. Ventricular tachycardias that require treatment include the following:
    - 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.
5. Ventricular events that do not require treatment, include the following:
    - 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.

Evidence

Bradycardic events that require atropine: Quality of Evidence = III; Strength of Recommendation = A (Ryan et al., 1996)

Bradycardic events that require a temporary transvenous pacemaker: Quality of Evidence = III; Strength of Recommendation = A (Ryan et al., 1996)

Supraventricular tachycardia events that require treatment: Quality of Evidence = III; Strength of Recommendation = A (Ryan et al., 1996)

Ventricular tachycardic events that require treatment: Quality of Evidence = III; Strength of Recommendation = A (Ryan et al., 1996)

Ventricular events that do not require treatment: Quality of Evidence = III; Strength of Recommendation = A (Ryan et al., 1996)

N. Assess Left Ventricular Function (LVF)

Objective

Identify overall LVF and other cardiac abnormalities that may complicate the patient's clinical course.

Annotation

Obtain an echocardiogram, if available, to assess for the following:

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

O. Is Patient At High Risk For Complications Or Death?

Objective

Identify those patients who are at high risk for recurrent infarction, CHF, life-threatening arrhythmia, or death following a MI.

Annotation

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 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)

Evidence

Recurrent angina: Quality of Evidence = I; Strength of Recommendation = A (Madsen et al., 1997)

CHF: Quality of Evidence = II-2; Strength of Recommendation = A ("Risk stratification and survival," 1983; Wilson et al., 1983)

Polymorphic ventricular tachycardia, monomorphic ventricular tachycardia, or ventricular fibrillation more than 48 hours from the infarct: Quality of Evidence = II-2; Strength of Recommendation = A (Bigger et al., 1984)

Prior MI: Quality of Evidence = II-2; Strength of Recommendation = A (Stevenson et al., 1985)

EF <0.40: Quality of Evidence = II-2; Strength of Recommendation = A ("Risk stratification and survival," 1983; Bigger et al., 1984)

Associated severe valvular disease: Quality of Evidence = III; Strength of Recommendation = A (American College of Cardiology (ACC)/American Heart Association (AHA), 1998)

P. Consider Non-Invasive Evaluation For Myocardial Ischemia

Objective

Identify patients at increased cardiovascular risk prior to discharge from the hospital.

Annotation

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 who are planned for catheterization may not need a stress test. The yield of performing the test should be evaluated for patients with major comorbidities 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.

Evidence

Obtain a non-invasive evaluation before discharge after MI for prognostic assessment and activity prescription of medical therapy (submaximal at 4 to 6 days): Quality of Evidence = II; Strength of Recommendation = A (Theroux et al., 1979; Schwartz et al., 1981)

Q. Is There Evidence Of Ischemia?

Objective

Identify and refer patients with ischemia for cardiac evaluation.

Annotation

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 >1 mm during a submaximal (low level) EST
- Reversible perfusion defect on sestamibi or thallium myocardial imaging
- Inducible wall motion abnormality during stress echocardiogram

Evidence

Refer patients with ischemia for further cardiac evaluation: Quality of Evidence = I; Strength of Recommendation = A (Rogers et al., 1990; Madsen et al., 1997)

R. Discharge Patient To Home

Objective

Discharge patient to home on appropriate therapy and with appropriate follow-up.

Annotation

Per the ACC/AHA AMI Guidelines, 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 (Clopidogrel if patient is unable to take aspirin because of hypersensitivity or gastrointestinal intolerance)
- 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 should continue in Module G.

Evidence

Activity following AMI: Quality of Evidence = III; Strength of Recommendation = A (Ryan et al., 1996)

Lipid-lowering therapy: Quality of Evidence = I; Strength of Recommendation = A (Sacks et al., 1991; "Randomized trial of cholesterol lowering," 1994; Rubins et al., 1999)

Oral ACE-inhibitor for post-MI patients with LVEF <0.40: Quality of Evidence = I; Strength of Recommendation = A (Yusuf et al., 2000)

Warfarin in patients with atrial fibrillation, thromboembolic events, or LV thrombus: Quality of Evidence = I; Strength of Recommendation = B (Ryan et al., 1996)

Warfarin in patients with larger, anterior wall MI: Quality of Evidence = II; Strength of Recommendation = B (Ryan et al., 1996)

Module B: Suspected Acute Coronary Syndrome (Unstable Angina or Non-ST Segment Elevation MI)

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

Annotation

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 (NSTE-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 are similar in UA and NSTEMI, 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.

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 in Module C: Management of Stable Angina or Module G: Follow-up and Secondary Prevention.

Risk stratification of patients with NSTE-ACS

The initial management of patients with 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. Short-Term Risk of Death or Nonfatal MI in Patients With UA

	High Risk	Intermediate Risk	Low Risk
Feature	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.
History	• Accelerating	• Prior MI,	

	High Risk	Intermediate Risk	Low Risk
	tempo of ischemic symptoms in the preceding 48 hours	peripheral or cerebro-vascular disease, or coronary artery bypass graft (CABG) • Prior aspirin use	
Character of Pain	• Prolonged ongoing rest pain (>20 minutes)	• Prolonged rest angina (>20 minutes), now resolved, with moderate or high likelihood of coronary artery disease (CAD) • Rest angina (<20 minutes or relieved with rest or sublingual NTG)	• New-onset CCS Class III or IV angina in the past 2 weeks without prolonged rest pain (>20 minutes), but with moderate or high likelihood of CAD
Clinical Findings	• Pulmonary edema, most likely related to ischemia • New or worsening mitral regurgitation (MR) murmur • S3 or new/worsening rales • Hypotension, bradycardia, or tachycardia • Age >75 years	• Age >70 years	
ECG Findings	• Dynamic ST-segment changes >0.05 mV • BBB, new or presumed new • Sustained ventricular tachycardia	• T-wave inversions >0.2 mV • Pathological Q-waves	• Normal or unchanged ECG during an episode of chest discomfort
Cardiac Markers	• Elevated (e.g., TnT or TnI	• Slightly elevated (e.g., TnT	• Normal

	High Risk	Intermediate Risk	Low Risk
	>0.1 ng/mL)	>0.01, but <0.1 ng/mL)	

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.

Evidence

ST-segment depression: Quality of Evidence = II-2; Strength of Recommendation = A (Herlitz & Hjalmarson, 1986; Maeda, 1994; Muller et al., 1988; Nyman et al., 1993; Boden et al., 1989; Hyde et al., 1999; Savonitto et al., 1999)

Elevated CK-MB: Quality of Evidence = II-2; Strength of Recommendation = A (Clyne, Medeiros, & Marton, 1989; Pettersson, Ohlsson, & Tryding, 1992; Zimmerman et al., 1999; Savonitto et al., 2002)

Elevated TnI and TnT: Quality of Evidence = II-2; Strength of Recommendation = A (Antman et al., 1996; Galvani et al., 1997; Ohman et al., 1996; Newby et al., 1998; Rao et al., 2003)

B. Ensure Emergency Intervention

Annotation

Institute specific interventions that are necessary early in the evaluation and treatment of acute myocardial infarction (AMI) and UA.

Annotation

1. Oxygen (O_2): 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_2 retention is not usually a concern with low flow nasal O_2, even in patients with severe chronic obstructive pulmonary disease (COPD).
2. Aspirin:
    - All patients should chew non-coated aspirin, 160 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 to 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 a patient with known or suspected ACS. For patients with ongoing symptoms, an urgent ECG should be obtained and interpreted within 10 minutes of presentation and followed up with 2 to 3 serial ECGs in the first 24 hours. ECG should be repeated for recurrent chest pain. 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 acute coronary syndromes (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) effectively 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): 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.

Evidence

Supplemental oxygen: pulse oximetry or arterial blood gas should be used to confirm adequate arterial oxygen saturation: Quality of Evidence = III; Strength of Recommendation = A (Braunwald et al., 2002)

Intravenous line(s) should be placed to ensure adequate venous access: Quality of Evidence = III; Strength of Recommendation = A (Working Group Consensus)

Consider chest radiograph: Quality of Evidence = III; Strength of Recommendation = B (Working Group Consensus)

Provide continuous ECG monitoring: Quality of Evidence = III; Strength of Recommendation = A (Braunwald et al., 2002)

C. Initiate

- Aspirin 160 to 325 mg, If Not Already Given (See Annotation B, 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

Objective

Provide prompt treatment for ACS patients with a high short-term risk of death or myocardial infarction.

Annotation

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 NSTE-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.

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

Evidence

Aspirin: Quality of Evidence = I; Strength of Recommendation = A ("Collaborative overview," 1994; Lewis et al., 1983; Cairns et al., 1985; Theroux et al., 1988; "Risk of myocardial infarction and death," 1990)

Clopidogrel: Quality of Evidence = I; Strength of Recommendation = A (Cadroy et al., 2000; Helft et al., 2000; Yusuf, 2001)

Unfractionated Heparin: Quality of Evidence = I; Strength of Recommendation = B (Theroux et al., 1993; Eikelboom et al., 2000; Cohen, 1994; Oler et al., 1996)

Beta Blockers: Quality of Evidence = II-1; Strength of Recommendation = A (Gottlieb et al., 1986; Yusuf, Wittes, & Friedman, 1988; "Randomised trial of intravenous atenolol," 1986)

Intravenous Nitrates: Quality of Evidence = II-1; Strength of Recommendation = C (Bussmann et al., 1981; Charvat, Kuruvilla, & al Amad, 1990; Jugdutt & Warnica, 1988; Yusuf, Wittes, & Friedman, 1988 ; Karlberg et al., 1998; Doucet et al., 2000)

LMWH Enoxaparin: Quality of Evidence = I; Strength of Recommendation = A (Cohen et al., 1997; Antman et al., 1999; Klein et al., 1997; "Comparison of two treatment durations," 1999)

Calcium Antagonists Diltiazem or Verapamil: Quality of Evidence = I; Strength of Recommendation = B (Pepine, Faich, & Makuch, 1998; "Verapamil in acute myocardial infarction," 1984; Gibson et al., 1986; Boden et al., 1991)

Fibrinolytics: Quality of Evidence = I; Strength of Recommendation = E (Anderson et al., 1995; "Randomized trial of intravenous streptokinase," 1988; "Indications for fibrinolytic therapy," 1994)

D. Admit To Monitored Bed, At Appropriate Level Of Care

Objective

Match intensity of care to the individual patient, continue risk assessment, determine if infarction has occurred, and begin secondary prevention by treatment of dyslipidemia, as appropriate.

Annotation

Patients with ACS who have an intermediate- or high-risk of death and/or MI (see Table 1) should be admitted to an inpatient unit with cardiac monitoring capabilities. In addition to continuous monitoring of the ECG, this unit should provide for the rapid availability of emergency medical care (e.g., Advanced Cardiac Life Support [ACLS]) and personnel trained in the recognition and management of cardiac arrhythmias.

E. Assess Serial ECGs, Cardiac-Specific Markers and Lipid Profile

Objective

Obtain key diagnostic information.

Annotation

- 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 to 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.

Evidence

Elevation of Troponin I: Quality of Evidence = II-2; Strength of Recommendation = A (Antman et al., 1996; Galvani et al., 1997)

Elevation of Troponin T: Quality of Evidence = II-2; Strength of Recommendation = A (Ohman et al., 1996; Newby et al., 1998)

Elevation in CK-MB: Quality of Evidence = II-2; Strength of Recommendation = A (Clyne, Medeiros, & Marton, 1989; Pettersson, Ohlsson, & Tryding, 1992)

F. Treat Exacerbating Non-Cardiac Causes Of Unstable Angina

Objective

Identify conditions that may provoke or exacerbate angina symptoms or angina-like symptoms.

Annotation

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 7. Conditions and Medications Provoking or Exacerbating Ischemia

Increased Oxygen Demand	Decreased Oxygen Supply

Increased Oxygen Demand	Decreased Oxygen Supply

Non-cardiac
 	
• Hyperthermia
• Hyperthyroidism
• Sympathomimetic toxicity (e.g., cocaine use)
• Hypertension
• Anxiety
• Arteriovenous fistulae
 	
Cardiac
 	
• Hypertrophic cardiomyopathy
• Aortic stenosis
• Dilated cardiomyopathy
• Tachycardia
  • Ventricular
  • Supraventricular
 	
Medications
 	
• Vasodilators
• Excessive thyroid replacement
	Non-cardiac
	
	• Anemia
	• Hypoxemia
	  • Pneumonia
	  • Asthma
	  • Chronic obstructive pulmonary disease
	  • Pulmonary hypertension
	  • Interstitial pulmonary fibrosis
	  • Obstructive sleep apnea
	• Sickle cell disease
	• Sympathomimetic toxicity (e.g., cocaine use)
	• Hyperviscosity
	  • Polycythemia
	  • Leukemia
	  • Thrombocytosis
	  • Hypergammaglobulinemia
	
	Cardiac
	
	• Aortic stenosis
	• Hypertrophic cardiomyopathy
	
	Medications
	
	• Vasoconstrictors

G. Provide Appropriate Antiplatelet And Anticoagulant Therapy?

Objective

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

Annotation

Patients with NSTE-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 8) 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 8. Antiplatelet and Anticoagulant Therapy

	Low Risk Possible ACS	Moderate Risk Likely/Definite ACS	High Risk Continuing Ischemia or Other High-Risk Featu		
			No Planned Intervention	Planned Interventio	
				PCI	
1	Aspirin	Aspirin	Aspirin	Aspirin	Aspirin
2	Clopidogrel	Clopidogrel	Clopidogrel		Smokin hyperte hyperli diabete history
3	-	LMWH Or UFH	LMWH Or UFH	LMWH Or UFH	UFH
4	-	-	Platelet GP IIb/IIIa antagonist: • Eptifibatide • Tirofiban	Platelet GP IIb/IIIa antagonist: • Abciximab • Eptifibatide	Platelet antago • •

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 hours.

