Sidebar D (Box 13): Results of Non-Invasive Testing

High-Risk

- Severe resting LV dysfunction (LVEF <0.35)
- High-risk Duke treadmill score (score ≤ -11)
- Severe exercise LV dysfunction (exercise LVEF <0.35)
- Stress-induced large perfusion defect (particularly if anterior)
- Stress-induced moderate-size multiple perfusion defects
- Large fixed perfusion defect with LV dilation or increased lung uptake (thallium-201)
- Stress-induced moderate-size perfusion defect with LV dilation 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 = 0.35 to 0.49)
- Intermediate-risk Duke treadmill score (greater than -11 and less than 5)
- Stress-induced moderate perfusion defect without LV dilation or increased lung uptake (thallium-201)
- Limited stress echocardiographic ischemia with wall motion abnormality only at higher doses of dobutamine involving ≤ two segments

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

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

Sidebar F (Box 19): Intermediate Probability of CAD

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

For Management of AMI, Unstable Angina/ NSTEMI, Stable Angina & Follow-Up of Patient with IHD See Respective Pocket Guides

Sidebar A: Symptoms/Signs Suggesting Ischemia

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

Sidebar B (Box 3): Emergency Status

Patient's vital signs (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 percent
- Irregular pulse

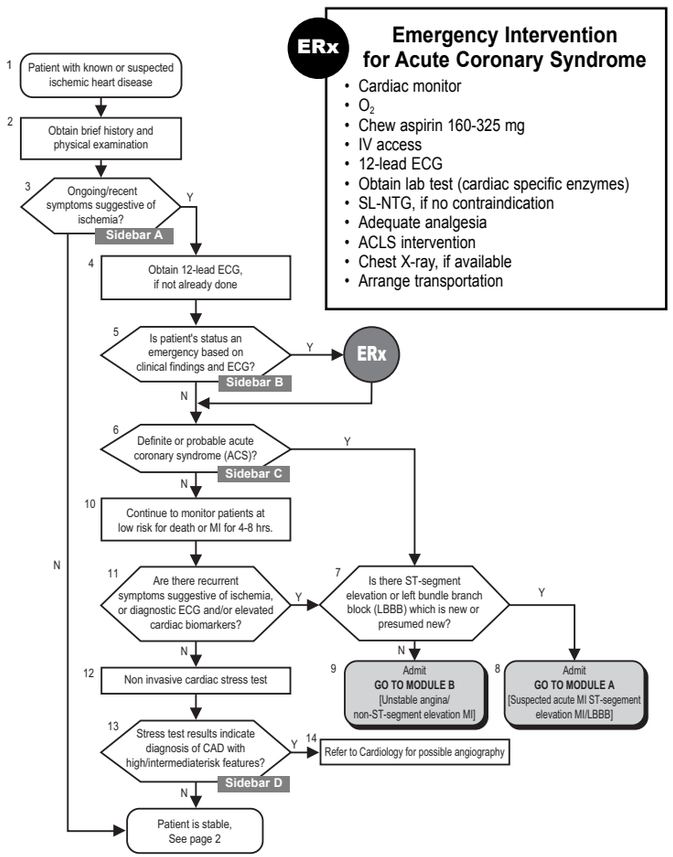
AND/OR

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

VA/DoD Clinical Practice Guideline Management of Ischemic Heart Disease (IHD) – Core Module Pocket Guide

Initial Evaluation



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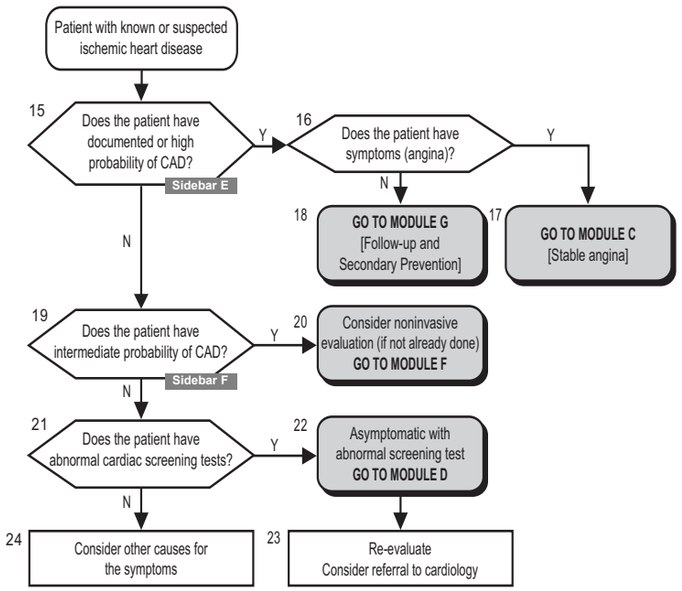


Sidebar C (Box 6): DIAGNOSIS OF ACS

A diagnosis of ACS is made if at least *one major criterion* or *at least one minor criterion from both columns I and II* is present

Major Criteria

A diagnosis of an ACS can be made if one or more of the following major criteria is present

- ST-elevation[a] or 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)

Minor Criteria

In the absence of a major criterion, a diagnosis of ACS requires the presence of at least one item from both columns

I	II
• 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 chest leads (V_1 to V_6) or ≥ 0.1 mV in all other leads. Contiguity in the limb leads (frontal plane) is defined by the lead sequence: I, aVL (lateral), and II, III, aVF (inferior).

(b) Use the following definitions to determine the likelihood that the presenting symptoms are angina

(c) These age and gender characteristics define a probability of CAD ≥10% in symptomatic patients

Pretest Likelihood of CAD in Symptomatic Patients According to Age and Sex[a]

	Non-anginal Chest Pain		Atypical (Probable) Angina		Typical (Definite) Angina	
Age (Years) [b]	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

[a] Each value represents the percent with significant CAD on catheterization. (Italic =Low Bold= High)

[b] 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.

Definitions of Angina Symptoms

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

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: (but do not exclude diagnosis of CAD)
- Pleuritic pain (i.e., sharp or knife-like pain brought on by respiratory movements or cough)
- Primary or sole location of discomfort in the middle or lower abdominal regions
- Pain that may be localized at the tip of one finger, particularly over costochondral junctions or the left ventricular (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

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

Sidebar B: Contraindications to Reperfusion Therapy

Absolute Contraindications to Thrombolysis

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

Relative Contraindications to Thrombolysis

- Severe, uncontrolled hypertension on presentation (i.e., blood pressure >180/110 mm Hg)
- Current use of anticoagulants in therapeutic doses
- Known bleeding problems
- Recent trauma (i.e., within 2 to 4 weeks) including head trauma or traumatic or prolonged (i.e., >10 minutes) cardiopulmonary resuscitation (CPR)
- Recent major surgery (i.e., within 3 weeks)
- Non-compressible vascular punctures
- Recent internal bleeding (i.e., within 2 to 4 weeks)
- Prior exposure to streptokinase (i.e., 5 days to 2 years), if that agent is to be administered
- 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

Suspected Acute Myocardial Infarction or New or Presumed New LBBB

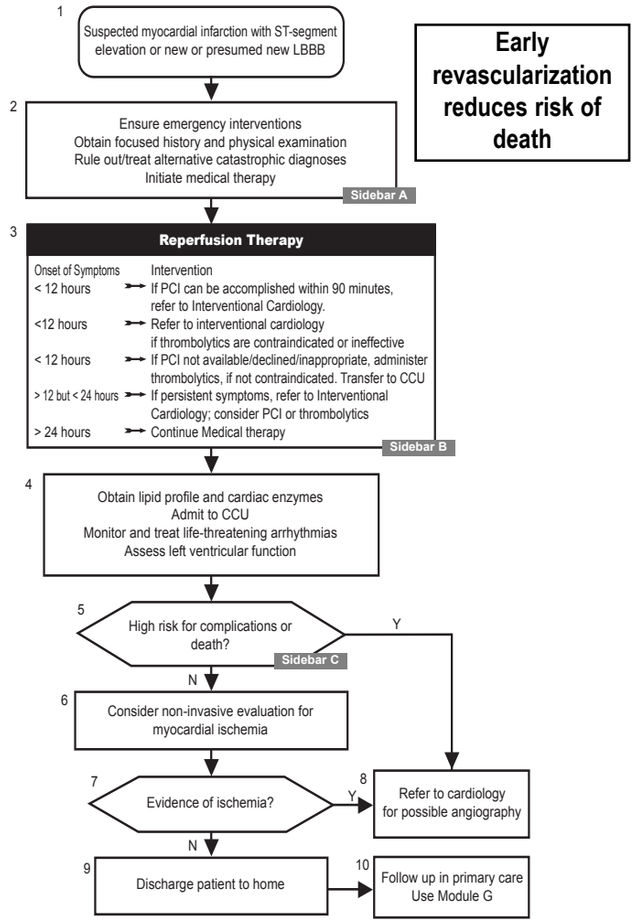
VA/DoD Clinical Practice Guideline Management of Ischemic Heart Disease (IHD) Module A Pocket Guide

Management of Patients with ST-Segment Elevation MI or New or Presumed New LBBB

1. Admit to an intensive care unit
2. Initiate heparin, low-molecular weight heparin, if indicated
3. Continue beta blockers
4. Consider ACE Inhibitor therapy in the absence of contraindications