Table 9: Antiplatelet and Anticoagulant Agents

Aspirin	160 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.
Clopidogrel	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
Abciximab	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.
Enoxaparin	Enoxaparin is given as 1 mg/kg subcutaneously (sq) b.i.d. 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.
UFH	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 hours. UFH is also preferred in patients with renal failure.
Eptifibatide	Eptifibatide is bolused at 180 micrograms/kg (maximum 22.6 mg) and then infused at 2 micrograms/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 > 2.0, but <4.0 mg/dL, the bolus should be reduced to 135 micrograms/kg and the infusion to 0.5 micrograms/kg/min. If the serum creatinine is >4.0, this agent should not be used.
Tirofiban	Tirofiban is given at 0.4 micrograms/kg/min for 30 minutes, then 0.1 micrograms/kg/min for 48 to 96 hours, or 12 to 24 hours post-PCI

H. Are there indications for Glycoprotein IIb/IIIa Receptor Antagonists?

Objective

Identify patients at increased risk of death or MI who would benefit most from more aggressive therapy.

Annotation

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).

Evidence

Eptifibatide: Quality of Evidence = I; Strength of Recommendation = A ("Inhibition of the platelet glycoprotein IIb/IIIa with eptfibatide," 1998; "Randomised placebo-controlled trial of effect of eptifibatide," 1997; O'Shea et al., 2001)

Tirofiban: Quality of Evidence = I; Strength of Recommendation = B ("A comparison of aspirin plus tirofiban," 1998; "Inhibition of the platelet glycoprotein IIb/IIIa receptor with tirofiban in unstable angina," 1998; "Effects of platelet glycoprotein IIb/IIIa blockade," 1997)

Abciximab in patient receiving PCI: Quality of Evidence = I; Strength of Recommendation = A ("Randomised placebo-controlled trial," 1997; "Use of a monoclonal antibody," 1994; "Randomised placebo-controlled and ballon-angioplasty-controlled," 1998; Roffi et al., 2002)

Abciximab in patient not planned for PCI: Quality of Evidence = I; Strength of Recommendation = D (Simoons, 2001)

I. Is There Indication For Urgent Angiography?

Objective

Identify patients who may benefit from early invasive therapy.

Annotation

An early invasive strategy is recommended in patients with UA/NSTEMI without serious comorbidity and who have 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 and no contraindications to revascularization
- 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 left ventricular (LV) systolic function (e.g., ejection fraction [EF] <0.40 on an 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.

Evidence

Early invasive therapy in patients with UA/NSTEMI: Quality of Evidence = II-1; Strength of Recommendation = A (Braunwald et al., 2000, 2002; "Effects of tissue plasminogen," 1994; "Invasive compared with non-invasive treatment," 1999)

J. Assess Left Ventricular Function, If Indicated

Objective

Select the most appropriate method for the assessment of LV systolic function.

Annotation

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 12.

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. 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

Table 12. Relative Advantages and Disadvantages of Echocardiography and Radionuclide Ventriculography for Assessing Left Ventricular Ejection Fraction (LVEF)

Test	Advantages	Disadvantages
Echocardiogram	• Permits concomitant assessment of valvular disease, ventricular hypertrophy, and left atrial size • Can detect pericardial effusion and LV thrombus • Usually less expensive and more widely available than radionuclide studies	• Provides only semi-quantitative estimate of EF • Technically inadequate study, in as many as 18% of patients, and particularly difficult in patients with emphysema
Radionuclide ventriculography	• More precise, reliable, and quantitative measurement of	• Limited assessment of valvular function and ventricular hypertrophy

Test	Advantages	Disadvantages
	ejection fraction, compared to echocardiography • Better assessment of right ventricular function	• Requires venipuncture and radiation exposure • Should generally not be used with patients with irregular heart rhythm

K. Ensure Pharmacotherapy For Congestive Heart Failure (CHF) or LV Dysfunction

Objective

Ensure that all patients with LV dysfunction are on optimal pharmacological therapies with proven morbidity and mortality benefits.

Annotation

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.

Multiple trials have convincingly demonstrated the benefit of ACE-inhibitor therapy in patients with CHF, due to LV systolic dysfunction (both ischemic and non-ischemic dysfunction). Clinical benefits include less dyspnea, improved exercise tolerance, reduced need for emergency care for heart failure, and improved survival. In both the SOLVD trial and the Veterans Heart Failure Trial (V-HeFT II), patients with reduced LVEF and symptoms of heart failure had improved survival with enalapril. In another trial in asymptomatic patients after MI with documented LV dysfunction, captopril reduced mortality and ischemic events compared with a placebo. A meta-analysis of 32 randomized controlled trials (RCTs) of ACE-inhibitors for

symptomatic heart failure found an overall decrease in mortality of 28% (absolute risk reduction, 6.1%, NNT=16). The greatest benefit was found for NYHA class IV failure, LVEF <25%, and CHF due to IHD.

Moderate to high doses of ACE-inhibitors were used in all the trials. In the ATLAS study, patients with moderate to severe heart failure were randomized to either a low dose (2.5 to 5 mg/day) or high dose (32.5 to 35 mg/day) of lisinopril. Those patients randomized to the higher dose regimen had a 12% lower risk of death or hospitalization at 3 to 5 years of follow-up. In a more recent study, patients with moderate CHF were randomized between moderate- (20 mg/day) and high-dose (60 mg/day) enalapril. Following 12 months of therapy, there were no differences in survival or other clinical variables. In patients intolerant of ACE-inhibitors, an angiotensin II receptor blocker (ARB) should be prescribed.

Results from a recent large-scale, randomized, placebo controlled clinical trial suggest that all patients with IHD, irrespective of EF, may benefit from routine treatment with an ACE-inhibitor (ramipril). If these results are confirmed by other ongoing trials, involving other ACE inhibitors, and in patients under the age of 55, treatment with an ACE-inhibitor will likely become the standard of care for all patients with IHD, irrespective of LV function. However, pending the outcome of these trials, no firm recommendations can be made at this time for the routine use of ACE inhibitors in all patients with IHD.

Evidence

ACE-inhibitors improve morbidity and mortality in patients with CHF or low EF: Quality of Evidence = I; Strength of Recommendation = A (Garg & Yusuf, 1995)

Asymptomatic patients, but with low EF, experience survival benefit from ACE-inhibitors: Quality of Evidence = I; Strength of Recommendation = B (Rutherford et al., 1994; "Effect of enalapril on mortality," 1991)

Doses of ACE Inhibitors should be optimized to obtain greatest benefit: Quality of Evidence = I; Strength of Recommendation = A (Packer et al., 1999)

Beta-blockers should be considered for all patients with NYHA class II or III CHF, and EF<0.40, after stabilization on ACE-inhibitors: Quality of Evidence = I; Strength of Recommendation = A (Lechat et al., 1998)

L. Consider Cardiac Stress Test

Annotation

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 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 pretest probability of 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, duration, 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

Objective

Refer patients who may benefit from coronary angiography or revascularization.

Annotation

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.

N. Discharge

Annotation

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

Module C: Management of Stable Angina

A. Patient With Known/High Likelihood of Ischemic Heart Disease (IHD) And Angina Symptoms

This module deals with the management of patients with known 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. 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 nitroglycerine. 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".

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).

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

Objective

Assess whether symptoms are due to non-cardiac conditions.

Annotation

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 nitroglycerine)
- History of prior myocardial infarction (MI)
- 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 (e.g., fatigue, weakness, bleeding disorders, menstrual flow, hematuria, hematochezia, and nutrition)
- Thyroid disease (e.g., diaphoresis, nervousness, insomnia, weight loss, and neck pain)
- Pulmonary disease (e.g., smoking, wheezing, coughing, pleuritic chest pain, exposure to tuberculosis, and hemoptysis)
- Gastrointestinal disorders (e.g., 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 (LFTs)
- Thyroid Function Tests (TFTs)
- 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 contains a partial list of conditions that can cause symptoms that mimic angina.

Table 1. Alternative Diagnoses to Angina for Patients with Chest Pain or Discomfort

Non-ischemic Cardiovascular	Pulmonary	Gastrointestinal	Chest Wall	Ps
Aortic dissection Pericarditis	Pulmonary embolus Pneumothorax Pneumonia Pleuritis	Esophageal • Esophagitis • Spasm • Reflux • Biliary • Colic • Cholecystitis • Choledo-cholithiasis	Costochondritis Fibrositis Rib fracture Sternoclavicular arthritis Herpes zoster (before the rash)	Anxiety d • • • Affective (e.g., de Somatofo Thought (e.g., fix

Non-ischemic Cardiovascular	Pulmonary	Gastrointestinal	Chest Wall	Ps
		• Cholangitis Peptic ulcer Pancreatitis		

C. Are There Any Medications Or Conditions That Provoke Or Exacerbate The Angina And The Underlying Ischemia?

Objective

Identify patients with conditions, other than significant coronary disease, that may provoke or exacerbate angina symptoms or angina-like symptoms.

Annotation

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

Increased Oxygen Demand	Decreased Oxygen Supply

Non-cardiac
 	
• Hyperthermia
• Hyperthyroidism
• Sympathomimetic toxicity (e.g., cocaine use)
• Hypertension
• Anxiety
• Arteriovenous fistulae
 	
Cardiac
 	
• Hypertrophic cardiomyopathy
• Aortic stenosis
• Dilated cardiomyopathy
• Tachycardia
  • Ventricular
  • Supraventricular
	Non-cardiac
	
	• Anemia
	• Hypoxemia
	  • Pneumonia
	  • Asthma
	  • Chronic obstructive pulmonary disease
	  • Pulmonary hypertension
	  • Interstitial pulmonary fibrosis
	  • Obstructive sleep apnea
	• Sickle cell disease
	• Sympathomimetic toxicity (e.g., cocaine use)
	• Hyperviscosity
	  • Polycythemia
	  • Leukemia
	  • Thrombocytosis
	  • Hypergammaglobulinemia

Increased Oxygen Demand	Decreased Oxygen Supply
Medications • Vasodilators • Excessive thyroid replacement	Cardiac • Aortic stenosis • Hypertrophic cardiomyopathy Medications • Vasoconstrictors

D. Ensure Patient Is Taking Antiplatelet Therapy:
Aspirin (ASA) 81-325 mg daily (qd)

Objective

Ensure that all patients receive antiplatelet therapy.

Annotation

Aspirin (ASA) 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 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).

Evidence

ASA 81 mg to 325 mg qd: Quality of Evidence = I; Strength of Recommendation = A ("Collaborative overview," 1994)

Clopidogrel if aspirin is contraindicated (75 mg qd): Quality of Evidence = I; Strength or Recommendation = A (Clopidogrel versus Aspirin in Patients at Risk of Ischemic Events [CAPRIE Steering Committee], 1996)

Combination of ASA and warfarin: Quality of Evidence = I; Strength of Recommendation = A ("Thrombosis prevention trial," 1998, Williams & Stewart, 1999)

E. Ensure Patient Is On Anti-anginal Therapy

Objective

Initiate treatment of suspected angina to complete, or nearly complete, elimination of anginal chest pain and return to normal activities, maintain the patient at a symptom level of CCS class I, with minimum adverse effects, BP <130/85 mmHg and pulse <70 bpm.

The main goal of antianginal therapy, however, is to reduce symptoms of cardiac ischemia and thus, improve physical function and quality of life.

Annotation

- Beta-blockers (if no contraindication)

  And / or long acting nitrate

  And / or calcium channel-blockers

- ACE inhibitor (especially for diabetes and LV dysfunction)

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 effect on long-term survival; therefore, emphasis should be place 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 well 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 inhibitors (ACEI) should be used for all patients with CAD who also have diabetes and or left ventricular systolic dysfunction. ACEI should also be considered in patient with CAD and other vascular disease in the absence of left ventricular dysfunction. ACEI has been shown to improve outcome in these patient, although ACE-inhibitors should not be considered antianginal drugs.

Evidence

Beta Blockers

First choice for control of angina: Quality of Evidence = II; Strength of Recommendation = A (Agency for Health Care Policy and Research & National Heart, Lung, and Blood Institute (NHLBI), 1994)

Atenolol decreases the number of ischemic episodes in patients with minimal symptoms (i.e., Class I or II angina): Quality of Evidence = II; Strength of Recommendation = A (Pepine et al., 1994)

Beta-blockers improve symptoms in patients with IHD: Quality of Evidence = I; Strength of Recommendation = A (Heidenreich et al., 1999)

Calcium Channel Blockers

May be added to beta-blockers to enhance control of anginal symptoms or in patients who do not tolerate beta-blockers: Quality of Evidence = I; Strength of Recommendation = A (Nadazdin & Davies, 1994; DiBianco et al., 1992; de Vries et al., 1994)

Short-acting nitrates

Prescribe on an as-needed basis to control exertional or unexpected angina: Quality of Evidence = III; Strength of Recommendation = A (Silber, 1990)

Long-acting nitrates

Prescribe on a daily basis with a 6 to 8 hour nitrate-free interval (to avoid the development of tachyphylaxis) to increase the antianginal effect of beta-blockers or calcium channel-blockers: Quality of Evidence = I; Strength of Recommendation = A (Bassan, Weiler-Ravell, & Shalev, 1983; Akhars & Jackson, 1991; AHCPR & NHLBI, 1994)

Combined use of sildenafil (Viagra) and nitrates may have significant life-threatening interactions (hypotension), especially when used within 24 hours of one another: Quality of Evidence = II; Strength of Recommendation = A. (American College of Cardiology (ACC)/American Heart Association (AHA), 1999).