5. ***If less than 12 hours from onset of symptoms***
   - Refer to PCI if intervention can be performed within 90 minutes of presentation in a high volume center by a high volume operator.
   - Initiate thrombolytic therapy, if not contraindicated and not referred for direct PCI
   - Refer to PCI, if thrombolytic therapy is contraindicated or response to thrombolysis is unsatisfactory

6. Consider non-invasive evaluation (cardiac stress test)
7. Refer to cardiology if at high risk for death or recurrent MI and/or LV dysfunction
8. Ensure pharmacologic therapy for ischemia, angina & CHF
9. Discharge patient to home with appropriate follow-up



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Sidebar A: Emergency Interventions

- Triage patients with possible acute MI or unstable angina for evaluation and treatment
- Initiate O_2, intravenous access and continuous ECG monitoring
- Institute advanced cardiac life support (ACLS), if indicated
- Obtain 12-lead electrocardiogram (ECG)
- Perform expedited history & physical to:
  - R/O alternative catastrophic diagnoses (Pericarditis, Pericardial tamponade, Thoracic aortic dissection, Pneumothorax, Pancreatitis, & Pulmonary embolus)
  - Elicit characteristics of MI
  - Contraindications to reperfusion therapy
- Administer the following:
  - Non-coated aspirin (160 to 325 mg).
  - Nitroglycerin (spray or tablet, followed by IV, if symptoms persist).
  - Beta-blockers in the absence of contraindications
  - Oral ACE-inhibitors in the absence of contraindications
  - Intravenous fractionated heparin if indicated
- Determine if patient meets criteria for emergent reperfusion therapy – if so, refer to Interventional Cardiology:
  - Hx of ischemia or infarction
  - ECG finding of LBBB or ongoing ST-segment elevation in 2 or more leads
- Ensure adequate analgesia (morphine, if needed)
- Obtain serum cardiac markers (troponin or CK-MD)
- Identify and treat other conditions that may exacerbate symptoms

Sidebar C: Thrombolytic Therapy

Current Thrombolytic Agents

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

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

Clinical Signs of Reperfusion Following Thrombolytic Administration

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

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

Table 4: Increased Risk for Complications or Death Following a MI

- Recurrent angina (i.e., spontaneous or inducible)
- Congestive Heart Failure (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)

For Management of Initial Evaluation, Unstable Angina/NSTEMI & Follow-Up of Patient with IHD - See Respective Pocket Guide

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

Initial Therapy for Patients with ACS

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

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

Sidebar A: Antiplatelet and Anticoagulant Therapy

DEFINITE ACS High Risk	LIKELY/ DEFINITE ACS Moderate Risk	POSSIBLE ACS Low Risk
Aspirin + IV heparin/ SQ LMWH + IV platelet GP IIb/IIIa receptor antagonist	Aspirin + SQ LMWH or IV heparin	Aspirin
Clopidogrel	Clopidogrel	

Sidebar B - Indications for IIb/IIIa and Early Invasive Therapy in High Risk Patients

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

Sidebar C - Indications for Angiography in Intermediate Risk Patients

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

Sidebar D: Results of Non-Invasive Testing

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

- Severe resting LV dysfunction (LVEF <0.35)
- High-risk Duke treadmill score (score ≤-11)
- Severe exercise LV dysfunction (exercise LVEF <0.35)
- Stress-induced large perfusion defect (particularly if anterior)
- Stress-induced moderate-size multiple perfusion defects
- Large fixed perfusion defect with LV dilation or increased lung uptake (thallium-201)
- Stress-induced moderate-size perfusion defect with LV dilation 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

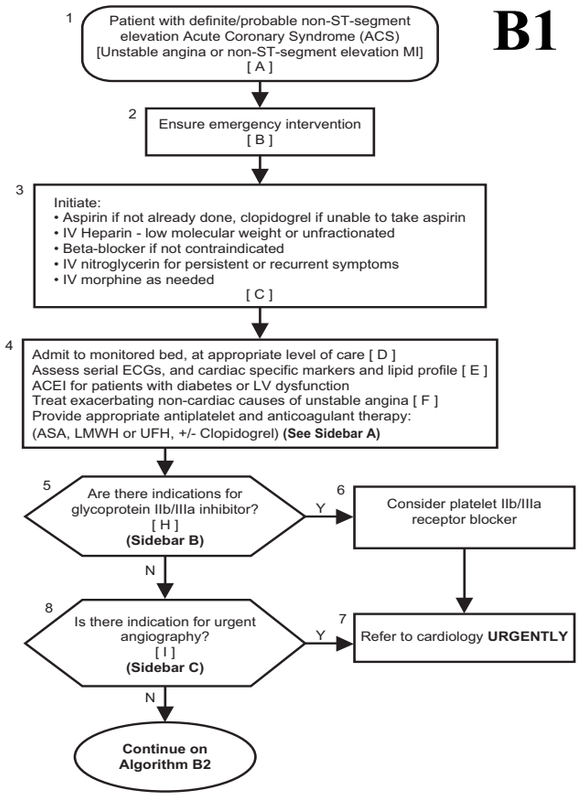
Intermediate-Risk (1% - 3% annual mortality rate)

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

VA/DoD Clinical Practice Guideline Management of Ischemic Heart Disease (IHD) Module B Pocket Guide

Definite/Probable Non-ST-Segment Elevation Acute Coronary Syndrome (NSTE-ACS)

B1



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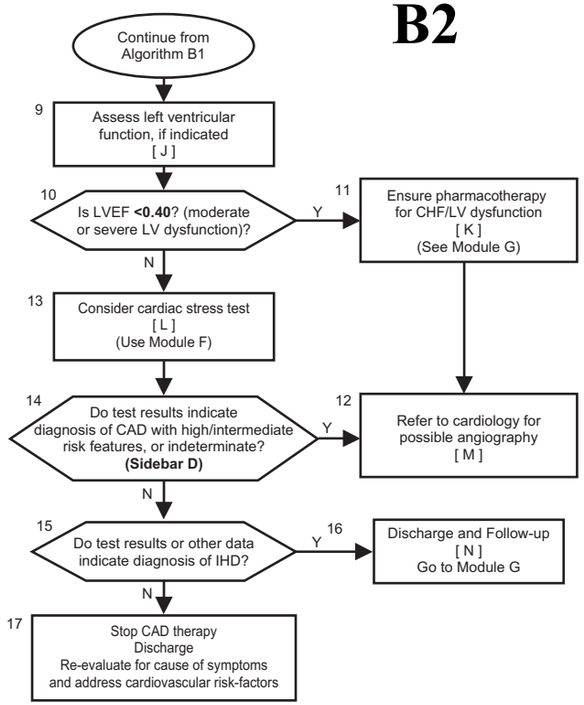
B2

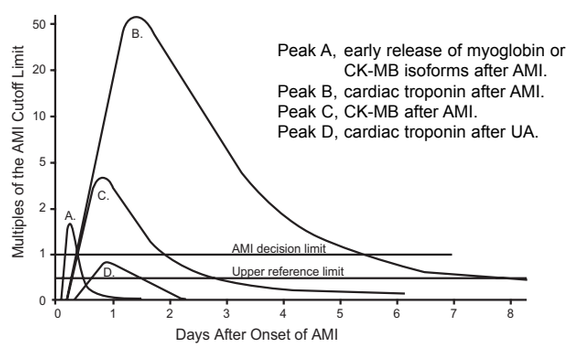


For Initial Evaluation – CORE, Management of AMI, and Follow-Up of Patient with IHD, See Respective Pocket Guides

Short-Term Risk of Death or Non-Fatal 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 tempo of ischemic symptoms in the preceding 48 hours	• Prior MI, peripheral or cerebrovascular 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) (see Table 6, Core Module) • 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 (see Table 6, Core Module)
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 >0.1 ng/mL)	• Slightly elevated (e.g., TnT >0.01, but <0.1 ng/mL)	• Normal

Cardiac Markers In Blood Vs. Time After Onset Of Symptoms*



Cardiac Troponins

- Powerful tool for risk stratification.
- Greater sensitivity and specificity than CK-MB.
- Useful for the selection of therapy.
- Best single test to efficiently diagnose NSTEMI
- Low sensitivity in very early phase of MI (i.e., <6 hours after onset of symptoms) and requires a repeat measurement at 8-12 hours, if negative.
- Limited ability to detect the late minor reinfarction.

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

Sidebar A - Anti-Anginal Therapy

Goals of Therapy:

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

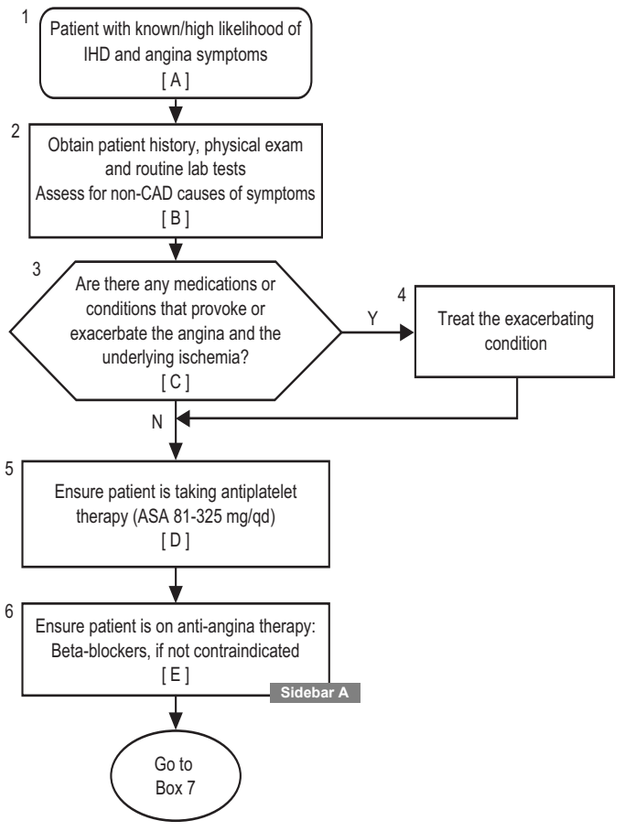
Recommended Medications for Patients with IHD