F. Does patient Experience Change In Symptoms And Had A Recent (<6 Months) Revascularization?

Objective

Identify patients who might benefit from a percutaneous intervention.

Annotation

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.

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 (PCI), or graft failure, following a coronary artery bypass graft (CABG). 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.

G. Are There Indications For The Assessment Of Left Ventricular Function (LVF)?

Objective

Identify patients with significant LV systolic dysfunction who could benefit from specific pharmacologic therapies.

Annotation

Left ventricular ejection fraction (LVEF) less than 0.40 is one of the strongest predictors of not only increased mortality, but also 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 impairments or 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 (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).

H. Assess LV Function

Objective

Select the most appropriate method for the assessment of LV systolic function.

Annotation

LV systolic function may be assessed by contrast angiography at cardiac catheterization, two dimensional echocardiogram, and radionuclide ventriculography. The relative advantages and disadvantages of cardiac ultrasound versus radionuclide ventriculography are presented in Table 5.

Table 5. Relative Advantages and Disadvantages of Echocardiography and Radionuclide Ventriculography for Assessing LVEF

Test	Advantages	Disadvantages
Echocardiogram	• Permits concomitant assessment of valvular disease, ventricular hypertrophy, and left atrial size • Can detect pericardial effusion and LV thrombus • Usually less expensive and more widely available than radionuclide studies	• Provides only semi-quantitative estimate of ejection fraction • Technically inadequate study, in as many as 18% of patients, and particularly difficult in patients with emphysema
Radionuclide ventriculography	• More precise, reliable, and quantitative measurement of ejection fraction,	• Limited assessment of valvular function and ventricular hypertrophy • Requires

Test	Advantages	Disadvantages
	compared to echocardiography • Better assessment of right ventricular function	venipuncture and radiation exposure • Should generally not be used with patients with irregular heart rhythm

An echocardiogram is preferable in evaluation of patients who also have physical findings suggestive of valvular heart disease to assess the severity of mitral regurgitation along with assessment of LV systolic function.

If the patient 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 on an outpatient basis. Of note, Silver et al., 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 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

I. Is LVEF <0.40 (Moderate Or Severe Left Ventricular Dysfunction?

Objective

Identify patients with systolic dysfunction who could benefit from therapy.

Annotation

Randomized trial evidence has consistently shown a survival benefit for patients with severe CHF and/or severe systolic dysfunction (LVEF <0.35 to 0.40) treated with ACE inhibitors, beta-blockers, or spironolactone. No mortality benefit has been found with the initiation of digoxin in patients with CHF from LV systolic dysfunction, though digoxin is frequently used in clinical practice. Both ACE inhibitors and beta-blockers have been proven to be beneficial in patients with both mild and more severe CHF. Spironolactone, on the other hand, at this time, has only been studied in patients already on an ACE inhibitor and in patients with severe heart failure. Because of the extensive data supporting the use of both ACE inhibitors and beta-blockers, these agents should be initiated prior to initiation of spironolactone.

J. Ensure Pharmacotherapy For CHF/LV Dysfunction

Objective

Ensure that all patients with LV dysfunction are on optimal doses of pharmacological therapies with proven morbidity and mortality benefits.

(See the National Guideline Clearinghouse (NGC summary of the VHA guideline The Pharmacologic Management of Chronic Heart Failure).

Annotation

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 CHF or evidence for 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.

Multiple trials have convincingly demonstrated the benefit of ACE-inhibitor therapy in patients with CHF, due to LV systolic dysfunction (both ischemic and non-ischemic dysfunction). Clinical benefits include less dyspnea, improved exercise tolerance, reduced need for emergency care for heart failure, and improved survival. In both the SOLVD trial and the Veterans Heart Failure Trial (V-HeFTII), patients with reduced LVEF and symptoms of heart failure had improved survival with enalapril. In another trial in asymptomatic patients after MI with documented LV dysfunction, captopril reduced mortality and ischemic events compared with a placebo. A meta-analysis of 32 random control trials (RCTs) of ACE-inhibitors for symptomatic heart failure found an overall decrease in mortality of 28% (absolute risk reduction, 6.1%, NNT=16). The greatest benefit was found for NYHA class IV failure, LVEF <25%, and CHF due to IHD.

Moderate to high doses of ACE-inhibitors were used in all the trials. In the ATLAS study, patients with moderate to severe heart failure were randomized to either a low dose (2.5 mg to 5 mg/day) or high dose (32.5 mg to 35 mg/day) of lisinopril. Those patients randomized to the higher-dose regimen had a 12% lower risk of death or hospitalization at 3 to 5 years of follow-up. In a more recent study, patients with moderate CHF were randomized between moderate- (20 mg/day) and high-dose (60 mg/day) enalapril. Following 12 months of therapy, there were differences in survival or other clinical variables. In patients intolerant of ACE-inhibitors, an angiotensin II receptor blocker (ARB) should be prescribed.

Results from a recent large-scale, randomized, placebo-controlled clinical trial suggest that all patients with IHD, irrespective of EF, may benefit from routine treatment with an ACE-inhibitor (i.e., ramipril). If these results are

confirmed by other ongoing trials involving other ACE inhibitors, and in patients under the age of 55, treatment with an ACE-inhibitor will likely become the standard of care for all patients with IHD, irrespective of LV function. Pending the outcome of these trials, no firm recommendations can be made at this time for the routine use of ACE-inhibitors in all patients with IHD. Therefore, the decision to use ACE-inhibitor therapy in IHD patients with normal (>0.40) EF should be individualized and left to the discretion of the provider.

Spironolactone

A randomized trial using a relatively low dose of spironolactone demonstrated significant improvement in outcomes in patients with severe CHF (i.e., Functional Class 3 to 4) who were already on ACE inhibitor therapy. Remarkably, in this trial, the incidence of hyperkalemia was not increased with this dose of spironolactone. The effect of spironolactone in patients with less severe CHF is unknown.

Digoxin

The VA DIG Study showed no benefit in terms of mortality but some reduction in frequency of hospitalization with the use of digoxin in patients with CHF. Discontinuing digoxin in patients with compensation heart failure results in worsening of symptoms.

Diuretics

While there is no evidence supporting mortality benefit of diuretics in patients with heart failure, diuretics are useful in the management of symptomatic volume overload.

Evidence

ACE-inhibitors improve morbidity and mortality in patients with CHF or low EF: Quality of Evidence = I; Strength of Recommendation = A (Garg & Yusuf, 1995)

Asymptomatic patients, but with low EF, experience survival benefit from ACE-inhibitors: Quality of Evidence = I; Strength of Recommendation = B (Rutherford et al., 1994; "Effect of enalapril on mortality," 1992)

Doses of ACE-inhibitors should be optimized to obtain greatest benefit: Quality of Evidence = I; Strength of Recommendation = A (Packer et al., 1999)

Beta-blockers should be considered for all patients with NYHA class II or III CHF, and EF<0.40, after stabilization on ACE-inhibitors: Quality of Evidence = I; Strength of Recommendation = A (Lechat et al., 1998)

Addition of spironolactone to ACE-inhibitors and diuretics in patients with severe heart failure improves morbidity and mortality: Quality of Evidence = I; Strength of Recommendation = A (Pitt et al., 1999)

Digoxin use in heart failure (EF<0.45) does not affect mortality, but decreases hospitalization due to heart failure: Quality of Evidence = II; Strength of Recommendation = A ("The effect of digoxin on mortality," 1997)

Diuretics improve symptoms of volume overload: Quality of Evidence = III; Strength of Recommendation = A ("Consensus recommendations for the management of chronic heart failure," 1999)

K. Referral to Cardiology?

Objective

Define patients who may benefit from a cardiology consultation for possible coronary angiography or revascularization.

Annotation

The safe use of beta-blockers in patients with moderate or severe CHF requires careful monitoring of symptoms and dose titration; this is best done by a clinician experienced in the therapy of such patients (i.e., a cardiologist or an internist specializing in the treatment of heart failure).

Patients at high risk for death or MI may benefit from a cardiology consultation to optimize medical therapy and consider the risks and benefits of a revascularization procedure. Such patients include those with the following symptoms:

- Moderate/severe LV dysfunction
- Persistence of CHF symptoms and after initial therapy
- Class III or IV angina, despite maximal medical therapy

Some patients with stable or asymptomatic IHD should be considered for referral to a cardiologist for possible coronary angiography, even after medical therapy has been optimized. The two general types of patients who should be considered for cardiology referral include the following:

1. Patients whose prior results from coronary angiography suggest a possible survival benefit from the use of coronary bypass surgery
2. Patients who have not yet had coronary angiography, but have Functional Class III to V angina or heart failure or whose non-invasive test results indicate a high risk for adverse outcomes

L. Are There Indications for Non-Invasive Risk Stratification Cardiac Stress Test?

Objective

Identify patients who should undergo stress testing for risk stratification.

Annotation

Patients with known IHD and angina 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

Evidence

Risk for death or MI can be stratified in stress testing: Quality of Evidence = II-2; Strength of Recommendation = A (Mark et al., 1991)

M. Optimize IHD Therapy

Objective

Optimize previously initiated therapy for angina to improve outcomes for lifestyle, morbidity, and mortality.

Annotation

The main goal of antianginal therapy is to reduce symptoms of cardiac ischemia and thus, improve physical function and quality of life, with minimum adverse effects, BP <130/85 mmHg and pulse <70 bpm.

Optimizing medical therapy should include anti-anginal medications, such as beta-blockers and nitroglycerin.

See Annotation D and E (Ensure antiplatelet and antianginal therapy)

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 low-density lipoprotein (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.

Evidence

Lipid-lowering therapy: Quality of Evidence = I; Strength of Recommendation = A (Sacks et al., 1996; "Prevention of cardiovascular events," 1998; "Randomized trial of cholesterol lowering," 1994)

N. Follow-up And Secondary Prevention

Objective

Identify patients whose symptoms require alternatives to medical therapy.

Annotation

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.

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 that 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.

Module G: Follow-up and Secondary Prevention

A. Patient With Known Ischemic Heart Disease (IHD)

Patients entering this module should already have been evaluated and treated using other modules in this guideline. This module G provides assistance in identifying areas for which there are effective interventions that reduce the risk of future coronary events.

Candidates for secondary prevention of IHD are patients who have a history of clinical coronary disease. Generally accepted criteria for a diagnosis of coronary artery disease (CAD) include the following:

- Prior myocardial infarction (MI) and/or pathologic Q-waves on the resting electrocardiogram (ECG)
- Typical stable angina in males older than 50 years of age or females older than 60 years of age
- 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 CAD by angiography
- Prior coronary revascularization (percutaneous coronary intervention or coronary artery bypass graft [CABG] surgery)

B. Obtain Focused History, Physical Exam, And Review Medication And Reversible Risk Factors

Objective

Assess clinical predictors for progression of IHD and identify areas for which there are effective interventions.

Annotation

A focused history should include assessment of risk factors for which interventions can improve outcome. All patients should be on appropriate medical therapy. Patients with IHD have a predictable prognosis, and efficacious treatment may be needed, depending on the stage and progression of the disease. Life-saving therapies, such as beta-blockers after MI, aspirin (ASA), angiotensin-converting enzyme (ACE) inhibitors, and lipid-lowering therapy, are under-prescribed in patients with known IHD. It is important to review whether such medications are prescribed, dosed appropriately, and actually taken. Medication compliance and adverse drug reactions should be addressed. When feasible, attempt to simplify medication regimens to improve compliance.

Evidence

Aspirin reduces cardiovascular (CV) events in patients with acute MI, previous MI, and unstable angina: Quality of Evidence = I; Strength of Recommendation = A ("Collaborative overview," 1994)

Aspirin reduces risk of MI in patients with chronic stable angina: Quality of Evidence = I; Strength of Recommendation = A (Juul-Moller et al., 1992; "Final report on the aspirin component," 1989; "Collaborative overview," 1994)

Beta-blockers improve symptoms in patients with IHD: Quality of Evidence = I; Strength of Recommendation = A (Heidenreich et al., 1999)

Beta-blockers improve morbidity and mortality in patients with IHD and previous MI: Quality of Evidence = I; Strength of Recommendation = A ("Timolol-induced reduction," 1981; "A randomized trial of propranolol," 1982)

Beta-blockers reduce CV events in patients with silent ischemia: Quality of Evidence = I; Strength of Recommendation = A (Pepine et al., 1994)

ACE inhibitors improve CV outcomes in patients with IHD, and are especially recommended in patients with diabetes or low LV ejection fraction: Quality of Evidence = I; Strength of Recommendation = A (Garg & Yusuf, 1995)

Lipid-lowering therapy improves CV outcomes in patients with IHD and elevated lipids: Quality of Evidence = I; Strength of Recommendation = A ("Randomised trial of cholesterol lowering," 1994; "Prevention of cardiovascular events," 1998)

Lipid-lowering therapy improves CV outcomes in patients with IHD and average cholesterol: Quality of Evidence = I; Strength of Recommendation = A (Sacks et al., 1996; "Prevention of cardiovascular events," 1998)

Gemfibrozil improves outcomes in patients with IHD and low high-density lipoproteins - cholesterol (HDL-C): Quality of Evidence = I; Strength of Recommendation = B (Rubins et al., 1999)

C. Are There Acute Symptoms, Changes In Symptoms Or Inadequately Controlled Symptoms?

Objective

Identify patients with a possible acute coronary syndrome (ACS) (i.e., ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), or unstable angina).