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

FOR
ADDITIONAL MEDICATION
RECOMMENDATIONS
SEE

Pharmacotherapy for Cardiovascular Disease in Primary Care

VA/DoD Clinical Practice Guideline
Management of Ischemic Heart Disease (IHD)
Module C Pocket Guide - Stable Angina



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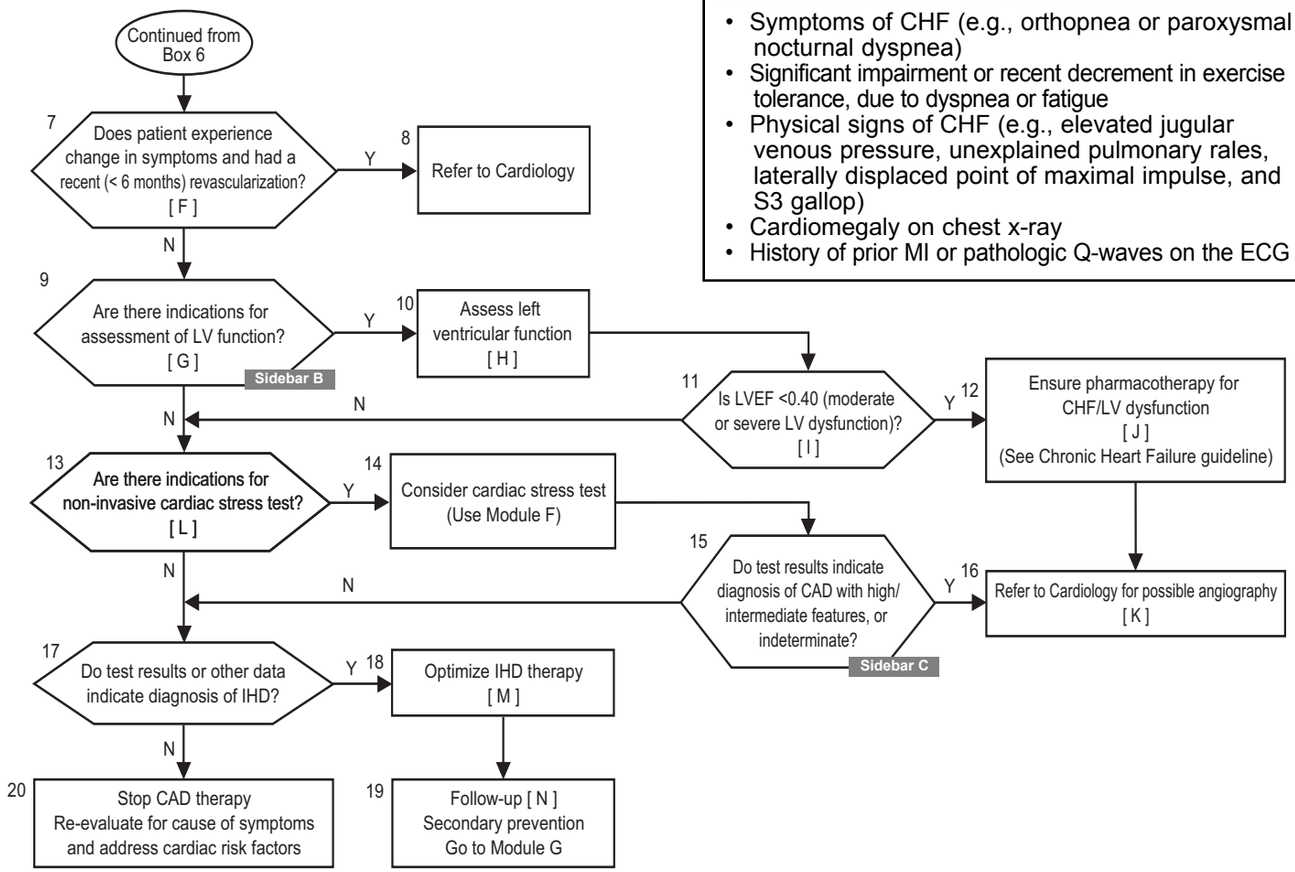

Sidebar B - Indication for Assessment of LVF

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

Sidebar C - Cardiac Stress Test

High-Risk Findings

- Duke treadmill score less than or equal to -11 (estimated annual mortality >3%)
- Large stress-induced perfusion defect
- Stress-induced, multiple perfusion defects of moderate size
- Large fixed perfusion defect with LV dilation or increased lung uptake (thallium-201)
- Stress-induced, moderate perfusion defect with LV dilation or increased lung uptake (thallium-201)
- Echocardiographic wall motion abnormality involving >2 segments at ≤10 mg/kg/min dobutamine or HR <120/min

Intermediate-Risk Findings

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

Sidebar A: SIGNS AND SYMPTOMS OF CORONARY ARTERY DISEASE (CAD)

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

Sidebar E: Recommended Medications for Patients with IHD

Aspirin (or clopidogrel) reduces cardiovascular (CV) events in patients with acute MI, previous MI, and unstable angina
Aspirin reduces risk of MI in patients with chronic stable angina
Beta-blockers improve symptoms in patients with IHD
Beta blockers improve CV outcomes in patients with IHD, previous MI and ischemic LV dysfunction
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Lipid-lowering therapy improves CV outcomes in patients with IHD and elevated lipids
Lipid-lowering therapy improves CV outcomes in patients with IHD and average cholesterol
Gemfibrozil improves outcomes in patients with IHD and low high-density lipoproteins – cholesterol (HDL-C)

Follow-Up and Prevention:

A = Aspirin and Anti-anginal therapy
B = Beta-blocker and Blood pressure
C = Cigarette smoking and Cholesterol
D = Diet and Diabetes
E = Education and Exercise

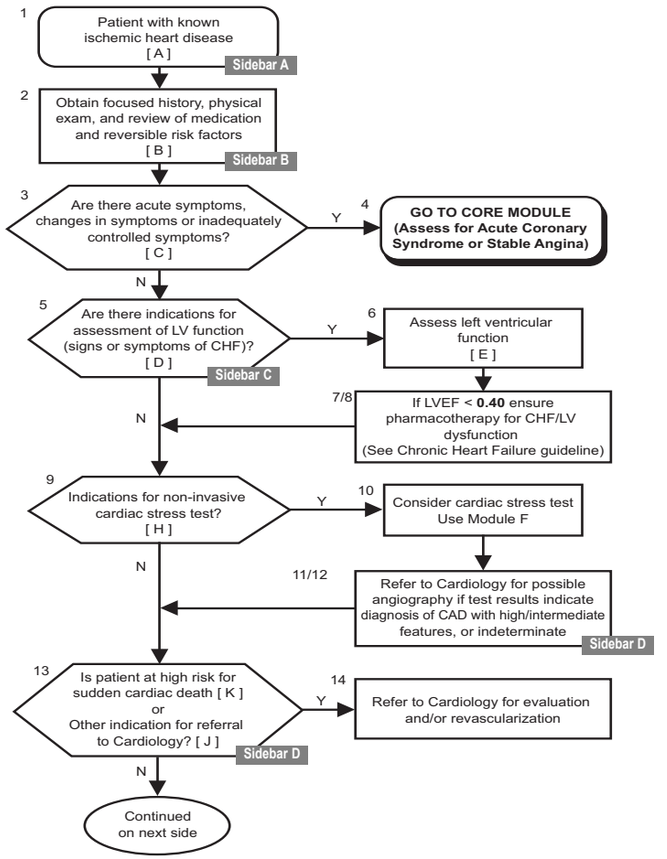
Sidebar F: Patient Education

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

FOR FURTHER MEDICATION INFORMATION SEE DOCUMENT,

PHARMACOTHERAPY FOR CARDIOVASCULAR DISEASES IN PRIMARY CARE POCKET GUIDE

VA/DoD Clinical Practice Guideline Management of Ischemic Heart Disease (IHD) Module G Pocket Guide Follow-Up & Secondary Prevention