Annotation

Stable patients with IHD may experience sudden or acute changes in their clinical status. (i.e., ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), or unstable angina).
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., CPK-MB, troponin I, or troponin T). Patients with symptoms that are new, acute, changed, or inadequately controlled should be evaluated according to the CORE Module

Symptoms that may represent ischemia

New or worsening symptoms suggestive of myocardial ischemia 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 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 (within 2 weeks) should be evaluated using the Core Module.

Symptom characteristics that suggest non-cardiac pain, (but do not exclude the diagnosis of CAD) include the following:

- 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

Are Stable Angina Symptoms Adequately Controlled?

The level of symptoms that constitute "adequate control" is highly dependent on several factors:

1. The stage of the CAD
2. Whether or not revascularization is feasible, at an acceptable risk
3. The patient's tolerance or intolerance of anti-anginal drugs
4. Patient preference.

Changes in exercise tolerance and symptoms, over time, are particularly useful in assessing adequacy of control of symptoms of myocardial ischemia. The Canadian Cardiovascular Society (CCS) classification (see Core Module) 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.

D. Are There Indications For The Assessment Of Left Ventricular Function (LVF) (e.g., Signs Or Symptoms Of Congestive Heart Failure (CHF)?

Objective

Identify patients with significant LV systolic dysfunction who could benefit from specific pharmacologic therapies.

Annotation

Left ventricular ejection fraction (LVEF) less than 0.40 is one of the strongest predictors of not only increased mortality, but also 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 impairments or 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.

E. Assess LV Function, If Indicated

Objective

Select the most appropriate method for the assessment of LV systolic function.

Annotation

LV systolic function may be assessed by contrast angiography at cardiac catheterization, two-dimensional echocardiogram, and radionuclide ventriculography. The relative advantages and disadvantages of cardiac ultrasound versus radionuclide ventriculography are presented in Table 2.

Table 2. Relative Advantages and Disadvantages of Echocardiography and Radionuclide Ventriculography for Assessing LVEF

Test	Advantages	Disadvantages
Echocardiogram	• Permits concomitant assessment of valvular disease, ventricular hypertrophy, and left atrial size • Can detect pericardial effusion and LV thrombus • Usually less expensive and more widely available than radionuclide studies	• Provides only semi-quantitative estimate of ejection fraction • Technically inadequate study, in as many as 18% of patients, and particularly difficult in patients with emphysema
Radionuclide ventriculography	• More precise, reliable, and quantitative measurement of ejection fraction, compared to echocardiography • Better assessment of right ventricular function	• Limited assessment of valvular function and ventricular hypertrophy • Requires venipuncture and radiation exposure • Should generally not be used with patients with irregular heart rhythm

An echocardiogram is preferable in evaluation of patients who also have physical findings suggestive of valvular heart disease to assess the severity of mitral regurgitation along with assessment of LV systolic function.

If the patient 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 on an outpatient basis. Of note, Silver et al. 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 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

F. Is LVEF <0.40 (Moderate Or Severe Left Ventricular Dysfunction?)

Objective

Identify patients with systolic dysfunction who could benefit from therapy.

Annotation

Randomized trial evidence has consistently shown a survival benefit for patients with severe CHF and/or severe systolic dysfunction (LVEF <0.35 to 0.40) treated with ACE inhibitors, beta-blockers, or spironolactone. No mortality benefit has been found with the initiation of digoxin in patients with CHF from LV systolic dysfunction, though digoxin is frequently used in clinical practice. Both ACE inhibitors and beta-blockers have been proven to be beneficial in patients with both mild and more severe CHF. Spironolactone, on the other hand, at this time, has only been studied in patients already on an ACE inhibitor and in patients with severe heart failure. Because of the extensive data supporting the use of both ACE inhibitors and beta-blockers, these agents should be initiated prior to initiation of spironolactone.

G. Ensure Pharmacotherapy For CHF/LV Dysfunction

Objective

Ensure that all patients with LV dysfunction are on optimal doses of pharmacological therapies with proven morbidity and mortality benefits.

(See the NGC summary of the VHA guideline http://www.deliciousdecisions.org).

Module E: Outpatient Cardiac Rehabilitation

A. Clinically Stable Patient With Known Ischemic Heart Disease (IHD)

The patients entering this module are clinically stable IHD outpatients in routine follow-up. This population includes patients who have undergone an evaluation of their symptoms and have a firm diagnosis and/or those who have undergone revascularization interventions, such as a coronary artery bypass graft (CABG), percutaneous transluminal coronary angioplasty (PTCA), or stent.

Exercise stress testing (EST) is recommended for all patients, prior to beginning an exercise program. A regular conditioning program can be initiated with a careful prescription of activity, based on the results of the exercise test.

B. Enroll Patient In Programs Aimed At Secondary Prevention, As Available

Objective

Optimize patient outcomes, given the available resources.

Annotation

Patients benefit, not only from direct interaction with their physicians, but also from formal cardiovascular risk-factor modification programs. The primary care provider may have initiated risk-factor modification, but additional programs, such as cardiac rehabilitation and health promotion/wellness centers, are frequently available and patient participation should be encouraged as an adjunct to primary care.

Secondary prevention of risk factors for cardiovascular disease is addressed in Module G. Also refer, as needed, to VHA /DoD guidelines for management of the following conditions:

- Dyslipidemia
- Hypertension
- Smoking cessation
- Depression
- Diabetes mellitus
- Weight management

Cardiac rehabilitation programs offer a comprehensive, multifactorial, and often, multidisciplinary approach to lifestyle management. This includes exercise training, smoking cessation, nutrition counseling, medication adherence, stress management, and behavioral intervention. Among the most substantial benefits are the following:

- Improvement in exercise tolerance, cardiovascular symptoms, and blood lipid levels
- Improvement in psychosocial well-being and reduction of stress
- Reduction in mortality

C. Does Patient Have Contraindications To An Exercise Test?

Objective

Identify patients with contraindications to exercise testing.

Annotation

The following absolute contraindications to exercise testing are adapted from the ACC/AHA Guidelines for Exercise Testing:

- Acute myocardial infarction (AMI), within 2 days
- Uncontrolled cardiac arrhythmias causing symptoms or hemodynamic compromise
- Symptomatic severe aortic stenosis
- Uncontrolled symptomatic heart failure

- Acute pulmonary embolus or pulmonary infarction
- Acute myocarditis or pericarditis
- Acute aortic dissection

In the past unstable angina was a contraindication to exercise testing. However, exercise treadmill and pharmacologic testing are safe in low-risk outpatients with unstable angina and in intermediate-risk patients in whom an MI has been ruled out and who are free of angina and congestive heart failure.

The following relative contraindications to exercise testing are adapted from the ACC/AHA Guidelines for Exercise Testing:

- Left main coronary stenosis
- Moderate stenotic valvular heart disease
- Electrolyte abnormalities
- Systolic hypertension >200 mm Hg
- Diastolic blood pressure >110 mm Hg
- Tachyarrhythmias or bradyarrhythmias
- Hypertrophic cardiomyopathy and other forms of outflow tract obstruction
- Mental or physical impairment leading to the inability to adequately exercise
- High-degree atrioventricular block

Relative contraindications to exercise testing can be overridden if the benefits of exercise outweigh the risks. These contraindications should be correlated with the results of a clinical evaluation, in consultation with a cardiologist, as needed.

D. Counsel Patient Regarding Activity Level

Objective

Educate and reassure patient about safe activity levels.

Annotation

Per the ACC/AHA AMI Guidelines, patients can begin regular walk 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.

Most patients with IHD, including those for whom an exercise program is contraindicated, benefit from some level of physical activity. The majority of patients who remain asymptomatic after an uncomplicated AMI can safely return to prior activities within 2 weeks, although scant data are available to guide this recommendation.

Post-CABG patients usually return to work within 6 to 8 weeks after surgery. It is important to individualize this decision, based upon specific job task

requirements, as well as upon environmental and psychological stressors encountered in the workplace. Increased participation in domestic, occupational, and recreational activities is the goal. For more impaired patients, facilitation of functional independence is the optimal outcome.

Activity prescription

The physician should provide explicit advice about when to return to previous levels of physical activity, sexual activity, and employment. Daily walking should be encouraged immediately. Patients should be instructed to notify their primary care provider if cardiac symptoms occur, such as chest discomfort or angina, palpitations, dyspnea, or excessive fatigue.

Prior to performing symptom-limited stress test

Patients should be encouraged to walk and return to activities of daily living that maintain the patients within their physical limitations and below their symptomatic threshold. The primary care provider may obtain rough estimations of exercise tolerance by using the metabolic equivalents (MET) activity table (see Table 1 below). (METs indicate metabolic equivalents and refer to a percentage of maximum oxygen required to perform a specific task or activity). The primary care provider should also question patients about those activities that induce fatigue or cardiac symptoms.

For IHD patients who have undergone an exercise stress test

The safety and scope of activity can be determined by comparing MET-level performance on a symptom-limited exercise test with the MET level required for the desired activity (Table 1 below). The MET table presents energy levels, expressed in METs, required to perform a variety of common activities. The MET table can be helpful in translating a patient's performance on an exercise test into daily activities that may be undertaken with reasonable safety. All activity recommendations must be below the onset of symptoms (e.g., angina and shortness of breath) and/or ischemic ECG changes.

Resumption of sexual activity

In stable patients without complications (Class I), sexual activity with the usual partner can be resumed within 7 to 10 days; typically, when the patient can climb 2 flights of stairs or perform 5 METs of activity.

Return to driving

Most post-MI patients can return to driving within a week of hospital discharge. Post-CABG patients, with midline sternotomy, may usually return to driving within 4 to 6 weeks after surgery.

Table 1: Energy Levels Required to Perform Common Activities

<3 METs	3-5 METs	5-7 METs	7-9 METs	>9 METs

<3 METs	3-5 METs	5-7 METs	7-9 METs	>9 METs
Walking (2 mph) Driving auto Standing (store clerk)	Level walking (3 to 4 mph) Sexual activity	Level walking (4.5 to 5.0 mph) Climbing stairs (slowly)	Level jogging (5 mph) Climbing stairs (moderate speed)	Walking uphill (5 mph) Running (>6 mph) Climbing stairs (quickly)
Stationary bike (with little or no tension) Very light calisthenics Golf (cart)	Level biking (6 to 8 mph) Light calisthenics Dancing (social) Golf (walking) Sailing Tennis (doubles) Volleyball (6 persons)	Swimming, breast stroke Badminton (competitive) Tennis (singles) Snow skiing (downhill) Light Backpacking Basketball Football Stream fishing	Bicycling (12 mph) Canoeing Mountain climbing Paddle ball Swimming (crawl stroke) Rowing machine Heavy calisthenics	Bicycling (>13 mph) Vigorous basketball Rope jumping Ski touring Handball/squash
Washing Shaving Dressing Desk work Washing dishes Light housekeeping	Carrying objects (15 to30 lbs) Stocking shelves (light objects) Auto repair Light welding/	Carrying objects (30 to 60 lbs) Easy digging in garden Level hand lawn mowing Digging	Carrying objects (60 to 90 lbs) Sawing wood Heavy shoveling Digging ditches (pick and shovel)	Carrying loads upstairs (objects >90 lbs) Shoveling heavy snow Lumber jack Heavy laborer

<3 METs	3-5 METs	5-7 METs	7-9 METs	>9 METs
Sitting (clerical) Typing Knitting Hand sewing	carpentry Cleaning windows Raking Power lawn mowing Bed making	vigorously Carpentry (exterior) Shoveling dirt Sawing wood Operating pneumatic tools		

METs indicate metabolic equivalents and refer to a percentage of maximum oxygen required to perform a specific task or activity. MET is a unit measuring functional capacity. As functional capacity increases, the MET level increases.

E. Perform Exercise Stress Test, If Not Done Within The Past 3 to 6 Months

Objective

Determine risk-stratification level and exercise heart-rate parameters.

Annotation

All IHD patients beginning an exercise program should be evaluated for exercise tolerance and functional capacity with an EST. A symptom-limited EST is often performed as soon as the patient's medical condition is stabilized (i.e., as early as 2 to 6 weeks after a coronary event). Consensus is that, if the patient is >1-year status post-acute coronary event, an exercise prescription may be based on stress testing performed within 3 to 6 months.

F. Does Patient Have Contraindications To An Exercise Program?

Objective

Identify patients who have contraindications to an exercise program.

Annotation

For the purpose of establishing a safe and effective exercise program, the patient should undergo a careful medical evaluation and review of the exercise test data, prior to participating in the program. The specific components of the medical evaluation should include a medical history, physical examination, and resting ECG. The exercise test should be repeated

any time symptoms or clinical changes warrant and in follow-up assessment of exercise training outcomes.