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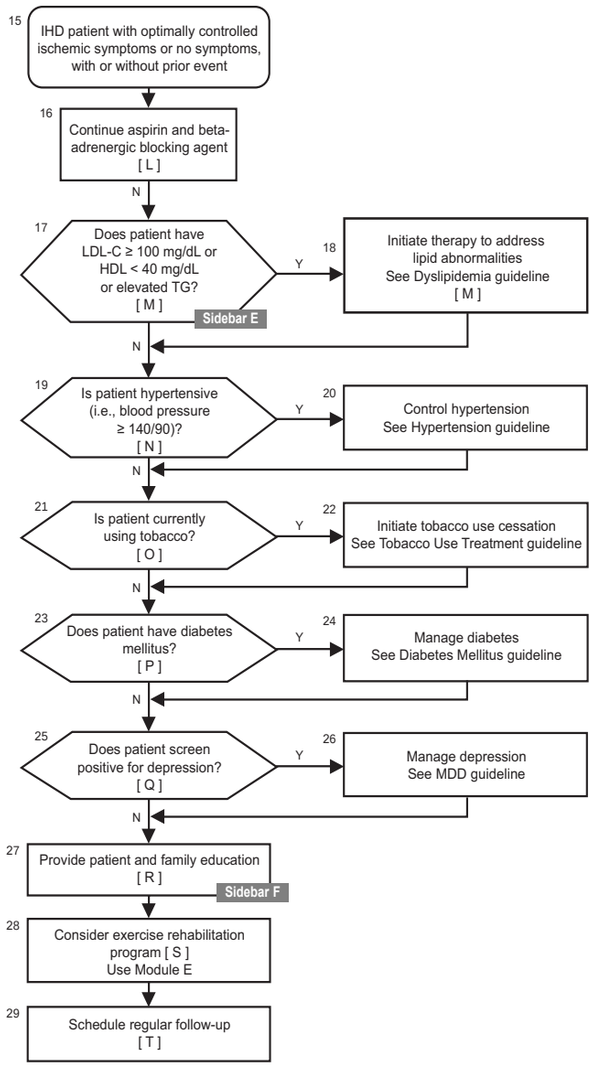

Sidebar B: Symptom Assessment

Symptoms that May Represent Ischemia or MI

- Chest pain, discomfort, pressure, tightness, or heaviness (defined as at least a one-class increase Canadian Cardiovascular Society classification)
- 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

Symptom Characteristics that Suggest Noncardiac Pain*

- 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

** Does not exclude the diagnosis of CAD*

Sidebar C: Indications for Assessment of Left Ventricular Function

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

Sidebar D: Referral to Cardiology

Class 3-4 symptoms of ischemia or heart failure on medical therapy
Recurrent symptoms following recent (<6 mo) revascularization
High-risk findings on noninvasive testing
Noninvasive test results that are inadequate for management
Increased risk for sudden cardiac death • History of sudden cardiac death • History of sustained monomorphic ventricular tachycardia • Reduced LVF (EF<0.40) and nonsustained ventricular tachycardia • Reduced LVF (EF<0.40) and syncope of undetermined etiology • Reduced LVF (EF <0.30) and prior history of MI

Pharmacotherapy for Cardiovascular Diseases in Primary Care

VA/DoD Medications Used in the Management of Cardiovascular Diseases in Primary Care

DRUG[a]	ORAL DOSE	POTENTIAL SIDE EFFECTS	PRECAUTIONS/CONTRAINDICATIONS/COMMENTS
ANTIPLATELET/ANTICOAGULANT			
Aspirin[b]	UA/MI 160 mg-325 mg (1st dose) Chronic 81 mg-325 mg qd	• GI intolerance: dyspepsia, nausea, GI bleeding, heartburn • Bronchospasm: prominent in patients with a history of asthma and nasal polyps • Tinnitus • Thrombocytopenia	• ASA hypersensitivity: bronchospasm, angioedema, and anaphylaxis • Active, severe bleeding • Clopidogrel should be used in patients who are unable to take ASA
Clopidogrel[b,c,d]	NSTE-ACS 300 mg oral load then 75 mg qd for at least 1 month & up to 9 months with elective PCI Post stent 300 mg oral load then 75 mg qd at least 1 month & up to 12 months Non acute conditions 75 mg qd May be given with aspirin (81-325 mg) unless aspirin is contraindicated or not tolerated	• Thrombolic thrombocytopenic purpura rarely reported (sometimes after less than 2 weeks exposure) • Bleeding • GI intolerance: diarrhea • Clopidogrel increases risk of major bleeding (i.e., requiring transfusion of ≥ 2 units) when combined with ASA	• History of bleeding diathesis • Chest pain without ECG changes in whom etiology of chest pain is unlikely to be ischemic in origin • Known hypersensitivity to ticlopidine, due to cross reactivity or any component of the product • Known hypersensitivity to clopidogrel or any component of the product • Active pathological bleeding (GI bleeding and intracranial hemorrhage) • Withhold clopidogrel for 5-7 days prior to elective CABG or other major surgical intervention
Warfarin[b,c]	Prevent systemic embolization: INR 2-3 Prevent recurrent MI within first 3 months: INR 2.5-3.5	• Bleeding (e.g., GU/GI) • Skin necrosis	• Pregnancy • Hemophilia • Cerebrovascular hemorrhage • History of warfarin induced skin necrosis • Vitamin K may decrease anticoagulant response; patient should be instructed on importance of consistent dietary intake of vitamin K
CARDIOVASCULAR			
ACE Inhibitors		• Hypotension, hyperkalemia, acute renal impairment, angioedema, cough • Monitor K+ and renal function	• Avoid in 2nd and 3rd trimesters of pregnancy due to possible fetal and neonatal morbidity and death • Hypersensitivity • Bilateral renal artery stenosis • Renal failure; use ACEI with caution in patients sCr >3.0 mg/dL • Take captopril 1 hr prior to food ingestion • Concomitant therapy with K+-sparing diuretics and/or K+ supplements may result in hyperkalemia
Captopril[b,c]	12.5–150 mg/day (divided bid-tid)		
Enalapril[b]	2.5–20 mg/day (divided qd-bid)		
Fosinopril[b]	5–40 mg qd		
Lisinopril[b,c]	2.5–40 mg qd		
Ramipril[b,c,d]	2.5–10 mg/day (divided qd-bid; qd for prevention of cardiovascular events)		