Patients with the following conditions should have medical evaluation/intervention before beginning an exercise-training program:

- Angina or other symptoms of cardiovascular insufficiency
- ECG evidence of ischemia, >2 mm ST-segment depression at low level of exercise (i.e., submaximal workloads)
- Plateau or decrease in systolic blood pressure associated with LV dysfunction
- Uncompensated heart failure
- Syncope or lightheadedness during exercise
- Exercise-induced ventricular tachycardia or other exercise-induced dysrhythmias causing symptoms
- Other significant ECG disturbances (e.g., new or uncontrolled atrial fibrillation and supraventricular tachycardia)
- Other conditions that could be aggravated by exercise (e.g., resting blood pressure >180 mm Hg systolic and/or >110 mm Hg diastolic, active or suspected myocarditis or pericarditis, and uncontrolled diabetes [i.e., exercise-induced hypoglycemia or resting blood glucose >400 mg/dl])
- Other clear signs or symptoms of exercise intolerance

Maximizing medical intervention or management for these conditions is necessary. A repeat stress test is recommended at the discretion of the referring physician. In patients with maximal medical management, the peak exercise training heart rate should be set sufficiently below the heart rate that occurred at the onset of the conditions described above (refer to Table 4 in Annotation H).

Exceptions to the list of contraindications to an exercise program should be considered, based on sound clinical judgment.

Consider physical therapy consultation for design of an exercise program for patients with special orthopedic adaptations (e.g., arthritis or lower extremities amputees).

G. Assess Level Of Risk For Exercise-Induced Event

Objective

Determine the appropriate level of exercise and surveillance required in an exercise program.

Annotation

Table 2. Risk Levels for Exercise-Induced Events

High Risk	Intermediate Risk	Low Risk
• Severely	• Mild to	• No significant

High Risk	Intermediate Risk	Low Risk
depressed left ventricular ejection function (LVEF) (<0.3) • Complex ventricular dysrhythmias • 3 or greater consecutive monomorphic ventricular complexes at rate >100, appearing or increasing with exercise* • Decrease in systolic blood pressure >15 mm Hg during exercise or failure to rise consistent with exercise workloads • Functional capacity <3 METs • MI complicated by congestive heart failure, cardiogenic shock, and/or complex ventricular dysrhythmias, recurrent ischemia • Clinically significant depression • Severe coronary artery disease and marked exercise-induced myocardial ischemia (>2mm ST-segment	moderately depressed LVEF (0.31 to 0.49) • Complex ventricular dysrhythmias • Less than 3 consecutive ventricular complexes at a rate >100, appearing or increasing with exercise** • Exercise-induced myocardial ischemia (1 to 2 mm ST-segment depression) or reversible ischemic defects (echocardiographic or nuclear radiography) • Functional capacity 3 to 5 METs, 3 or more weeks after clinical event • Failure to comply with exercise prescription	depression of LVEF (>0.5) • No resting or exercise-induced complicated dysrhythmias • No resting or exercise-induced myocardial ischemia manifested as angina and/or ST-segment displacement • Functional capacity >5 METs on EST, 3 or more weeks after clinical event • Uncomplicated MI, CABG, PTCA, stent, or arthrectomy • Absence of clinical depression

High Risk	Intermediate Risk	Low Risk
depression) • Patient with severe valvular disease • Survivor of sudden cardiac arrest		

* A combination of LVEF and increased ventricular ectopy or non-sustained monomorphic ventricular complexes is a poor prognostic indicator (suggest evaluation by a cardiologist).

H. Prescribe Exercise Program And Level Of Monitoring

Objective

Prescribe exercise program based on risk status.

Annotation

Exercise programs may be supervised or unsupervised.

- Supervised group exercise sessions, such as provided in outpatient cardiac rehabilitation programs, are recommended initially to enhance the exercise educational process, ensure that the patient is tolerating the exercise program, confirm progress, and provide medical supervision, particularly in high- to intermediate-risk patients.
- Unsupervised home exercise programs are acceptable for persons at low risk who are motivated, understand the basic principles of exercise training, and can reliably report untoward effects of exercise.

It is desirable that intermediate- to high-risk patients have medically supervised cardiac rehabilitation and reevaluation to "re-stratify" them to a lower level of risk (see Table 3 below). Most patients in secondary prevention can soon be re-stratified as low risk and can implement their exercise prescription at home or in a community program. In addition, secondary prevention efforts should be aggressive. There is considerable evidence that multiple risk-factor reduction in patients with known coronary artery disease stabilizes atherosclerotic plaque, improves endothelial function, and reduces risk for clinical events.

Table 3. Prescribed Exercise and Monitoring

Risk for Exercise-Induced Event	Monitored by Telemetry[(a)]	Supervised by Professionals	Home Exercise Program
High Risk	Yes	Yes	Not advised initially
Intermediate Risk	Yes	Yes	Not advised

Risk for Exercise-Induced Event	Monitored by Telemetry[a]	Supervised by Professionals	Home Exercise Program
			initially
Low Risk	Optional	Yes[b]	Yes

[a] Telemetry-monitored exercise is recommended if an outpatient cardiac rehabilitation program is available.
[b] Supervised exercise is recommended if it is determined that a patient will not adhere to a home exercise program.

Module F: Non-invasive Evaluation for Diagnosis, Risk Stratification, and Guidance of Medical Therapy

A. Patient Referred For Non-invasive Evaluation

Two of the primary determinants of outcome among patients with known or suspected coronary artery disease are the amount of myocardium at jeopardy because of obstructive coronary artery disease (CAD) and left ventricular (LV) function. This module provides the logic and presents the evidence behind the logic for the use of cardiac stress testing. Cardiac stress testing is commonly recommended for the following three major indications: (1) to assess the risk of a future coronary event which is closely tied to the amount of myocardium at jeopardy (i.e., to assess prognosis), (2) to make or confirm a diagnosis of ischemic heart disease (IHD), and (3) to assess the effects of therapy on exercise capacity and stress-induced ischemia. Stress testing to assess prognosis is recommended for most patients with known or suspected IHD (who are not candidates for prompt coronary arteriography) at their initial evaluation, and subsequently, if there has been a worsening in symptoms or signs of ischemia. Cardiac stress testing for diagnostic reasons is most useful in patients with an intermediate pretest probability of IHD. It is less useful among patients with a very low or very high pre-test probability of IHD, because there is already a high degree of certainty of the diagnosis.

This module does not discuss details of stress testing itself; such information can be found in the American College of Cardiology/American Heart Association (ACC/AHA) guidelines for exercise testing. Modules A, B, C, and G provide the indications for other major types of cardiac non-invasive evaluation and radionuclide ventricular angiography, sometimes referred to as MUGA.

B. Obtain Focused History And Physical Examination To Assess For Contraindications To Stress Testing

Objective

Elicit any findings that would contraindicate stress testing.

Annotation

Evaluate historical and objective patient characteristics that would contraindicate exercise stress testing (see Annotation D).

A patient with a relative contraindication--particularly the inability to adequately exercise--may still benefit by pharmacologic stress testing for diagnosis and prognosis (see Annotation H). Some patients, however, should proceed directly to cardiology for coronary angiography (see Annotation C, Table 1).

C. Are There Symptoms And/Or Clinical Findings Warranting Coronary Angiography?

Objective

Identify those patients who should be referred for coronary angiography as a means of diagnosis and risk stratification, without either exercise or pharmacologic stress testing.

Annotation

Patients should be referred to coronary angiography when prior non-invasive evaluation suggests a high risk for adverse outcomes. High risk results of non-invasive evaluation include:

- Severe resting left ventricular (LV) dysfunction (e.g., left ventricular ejection fraction (LVEF)<0.35)
- High-risk treadmill score (score <-11)
- Severe exercise LV dysfunction (e.g., exercise LVEF<0.35)
- Large, stress-induced perfusion defect (particularly if anterior)
- Stress-induced, multiple perfusion defects of moderate size
- Large, fixed perfusion defect with LV dilation or increased lung uptake (thallium-201)
- Stress-induced moderate perfusion defect with LV dilation or increased lung uptake (thallium-201)
- Echocardiographic wall motion abnormality involving greater than 2 segments and developing at a low dose of dobutamine (<10 mg/kg/minute) or at a low heart rate (<120 beats/minute)
- Stress echocardiographic evidence of extensive ischemia

Patients with any of the characteristics listed in Table 1 in the original guideline document (and in the "Evidence" list below) should be referred for coronary angiography, with patient consent and in the absence of major contraindications. They should not undergo stress testing, since they are at high risk for a cardiovascular event.

Evidence

Persistent or recurrent ischemic pain and Canadian Cardiovascular Society (CCS) Class III, or IV angina, despite medical therapy: Quality of Evidence = I; Strength of Recommendation = A (Scanlon et al., 1999)

CAD (post-myocardial infarction (MI) or angina) and/or LV dysfunction or heart failure (LVEF quantified at <0. 5 by prior LV angiogram, MUGA, or 2-D ECHO; other clinical evidence of LV dysfunction [e.g., S3, elevated jugular venous pressure, cardiomegaly, and history of congestive heart failure (CHF)]; pulmonary venous engorgement or edema on chest X-ray): Quality of Evidence = I; Strength of Recommendation = A (AHCPR & NHLBI, 1994)

Evidence of hemodynamically significant mitral or aortic valve disease: Quality of Evidence = III; Strength of Recommendation = A (AHCPR & NHLBI, 1994)

History of successful resuscitation from sudden cardiac death or sustained (e.g., >30 seconds) monomorphic ventricular tachycardia (VT) or nonsustained (e.g., <30 seconds) polymorphic VT: Quality of Evidence = II; Strength of Recommendation = A (AHCPR & NHLBI, 1994)

Intolerance to anti-anginal medical therapy due to uncontrollable side effects and continued angina or ischemia: Quality of Evidence = III; Strength of Recommendation = B (Scanlon et al., 1999)

CCS Class III or IV angina that improves to Class I or II with medical therapy: Quality of Evidence = III; Strength of Recommendation = B (Scanlon et al., 1999)

Non-diagnostic previous non-invasive evaluation or multiple admissions for atypical chest pain: Quality of Evidence = II; Strength of Recommendation = C (Scanlon et al., 1999)

Evidence of multi-vessel disease: Quality of Evidence = III; Strength of Recommendation = B (VA/DoD IHD Working Group)

Patients with recent revascularization (e.g., coronary bypass surgery or percutaneous coronary intervention and recurrent ischemia): Quality of Evidence = III; Strength of Recommendation = A (Scanlon et al., 1999)

Variant angina (transient ST-segment elevation with pain): Quality of Evidence = III; Strength of Recommendation = A (Scanlon et al., 1999)

There are no absolute contraindications for coronary angiography. Commonly accepted relative contraindications are widely used, although few data exist as to the inherent risks of performing the procedure when these problems are present. Relative contraindications to coronary angiography include the following:

- Acute renal failure
- Chronic renal failure secondary to diabetes
- Active gastrointestinal bleeding
- Unexplained fever, possibly due to infection
- Untreated active infection
- Acute stroke
- Severe anemia

- Severe uncontrolled hypertension
- Severe symptomatic electrolyte imbalance
- Severe lack of cooperation by patient, attributed to psychological or severe systemic illness
- Severe concomitant illness that drastically shortens life expectancy or increases risk of therapeutic interventions
- Refusal of patient to consider definitive therapy such as percutaneous transluminal coronary angioplasty (PTCA), coronary artery bypass graft (CABG), or valve replacement
- Digitalis intoxication
- Documented anaphylactoid reaction to angiographic contrast media
- Severe peripheral vascular disease limiting vascular access
- Decompensated CHF or acute pulmonary edema
- Severe coagulopathy
- Aortic valve endocarditis

D. Does Patient Have A Contraindication To Stress Test?

Objective

Identify patients with contraindications to exercise testing.

Annotation

The following absolute contraindications to exercise testing are adapted from the ACC/AHA Guidelines for Exercise Testing:

- Acute myocardial infarction (AMI), within 2 days
- Uncontrolled cardiac arrhythmias causing symptoms or hemodynamic compromise
- Symptomatic severe aortic stenosis
- Uncontrolled symptomatic heart failure
- Acute pulmonary embolus or pulmonary infarction
- Acute myocarditis or pericarditis
- Acute aortic dissection

In the past, unstable angina was a contraindication to exercise testing. However, exercise treadmill and pharmacologic testing are safe in low-risk outpatients with unstable angina and in intermediate-risk patients in whom an MI has been ruled out and who are free of angina and congestive heart failure.

The following relative contraindications to exercise testing are adapted from the ACC/AHA Guidelines for Exercise Testing:

- Left main coronary stenosis
- Moderate stenotic valvular heart disease
- Electrolyte abnormalities
- Systolic hypertension >200 mm Hg
- Diastolic blood pressure >110 mm Hg
- Tachyarrhythmias or bradyarrhythmias

- Hypertrophic cardiomyopathy and other forms of outflow tract obstruction
- Mental or physical impairment leading to the inability to adequately exercise
- High-degree atrioventricular block

Relative contraindications to exercise testing can be overridden if the benefits of exercise outweigh the risks. These contraindications should be correlated with the results of a clinical evaluation, in consultation with a cardiologist, as needed.

E. Is Patient Able To Exercise Adequately?

Objective

Identify those patients able to undergo exercise stress testing.

Annotation

Patients with significant non-cardiac impairment of ambulation cannot undergo meaningful treadmill exercise testing. Such physical impairment includes lower extremity amputation; hip, knee, or ankle arthritis; significant peripheral vascular disease with limiting claudication; lung disease with significant dyspnea on exertion; and generalized deconditioning. For patients with lower extremity limitations to exercise, substituting arm exercise for walking on a treadmill has not proven to be very useful, because (1) the maximum achievable workload (i.e., maximum oxygen consumption) with arm exercise is much less than with leg exercise, and (2) the arm and chest motion creates motion artifact in the electrocardiogram (ECG). Patients who can exercise and who meet the indications listed in Annotation A, should undergo exercise stress testing.

F. Does Pre-Test ECG Indicate Impaired Sensitivity And/Or Specificity or Patient Had Previous Revascularization?

Objective

Identify patients who should undergo stress testing with an imaging modality.

Annotation

The following abnormalities on the resting ECG significantly impair the sensitivity and/or specificity of exertional ST-segment depression for the diagnosis of CAD:

- Ventricular pre-excitation (Wolff-Parkinson-White Syndrome)
- Electronically paced ventricular rhythm
- Greater than 1 mm of resting ST-segment depression
- Complete left bundle branch block (LBBB)

These patients should undergo an exercise imaging study (e.g., exercise-rest myocardial perfusion imaging or rest-exercise echocardiography).

There is controversy about the diagnostic value of ST-segment depression in patients taking digoxin or who have LV hypertrophy on the resting ECG. These patients should be considered for an exercise imaging study.

Evidence

For Patients Who Are Able To Exercise

Patients who do not have LBBB or an electronically paced ventricular rhythm and have >1 mm ST-segment depression or pre-excitation on the resting ECG or are using digoxin: Quality of Evidence = II-1; Strength of Recommendation = A

Dipyridamole or adenosine myocardial perfusion imaging in patients with LBBB or electronically paced ventricular rhythm: Quality of Evidence = II-1; Strength of Recommendation = A

Exercise myocardial perfusion imaging or exercise echocardiography to assess the functional significance of coronary lesions (if not already known) in planning PTCA: Quality of Evidence = II-1; Strength of Recommendation = A

For Risk Stratification of Patients With Chronic Stable Angina Who Are Unable To Exercise

Dipyridamole or adenosine myocardial perfusion imaging or dobutamine echocardiography in patients who do not have LBBB or electronically paced ventricular rhythm: Quality of Evidence = II; Strength of Recommendation = A

Dipyridamole or adenosine myocardial perfusion imaging in patients with LBBB or electronically paced ventricular rhythm: Quality of Evidence = II; Strength of Recommendation = A

Dipyridamole or adenosine myocardial perfusion imaging or dobutamine echocardiography to assess the functional significance of coronary lesions (if not already known) in planning PTCA: Quality of Evidence = II; Strength of Recommendation = A

G. Perform Exercise Imaging Stress Test

Objective

Perform appropriate exercise imaging stress test.

Annotation

Stress imaging studies are generally more expensive than the standard exercise stress test, and should usually be reserved for the subsets of

patients defined in Table 2, Annotation F. Determining which imaging modalities to combine with exercise is partly dependent on local expertise and available technological support. However, each modality or set of modalities also has its particular advantages. The comparative advantages of stress radionuclide perfusion imaging and stress echocardiography for diagnosis of CAD are listed below.

Advantages of stress perfusion imaging include the following:

- Higher technical success rate
- Higher sensitivity, especially for single vessel coronary disease, involving the left circumflex
- Better accuracy in evaluating possible ischemia, when multiple resting LV wall motion
  abnormalities are present
- More extensive published database, especially in evaluation of prognosis

Advantages of stress echocardiography include the following:

- Higher specificity
- Versatility, with more extensive evaluation of cardiac anatomy and function
- Greater convenience, efficacy, and availability
- Lower cost

H. Perform Exercise Stress Test

Objective

Perform exercise stress test.

Annotation

Several exercise protocols are currently in use. Both treadmill and cycle ergometer devices are used for exercise testing. Although cycle ergometers have important advantages, the quadriceps muscles become fatigued in patients who are not experienced cyclists, causing them to stop before reaching their maximum oxygen uptake. As a result, treadmills are more common in the United States.

I. Perform Pharmacologic Stress Test With Imaging Modality

Objective

Perform appropriate pharmacologic imaging stress test.

Annotation

Currently, the most commonly used agents to induce pharmacologic stress are adenosine, dipyridamole, and dobutamine. These agents enhance

coronary blood flow, making it possible to obtain diagnostic and prognostic information from myocardial perfusion imaging in patients who are unable to perform adequate exercise.

Contraindications for pharmacologic stress testing include the use of adenosine and dipyridamole in patients with reactive airway disease or a reactive component to chronic obstructive pulmonary disease (COPD).

J. Is There Adequate Information For Diagnosis Or Prognosis?

Objective

Identify those patients who undergo stress testing that results in data with diagnostic or prognostic value.

Annotation

Although heart rate criteria (e.g., 85% of the maximum predicted heart rate [MPHR]) are commonly used as an end-point for stopping exercise, maximum heart rates are highly variable across patients. Therefore, the criteria listed in Table 3, Annotation H are much preferred as indications for terminating exercise. Nevertheless, the maximum heart rate has some value in assessing the adequacy of exercise in patients not taking a beta-blocker.

Exercise stress test results should be reported as follows:

- Maximum workload achieved in metabolic equivalents (METs) and/or the total duration of exercise plus the specific exercise protocol used (e.g., standard Bruce)
- Blood pressure while standing quietly, before the test, and at maximum exercise
- Pulse rate while standing quietly, before the test, and at maximum exercise
- Maximum amount of ST-segment depression and the leads in which ST-segment depression >1 mm occurred
- Exercise duration at which ST-segment depression >1 mm first occurred
- Whether the patient developed chest, arm, shoulder, or throat discomfort/pain
- Classification of the pain/discomfort as typical (definite) angina, atypical (probable) angina, or non-cardiac pain, according to the definitions given in the Core Module
- Whether the pain/discomfort was the limiting symptom causing termination of exercise

K. Do Test Results Indicate High Or Intermediate Risk For A Coronary Event?

Objective

Identify those patients who, on the basis of the stress testing, can be classified as having high or intermediate risk for subsequent cardiovascular events.

Annotation

Stress test parameters associated with an increased risk of a cardiovascular event, include the following:

- Low exercise workload in a symptom-limited test
- Impaired systolic blood pressure and heart rate response to exercise, in the absence of modifying drugs such as beta-blockers
- Amount of ST-segment depression
- Development of angina
- Exertional hypotension, usually defined as a drop >10 mm Hg during exercise compared to the baseline.

Despite the universal focus on ST-segment depression, the workload capacity (METs or duration of exercise) and hemodynamic response to exercise (pressure-rate product) are more powerful predictors of outcome. The Duke Treadmill Score synthesizes several of these parameters and is useful for estimating prognosis and for clinical decision making.

Evidence

High Risk (>3% annual mortality rate)

High-risk treadmill score (score <-11): Quality of Evidence = I; Strength or Recommendation = B

Large, stress-induced perfusion defect (particularly if anterior): Quality of Evidence = I; Strength or Recommendation = B

Stress-induced, multiple perfusion defects of moderate size: Quality of Evidence = I; Strength or Recommendation = B

Large, fixed perfusion defect with LV dilation or increased lung uptake (thallium-20)1: Quality of Evidence = I; Strength or Recommendation = B

Stress-induced moderate perfusion defect with LV dilation or increased lung uptake (thallium-201): Quality of Evidence = I; Strength or Recommendation = B

Echocardiographic wall motion abnormality involving greater than 2 segments and developing at a low dose of dobutamine (<10 micrograms/kg/minute) or at a low heart rate (<120 beats/minute): Quality of Evidence = I; Strength or Recommendation = B

Stress echocardiographic evidence of extensive ischemia: Quality of Evidence = I; Strength or Recommendation = B

Intermediate Risk (1% to 3% annual mortality rate)

Intermediate-risk treadmill score (-11 < score < 5): Quality of Evidence = I; Strength or Recommendation = B

Stress-induced moderate perfusion defect without LV dilation or increased lung uptake (thallium-201): Quality of Evidence = I; Strength or Recommendation = B

Limited stress echocardiographic ischemia with a wall motion abnormality only at higher doses of dobutamine involving less than or equal to two segments: Quality of Evidence = I; Strength or Recommendation = B

To improve the ease of use, the Duke Treadmill Score was converted to a nomogram (See Figure 1 of the original guideline document).

Determination of prognosis proceeds in five steps. First, the observed amount of exercise-induced ST-segment deviation (the largest elevation or depression after resting changes have been subtracted) is marked on the line for ST-segment deviation during exercise. Second, the observed degree of angina during exercise is marked on the line for angina. Third, the marks for ST-segment deviation and degree of angina are connected with a straight edge. The point where this line intersects the ischemia-reading line is noted. Fourth, the total number of minutes of exercise in treadmill testing according to the Bruce protocol (or the equivalent in multiples of resting oxygen consumption [METS] from an alternative protocol) is marked on the exercise-duration line. Fifth, the mark for ischemia is connected with that for exercise duration. The point at which this line intersects the line for prognosis indicates the five-year survival rate and average annual mortality for patients with these characteristics.

L. Is The Patient A Candidate For A Revascularization Procedure?

Objective

Identify those high- and intermediate-risk patients who are candidates for a revascularization procedure (PCI or CABG), and who should be referred for coronary arteriography.

Annotation

The ACC/AHA Guidelines for the Management of Patients with Chronic Stable Angina and ACC/AHA Guidelines for Coronary Angiography state that coronary arteriography should be avoided in patients who, by virtue of age or other comorbidity, are poor candidates for revascularization by CABG or angioplasty. In addition, patients with the conditions listed in Table 5 should also be considered unlikely candidates for coronary angiography.

Evidence

Review of prior coronary angiogram by current clinician shows disease not amenable to revascularization by current standards: Quality of Evidence = III; Strength of Recommendation = D (VHA/DoD IHD Working Group Consensus)

Patient refusal of catheterization and/or revascularization and/or patient and physician prefer medical therapy alone, without further evaluation: Quality of Evidence = III; Strength of Recommendation = D (Scanlon et al., 1999; VHA/DoD IHD Working Group Consensus)

Non-cardiac disease with projected life expectancy <6 months or quality of life unlikely to be improved by revascularization: Quality of Evidence = III; Strength of Recommendation = D (Scanlon et al., 1999; AHCPR & NHLBI, 1994)

M. Do Test Results Indicate Myocardial Ischemia, But Low Risk?

Objective

Define patients with low risk for cardiovascular events after stress testing who can be managed medically.

Annotation

If results are not high- or intermediate-risk, as defined in Annotation K, the patient may be treated medically and observed for further symptoms that would warrant additional testing. If the stress test result indicates no CAD, the patient should be referred back to the provider for evaluation of non-ischemic causes of angina or chest pain.

N. Consider Imaging Stress Test Or Referral To Cardiology

Objective

Ensure the proper referral of patients with inadequate stress test results to cardiology for further consideration of invasive testing or medical therapy.

Annotation

If the clinician who performed a stress test is unable to make a diagnosis or risk assessment for the patient based on the data and historical features, further consultation is warranted.

Module D: Evaluation and Management of the Asymptomatic Patient
(There is no algorithm associated with this module.)

Part 1: Test Abnormalities Indicative of Possible Subclinical Coronary Artery Disease (CAD)

A. Resting Electrocardiogram (ECG)

Abnormalities

The following ECG test abnormalities in an asymptomatic patient suggest possible subclinical CAD:

- New pathologic Q waves in 2 or more contiguous leads
- New or previously unidentified left bundle branch block (LBBB)
- Horizontal or down-sloping ST depression >1 mm or ST-segment elevation >1 mm (in the absence of digoxin, or valvular, hypertensive, or myopathic heart disease or female gender)
- Symmetric, deep (>5 mm) T-wave inversions in the right precordial leads
- Sustained wide-complex tachycardia
- Acquired long QTc (corrected QT interval) (male >450 msec, female >460 msec) in patients >50 years

B. Exercise Test

Abnormalities

Asymptomatic ST depression during exercise is relatively common and should raise the suspicion for occult CAD. However, the accuracy of exercise testing in asymptomatic patients has never been defined. Therefore, an abnormal exercise test result in an asymptomatic patient is most appropriately viewed within the context of the pre-test probability of CAD based on age, gender, and the presence of coronary risk factors.

Several studies have examined the prognostic significance of an abnormal exercise test in asymptomatic subjects. For example, in a study of 2,365 healthy men by Bruce et al., exercise-induced ST segment depression was associated with a 4.7% incidence of coronary events over the subsequent follow-up period of 5.6 years. The rate among those with normal ST responses was 1.4%. Most of these studies indicate that the relative risk of future coronary events is increased (2 to 5 times) in the presence of an abnormal exercise test, although the absolute risk is in the range of 1% per year.

Asymptomatic ST elevation in healthy subjects during exercise testing is uncommon. In a study by Bruce et al., only 0.5% of 1,275 asymptomatic subjects had ST-segment elevation during exercise. The incidence of CAD among those subjects is unknown.

The significance of exercise-induced LBBB in asymptomatic patients is unknown. However, among patients with symptoms, exercise-induced LBBB independently predicts a higher risk of death and major cardiac events.

The prognostic implications of exercise-induced ventricular tachycardia are unclear in patients without symptoms. In a study by Froelicher et al., exercise-induced ventricular arrhythmias among asymptomatic subjects had no predictive value for CAD. On the other hand, a recent follow-up of more than 6,000 asymptomatic men, ages 42 to 53 years, found that men who had

frequent exercise induced ventricular depolarization abnormalities (e.g., ventricular couplets, nonsustained ventricular tachycardia, or PVCs representing 10% or more of ventricular depolarization during any 30-second period of exercise) had an increased risk of cardiovascular death (relative risk = 2.67, CI = 1.76 to 4.07) independent of typical ischemic changes. Importantly, those men who had only ventricular depolarization abnormalities at rest or during recovery did not have an increased risk of cardiovascular death.

C. Abnormal Myocardial Perfusion Study

Abnormalities

The probability of significant CAD in a patient with a positive myocardial perfusion scan (i.e., single photon emission computed tomography [SPECT] or positron emission tomography [PET]) depends on the pre-test probability of CAD, based on gender and the presence of coronary risk factors. The diagnostic accuracy of perfusion imaging in totally asymptomatic subjects is not well defined.

D. Abnormal Regional or Global Left Ventricular Wall Motion

Abnormalities

Global and/or regional left ventricular (LV) systolic wall motion can be measured using a number of non-invasive imaging modalities, including echocardiography, radionuclide ventriculography (RNVG), or magnetic resonance imaging (MRI), either at rest or with exercise or pharmacological stress. In general, the finding of abnormal global and/or regional systolic wall motion by non-invasive testing is highly suggestive of underlying structural heart disease and warrants further diagnostic evaluation. Although IHD is a leading cause, systolic wall motion abnormalities may also occur as a consequence of hypertensive, valvular, or nonischemic myopathies. The possibility of a falsely abnormal test should be considered. However, the true diagnostic accuracy of many of these modalities in the asymptomatic subject is unknown.

E. Coronary Calcification

Abnormalities

Pathologic studies have shown coronary calcification to be associated with the presence of atherosclerosis. Electron beam computed tomography (EBCT), which is used to measure coronary artery calcium, is being used with increasing frequency to screen for IHD. The extent of coronary calcification measured by EBCT is positively related to the severity of coronary stenosis among patients with proven CAD. In asymptomatic subjects, the presence of coronary calcification by EBCT correlates positively with the presence of coronary risk factors, but the relationship between a positive EBCT scan and the likelihood of subsequent coronary events is not well defined. Furthermore,

reproducibility within an individual is limited, particularly at low calcium scores typical of most asymptomatic individuals without risk factors.

F. Abnormal Ankle/Brachial Index (ABI) or Toe/Brachial Index (TBI)

Abnormalities

The ankle/brachial (ABI) and toe/brachial (TBI) indices are measures of the status of the large and small arteries of the lower extremity. Abnormalities of these indices are highly correlated with the presence of either symptomatic or asymptomatic peripheral vascular disease (PVD) and are strongly associated with the presence of traditional coronary risk factors.

G. Abnormal Carotid Duplex Ultrasound

Abnormalities

Carotid artery atherosclerosis correlates strongly with the presence of coronary artery risk factors, the presence of CAD, and the incidence of IHD events. However, no specific recommendations can be made at this time for the diagnostic or therapeutic management of patients with abnormal carotid artery duplex scans, who are asymptomatic for IHD.

Part 2: Diagnostic Follow-Up Recommendations

A. If not already done, the primary physician should take a history and conduct a physical examination, chest radiograph, and ECG in all patients with suspected IHD.
   - The history determines the presence/severity of coronary risk factors or the presence of symptoms suggestive of congestive heart failure (CHF).
   - The physical examination determines the presence of physical findings of valvular heart disease or cardiomyopathy. These include significant murmurs, abnormalities of carotid pulse, jugular venous distention, abdominal-jugular reflux, S3 gallop, pulmonary or hepatic congestion, peripheral edema, or laterally displaced apex.
   - The ECG may identify the presence of chamber enlargement, hypertrophy, or ischemia.
   - The chest x-ray evaluates for enlargement of the cardiac silhouette, pulmonary vascular engorgement, and valvular or pericardial calcification.

B. Certain clinical findings suggest not only a high probability of CAD, but also a high risk of poor outcomes. Patients with the following findings have a high probability of significant CAD and should be considered for cardiology consultation for further evaluation:
   - Wellens T waves on ECG
   - Exercise-induced hypotension
   - Sustained ventricular tachycardia (>30 seconds) on treadmill or Holter
   - Exercise treadmill results predicting an average annual mortality of >1.5%

- ST-segment elevation during exercise treadmill testing
- Ischemic myocardial perfusion scan
- Wall motion abnormality on echocardiogram or nuclear study

C. Certain clinical findings suggest that the probability of IHD is sufficiently high to warrant further diagnostic testing that can be done by the primary care provider.
   - Resting ST-segment depression >1 mm (in the absence of digoxin, or valvular, hypertensive, or myopathic heart disease or female gender) is a marker for a higher prevalence of severe CAD and is associated with a poor prognosis. In the presence of baseline ECG abnormalities, the diagnostic accuracy of standard exercise testing is reduced. These patients should be considered for cardiology consultation, myocardial nuclear perfusion scan, or exercise stress echocardiography. Patients with marked resting ST-segment depression should be considered high risk, until proven otherwise.
   - Patients with >1 mm ST dynamic segment depression on Holter monitor, for more than 120 seconds, should be referred for an appropriate ischemic work-up.
   - There is little evidence to support screening asymptomatic individuals for IHD. Although LBBB is frequently associated with CAD, there are no retrospective or prospective trials that support evaluating patients with LBBB who are asymptomatic and who have a normal echocardiogram. Likewise, asymptomatic individuals with Q-waves on ECG, but a normal echocardiogram, do not require further evaluation.

   Evidence

   ST depression >1 mm on resting ECG: Quality of Evidence = II; Strength of Recommendation = B (Cheitlin et al., 1997)

   Abnormal Holter monitor with ST depression: Quality of Evidence = I; Strength of Recommendation = B (Cheitlin et al., 1997)

D. Asymptomatic patients with suspected IHD and with one or more of the indications in Table 1 should be considered for referral for echocardiography, if it has not already been performed.

   Indications for echocardiography (ACC/AHA Guideline for the Clinical Application of Echocardiography):

   - Holosystolic or late systolic murmur
   - Grade 3 or midsystolic murmurs
   - Murmurs associated with an abnormal ECG or chest x-ray
   - Physical signs of LV dysfunction or CHF
   - Enlarged cardiac silhouette and/or signs of pulmonary venous congestion on chest x-ray
   - New Q-waves in 2 or more contiguous leads or new LBBB

E. The finding of coronary calcification by non-invasive testing in an asymptomatic patient suggests the possibility of underlying CAD. Similarly, the finding of peripheral vascular or carotid artery disease

raises the suspicion for CAD since, in cross-sectional studies, there is a strong association between atherosclerosis involving the peripheral, carotid, and coronary vasculature.

No specific recommendations for the management of such patients can be made at this time. These patients should be made aware of their increased likelihood of CAD and strongly considered for risk-factor modification, in accordance with current recommendations for the primary prevention of acute coronary events.

Definitions:

Strength of Recommendation:

A. A strong recommendation, based on evidence or general agreement, that a given procedure or treatment is useful/effective, always acceptable, and usually indicated
B. A recommendation, based on evidence or general agreement, that a given procedure or treatment may be considered useful/effective
C. A recommendation that is not well established, or for which there is conflicting evidence regarding usefulness or efficacy, but which may be made on other grounds
D. A recommendation, based on evidence or general agreement, that a given procedure or treatment may be considered not useful/effective
E. A strong recommendation, based on evidence or general agreement, that a given procedure or treatment is not useful/effective, always acceptable, and usually indicated

Quality of Evidence

I: Evidence is obtained from at least one properly randomized controlled trial (RCT).

II-1: Evidence is obtained from well-designed controlled trials without randomization.

II-2: Evidence is obtained from well-designed cohort or case-control analytical studies, preferably from more than one center or research group

II-3: Evidence is obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.

III: Opinion of respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees.

Abbreviations

AACVPR: American Association of Cardiovascular and Pulmonary Rehabilitation
ABI: Ankle/Brachial Index

ACC: American College of Cardiology
ACE: Angiotensin-Converting Enzyme
ACE-I: Angiotensin-Converting Enzyme-Inhibitor
ACLS: Advanced Cardiac Life Support
ACS: Acute Coronary Syndrome
AF: Atrial Fibrillation
AHA: American Heart Association
AHCPR: Agency for Health Care Policy and Research
AHRQ: Agency of Health Care Research and Quality
AICD: Automatic Implantable Cardioverter Defibrillator
AIVR: Accelerated Idioventricular Rhythm
AMI: Acute Myocardial Infarction
APTT: Activated Partial Thromboplastin Time
ARB: Angiotensin II Receptor Blocker
ASA: Aspirin
AV: Atrioventricular
BBB: Bundle Branch Block
BMI: Body Mass Index
BPM: Beats Per Minute
CABG: Coronary Artery Bypass Graft
CAD: Coronary Artery Disease
CARF: Commission on Accreditation of Rehabilitation Facilities
CBC: Complete Blood Count
CCB: Calcium Channel Blockers
CCS: Canadian Cardiovascular Society
CCSC: Canadian Cardiovascular Society Classification
CHD: Coronary Heart Disease
CHF: Congestive Heart Failure
CK: Creatine phosphokinase
COPD: Chronic Obstructive Pulmonary Disease
CPG: Clinical Practice Guideline
CPR: Cardiopulmonary Resuscitation
CV: Cardiovascular
DM: Diabetes Mellitus
DoD: Department of Defense
DSM-IV: Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition
EBCT: Electron Beam Computed Tomography
ECG: Electrocardiogram
ED: Emergency Department
EF: Ejection Fraction
EP: Electrophysiology
EPC: Evidence Based Practice Center
ESC: European Society of Cardiology
EST: Exercise Stress Test
FTT: Fibrinolytic Therapy Trialists' Collaborative Group
HDL: High Density Lipoproteins
IABP: Intraaortic Balloon Pump
ICU: Intensive Care Unit
IHD: Ischemic Heart Disease
INR: International Normalized Ratio
ISMN: Isosorbide Mononitrate
IV: Intravenous
IVCD: Intraventricular Conduction Delay

JAMA: Journal of the American Medical Association
JVD/AJR: Jugular Vein Distention/Abdominal Jugular Reflux
LAD: Left Anterior Descending
LAFB: Left Anterior Fascicular Block
LAHB: Left Anterior Hemiblock
LBBB: Left Bundle Branch Block
LDH: Low-Dose Subcutaneous Heparin
LDL: Low Density Lipoproteins
LDL-C: Cholesterol Low Density Lipoproteins
LFHB: Left Fascicular Hemiblock
LFT: Liver Function Test
LMWH: Low Molecular Weight Heparin
LPFB: Left Posterior Fascicular Block
LV: Left Ventricular
LVEF: Left Ventricular Ejection Fraction
LVF: Left Ventricular Fraction
LVH: Left Ventricular Hypertrophy
METs: Metabolic Equivalents
MI: Myocardial Infarction
MIR: Myocardial Infarction Registry
MITRA: Maximal Individual Therapy in Acute Myocardial Infarction Registry
MPHR: Maximum Predicted Heart Rate
MR: Mitral Regurgitation
MRI: Magnetic Resonance Imaging
MU: Million Units
MUGA: Multiple-Gated Acquisition Scanning
NEJM: New England Journal of Medicine
NNT: Number Needed to Treat
NO: Nitric Oxide
NRMI-2: Second National Registry of Myocardial Infarction
NSTEMI: Non St-Segment Myocardial Infarction
NSVT: Nonsustained Ventricular Tachycardia
NTG: Nitroglycerin
NYHA: New York Heart Association
O2: Oxygen
PBM: Pharmacy Benefits Management
PCI: Percutaneous Coronary Intervention
PET: Positron Emission Tomography
PMI: Point of Maximal Impact
PRN: As needed
PSVT: Paroxysmal Supraventricular Tachycardia
PTCA: Percutaneous Transluminal Coronary Angioplasty
PVC: Premature Ventricular Contractions
PVD: Peripheral Vascular Disease
QE: Quality of Evidence
R: Recommendation
RCTs: Randomized Controlled Trials
RNVG: Radionuclide Ventriculography
RPA: Reteplase
SBP: Systolic Blood Pressure
SL: Sublingual
SPECT: Single Photo Emission Computed Tomography
SR: Strength of Recommendation

STEMI: ST-Elevation Myocardial Infarction
SVT: Supraventricular Tachycardia
TBI: Toe/Brachial Index
TFT: Thyroid Function Test
THR: Threshold
TPA: Alteplase
UA: Unstable Angina
USA: Unstable Angina
VA: Veterans Administration
VHA: Veterans Health Administration
VT: Ventricular Tachycardia
WPW: Wolff-Parkinson-White Syndrome or Ventricular Preexcitation

CLINICAL ALGORITHM(S)

Algorithms are provided for:

- Core: Initial Evaluation/Triage
- Module A: Suspected Acute Myocardial Infarction
- Module B: Suspected Acute Coronary Syndrome (Unstable Angina or Non-ST Segment Elevation MI)
- Module G: Follow-up and Secondary Prevention
- Module E Outpatient Cardiac Rehabilitation
- Module F Non-invasive Evaluation

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The quality and strength of evidence are provided for selected recommendations (see "Major Recommendations" field). Where evidence was ambiguous or conflicting, or scientific data were lacking, the clinical experience within the multidisciplinary group guided the development of consensus-based recommendations. The guideline contains a bibliography and discussion of the evidence supporting each recommendation.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

The system-wide goal of evidence-based guidelines is to improve the patient's outcome. In general, the overall expected outcome of successful implementation of the ischemic heart disease (IHD) guideline is to reduce death and recurrence of adverse events.

POTENTIAL HARMS

The use of fibrinolytic agents may be potentially harmful in unstable angina (UA) and non ST-segment myocardial infarction (NSTEMI)

CONTRAINDICATIONS

CONTRAINDICATIONS

Contraindications to aspirin include a documented allergy to salicylates, active bleeding, or active peptic ulcer disease.

Contraindications to Reperfusion Therapy include:

- Medication allergies
- Prior use of thrombolytic agents
- Contraindications to thrombolytic therapy

Relative contraindications to beta-blockers, include heart rate <60 beats per minute (bpm), systolic blood pressure <100 mm Hg, moderate or severe congestive heart failure (CHF), signs of peripheral hypoperfusion, PR interval >0.24 seconds on the electrocardiogram (ECG), second or third degree atrioventricular (AV) block, severe chronic obstructive pulmonary disease (COPD), and history of asthma.

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).

Angiotensin-converting enzyme (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.

Beta-blockers should not be used in uncompensated congestive heart failure (CHF) and should be used with great caution in patients with Class IV congestive heart failure.

Absolute contraindications to thrombolysis, include the following:

- 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, include the following:

- 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., >10minutes) 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 ≥4 risk factors:
    - Age ≥75 years
    - Female
    - African American descent
    - Prior stroke
    - Admission systolic blood pressure ≥160 mm Hg
    - Use of alteplase
    - Excessive anticoagulation (i.e., INR ≥4; APTT ≥24)
    - Below median weight (≤65 kg for women; ≤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

The following absolute contraindications to exercise testing are adapted from the ACC/AHA Guidelines for Exercise Testing (1997):

- Acute myocardial infarction (AMI), within 2 days
- Uncontrolled cardiac arrhythmias causing symptoms or hemodynamic compromise
- Symptomatic severe aortic stenosis
- Uncontrolled symptomatic heart failure
- Acute pulmonary embolus or pulmonary infarction
- Acute myocarditis or pericarditis
- Acute aortic dissection

The following relative contraindications to exercise testing are adapted from the ACC/AHA Guidelines for Exercise Testing (1997):

- Left main coronary stenosis
- Moderate stenotic valvular heart disease
- Electrolyte abnormalities
- Systolic hypertension >200 mm Hg
- Diastolic blood pressure >110 mm Hg
- Tachyarrhythmias or bradyarrhythmias
- Hypertrophic cardiomyopathy and other forms of outflow tract obstruction
- Mental or physical impairment leading to the inability to adequately exercise
- High-degree atrioventricular block

Contraindications for pharmacologic stress testing include the use of adenosine and dipyridamole in patients with reactive airway disease or a reactive component to chronic obstructive pulmonary disease (COPD).

Relative contraindications to coronary angiography include the following:

- Acute renal failure
- Chronic renal failure secondary to diabetes
- Active gastrointestinal bleeding
- Unexplained fever, possibly due to infection
- Untreated active infection
- Acute stroke
- Severe anemia
- Severe uncontrolled hypertension
- Severe symptomatic electrolyte imbalance
- Severe lack of cooperation by patient, attributed to psychological or severe systemic illness
- Severe concomitant illness that drastically shortens life expectancy or increases risk of therapeutic interventions
- Refusal of patient to consider definitive therapy such as percutaneous transluminal coronary angioplasty (PTCA), coronary artery bypass graft (CABG), or valve replacement
- Digitalis intoxication
- Documented anaphylactoid reaction to angiographic contrast media
- Severe peripheral vascular disease limiting vascular access
- Decompensated CHF or acute pulmonary edema
- Severe coagulopathy
- Aortic valve endocarditis

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- Clinical practice guidelines, which are increasingly being used in health care, are seen by many as a potential solution to inefficiency and inappropriate variations in care. Guidelines should be evidenced-based as well as based upon explicit criteria to ensure consensus regarding their internal validity. However, it must be remembered that the use of guidelines must always be in the context of a health care provider's clinical judgment in the care of a particular patient. For that reason, the guidelines may be viewed as an educational tool analogous to textbooks and journals, but in a more user-friendly format.
- The guideline is not intended to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advances and patterns evolve. The ultimate judgement regarding a particular clinical procedure or treatment course must be made by the individual clinician, in light of the patient's clinical presentation, patient preferences, and the available diagnostic and treatment options. The guideline can assist primary medical care providers in all aspects of care for ischemic heart disease (IHD), but the use of a clinical practice guideline (CPG) must always be considered as a recommendation, within the context of a provider's clinical judgment, in the care for an individual patient.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm
Pocket Guide/Reference Cards
Quality Measures

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

RELATED NQMC MEASURES

- Ischemic heart disease: percent of patients hospitalized with acute coronary syndrome (ACS) with cardiac symptoms prior to or on arrival to the acute care setting who had an electrocardiogram (ECG, EKG) performed 15 minutes prior to arrival in acute setting or within 10 minutes after arrival (inpatient AMI JCAHO, inpatient AMI all, and inpatient NST-ACS/UA cohorts).
- Ischemic heart disease: percent of patients hospitalized with acute coronary syndrome (ACS) found to be high risk ST-segment elevation myocardial infarction (STEMI) or moderate-high risk non-ST-segment elevation myocardial infarction (NSTEMI) patients with cardiology involvement in care within 24 hours of acute arrival or if acute myocardial infarction (AMI) as inpatient, within 24 hours of initial electrocardiogram (ECG) or first positive troponin whichever is earlier (inpatient AMI all cohort [inclusive
- Ischemic heart disease: percent of patients with first troponin result returned within 60 minutes of order time (inpatient AMI JCAHO, inpatient AMI all, and inpatient NST-ACS/UA cohorts).
- Ischemic heart disease: percent of patients hospitalized with acute coronary syndrome (ACS) found to be ST-segment elevation myocardial infarction (STEMI) patients who met criteria for reperfusion and received interventional reperfusion (inpatient AMI all cohort [inclusive of JCAHO AMI]).
- Ischemic heart disease: percent of patients hospitalized with acute coronary syndrome (ACS) found to be ST-segment elevation myocardial infarction (STEMI) patients who met criteria for reperfusion and received percutaneous transluminal coronary angioplasty (PTCA)/primary percutaneous coronary intervention (PCI) within 120 minutes of acute arrival (inpatient AMI all cohort [inclusive of JCAHO AMI]).
- Ischemic heart disease: percent of patients hospitalized with acute coronary syndrome (ACS) found to be ST-segment elevation myocardial infarction (STEMI) patients who met criteria for reperfusion and received thrombolytic therapy within 30 minutes of acute arrival or electrocardiogram (ECG) if acute myocardial infarction (AMI) as inpatient (inpatient AMI all cohort [inclusive of JCAHO AMI]).
- Ischemic heart disease: percent of patients hospitalized with acute coronary syndrome (ACS) found to be moderate/low risk ACS patients who had a plan prior to discharge that includes further outpatient stress testing and possible

catheterization (inpatient AMI all [inclusive of JCAHO AMI] and inpatient NST-ACS/UA cohorts).
- Ischemic heart disease: percent of patients hospitalized with acute coronary syndrome (ACS) found to be high ST-segment elevation myocardial infarction (STEMI) or moderate-high risk non-ST-segment elevation myocardial infarction (NSTEMI) patients who receive a diagnostic catheterization prior to discharge (inpatient AMI all cohort [inclusive of JCAHO AMI]).
- Ischemic heart disease: percent of patients previously hospitalized with acute coronary syndrome (ACS) found to be high or moderate-high risk patients while hospitalized who are seen by a cardiologist within 60 days after discharge (follow-up for inpatient AMI all cohort).
- Ischemic heart disease: percent of patients with previous acute myocardial infarction (AMI), full lipid panel in the past two years, and low-density lipoprotein cholesterol (LDL-C) less than 100 on most recent test in past two years (NEXUS clinics, outpatient heart failure, AMI follow-up, SCI&D, and SMI cohorts).
- Ischemic heart disease: percent of patients with previous acute myocardial infarction (AMI) and low-density lipoprotein cholesterol (LDL-C) greater than or equal to 120 on most recent test in past two years (lower is better) (NEXUS clinics, outpatient heart failure, AMI follow-up, SCI&D, and SMI cohorts).

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness
Timeliness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Veterans Health Administration, Department of Defense. VA/DoD clinical practice guideline for the management of ischemic heart disease. Washington (DC): Veterans Health Administration, Department of Defense; 2003 Nov. Various p. [35 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2003 Nov

GUIDELINE DEVELOPER(S)

Department of Defense - Federal Government Agency [U.S.]
Department of Veterans Affairs - Federal Government Agency [U.S.]
Veterans Health Administration - Federal Government Agency [U.S.]

SOURCE(S) OF FUNDING

United States Government

GUIDELINE COMMITTEE

The Management of Ischemic Heart Disease Working Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Members of the Working Group: Catherine Bard, MD, Family Practitioner; Mark Brouker, CDR, USN, Deputy Director, DoD PEC; Lorie A. Brown, MAJ, NC, USA, Family Practitioner; James Caldwell, MD, Chief, Cardio Care Services, VAMC; Jan M. Carrio, CDR, NC, USN, Health Care Analyst, Bureau of Medicine and Surgery; Dale A. Carroll, COL, MC, USA, Chief, Clinical Services Division, US Army Medical Command; Pat Comoss, RN, BS, FAACVPR, Nurse Consultant for Cardiac Rehabilitation, Nursing Enrichment Consultants, Inc.; Ken Conrad, CDR, MC, USN, Waterfront Support Unit; Margretta Diemer, COL, MC, USA, Staff Internist; Kathryn J. Dolter, RN, PhD, LTC, USA, Chief, Outcomes Management, Quality Management; Christine Edwards, CPT, NC, USA, Clinical Instructor, Nutrition Care Division; Rosalie Fishman, RN, MSN, CPHQ, Clinical Coordinator; Ross D. Fletcher, MD, Chief, Cardiology, VAMC; Chester B. Good, MD, MPH, Chairperson, Medical Advisory Panel, Pittsburgh VAMC; Karl Hammermeister, MD, Staff Cardiologist, Denver VAMC; Thomas Harrell, MAJ, MC, USAF, Chief, Cardiology, M. O'Calleghan Federal Hospital; Susan Herrold, CDR, NC, USN, BUMED; Robert L. Jesse, MD, Chief, Cardiology, VAMC; David Lantz, COL, MC, USAF, Cardiology Consultant to AF/SG, Wright Patterson AFB; Wendy Larson, MAJ, USAF, MPH, RD, Manager, Nutrition Programs; John Leroy, CDR, MSC, USN, Naval Medical Clinic; Susan Manship, LTC, USA, Dietitian, Brooke Army Medical Center; Joanne Marko, SLP, Clinical Coordinator; Gary Martin, MD, VA Puget Sound Health Care System; Jennifer S. Menetrez, MAJ, MC, USA, Physical Medicine & Rehabilitation; Charles Miller, MD, USA Medcom MCHO-CL-C; Michael E. Mollerus, CDR, MC, USN, Naval Medical Center; Kenneth G. Morris, MD, Chief of Cardiology, Department of Veterans Affairs; Patrick G. O'Malley, MAJ, MC, USA, Staff, General Internal Medicine Service, Walter Reed Army Medical Center; Deborah M. Newsome, LTC, NC, USA, Head Nurse CICU, Tripler Army Medical Center; Daniel Parks, MAJ, MC, USA, Family Practice, Womack Army Medical Center; Jesse Ortel, MPT; Daniel Remund, COL, MSC, USA, Pharmacist, Director, DoD Pharmacoeconomic Center, DoD PEC; Susan Russell, LT, MSC, USN, Pharmacist, Naval Medical Clinic; John T. Schindler, LCDR, MC, USN, Internal Medicine, National Naval Medical Center; Frances Sawyer, RD, Perry Point VAMC; Robert J. Sullivan, Jr., MD, MPH, Director, National Center for Health Promotion; Frances Stewart, CDR, USN, Program Director, Patient Advocacy/Medical Ethics; Robert W. Swisher, MD, Research Coordinator, Department of Veterans Affairs; Ali F. Sonel, MD, FACC, FACP,

Chairman, VA Pittsburgh Healthcare Systems; Debby Walder, RN, MSN, Performance Management Facilitator, Department of Veterans Affairs; Oded Susskind, MPH, Medical Education Consultant; Iris West, COL, NC, USA, Nurse Staff Officer, US Army/Office of the Surgeon General; Karen Ulisney, RNC, BSN, Clinical Nurse Specialist, Cardiac Rehab Program Director, National Naval Medical Center; Robert G. Zoble, MD, PhD, Director, CCU, James A. Haley VA Hospital; Lynn Welling, CDR, MC, USN, Head, Department of Emergency Medicine, Naval Hospital Great Lakes; John M. Westfall, MD, MPH, Associate Professor of Medicine, University of Colorado Health Sciences Center; Judy A. Young, MAJ, USAF, Special Care/Intensive Care, Flight Commander, 96th Medical Group

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the Department of Veterans Affairs Web site.

Print copies: Available from the Department of Veterans Affairs, Veterans Health Administration, Office of Quality and Performance (10Q) 810 Vermont Ave. NW, Washington, DC 20420.

AVAILABILITY OF COMPANION DOCUMENTS

Various companion documents are available from the Veterans Health Administration (VHA) Web site.

In addition, the VHA Web site provides references to related guidelines, performance measures, and other resources.

Also available:

- Guideline for Guidelines. Draft. Washington (DC): Veterans Health Administration, Department of Veterans Affairs. Available at: VHA Web site.

Print copies: Department of Veterans Affairs, Veterans Health Administration, Office of Quality and Performance (10Q) 810 Vermont Ave. NW, Washington, DC 20420.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on August 4, 2004.

COPYRIGHT STATEMENT

No copyright restrictions apply.

© 1998-2005 National Guideline Clearinghouse

Date Modified: 5/16/2005