VA access to full guideline: http://www.oqp.med.va.gov/cpg/cpg.htm *December 2003*
DoD access to full guideline: http://www.QMO.amedd.army.mil
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VA/DoD Medications Used in the Management of Cardiovascular Diseases in Primary Care

DRUG[a]	ORAL DOSE	POTENTIAL SIDE EFFECTS	PRECAUTIONS/CONTRAINDICATIONS/COMMENTS
CARDIOVASCULAR			
Angiotensin II Receptor Blockers[d,e]		• Hypotension, hyperkalemia, acute renal impairment, angioedema, dyspnea • Less incidence of cough than ACEIs • Monitor K+ and renal function	• Avoid in 2nd and 3rd trimesters of pregnancy due to possible fetal and neonatal morbidity and death • Hypersensitivity • Bilateral renal artery stenosis • Renal failure • Alternative to ACEIs in patients who cannot tolerate ACEIs • Concomitant therapy with K+-sparing diuretics and/or K+ supplements may result in hyperkalemia • Losartan/valsartan reported to ↑ reabsorption of lithium; monitor levels and for signs of toxicity • Telmisartan may ↑ peak and trough digoxin levels by 49% and 20%, respectively; monitor trough digoxin levels at steady-state
Candesartan	4-32 mg/day (divided qd-bid)		
Eprosartan	400-800 mg/day (divided qd-bid)		
Irbesartan	75-300 mg qd		
Losartan	25-100 mg/day (divided qd-bid)		
Olmesartan	5-40 mg qd		
Telmisartan	20-80 mg qd		
Valsartan	80-320 mg qd		
β-Blockers		• Bradycardia, hypotension, fatigue, insomnia, depression, sexual dysfunction, cold extremities, masking of hypoglycemia, nightmares/ vivid dreams • Wheezing and dyspnea seen with larger doses	• Sinus bradycardia • SBP< 90mmHg • 2nd or 3rd degree heart block • Cardiogenic shock • Severe bronchospastic disease • Sick sinus syndrome • Overt, decompensated HF • May cause growth retardation in 1st trimester • Discontinue with slow taper over 1 wk • Verapamil/diltiazem may potentiate pharmacologic effects of β-blockers; additive effects on cardiac conduction • Adjust dose of atenolol in chronic kidney disease
Propranolol[b]	IR: 40-480 mg/day (divided qd-bid) SR: 80-160 mg qd		
Atenolol[b,c]	25mg-100 mg qd (may require 200 mg qd for angina)		
Metoprolol IR[b,c]	50-300 mg/day (divided qd-bid) (6.25-100 mg bid for HF)		
Metoprolol XL[b,d]	50-400 mg qd (12.5-200 mg qd for HF)		
Alpha-beta blocker			
Carvedilol[b,d]	3.125-25mg bid (patients ≥ 85kg may be titrated to 50mg bid with caution)		
Calcium Channel Blockers		• Verapamil may cause constipation • DHPs may cause ankle edema, dizziness, flushing, headache	• CCBs should be used with caution in patients with HF • Diltiazen & verapamil may decrease heart rate, cause heart block and/or are contraindicated in AV node dysfunction (2nd or 3rd degree heart block), systolic HF and decreased LV function • Use all CCBs with caution in patients with liver dysfunction; use diltiazem & verapamil with caution in patients with impaired kidney function • Verapamil/diltiazem may potentiate pharmacologic effects of β-blockers; additive effects on cardiac conduction • Short-acting nifedipine should be avoided due to its potential to precipitate acute and life-threatening hypotension
Diltiazem IR[b,c]	90-360 mg/day (divided tid-qid)		
Diltiazem SR[b,c]	120-540 mg qd		
Verapamil IR[b,c]	120-360 mg/day (divided bid-tid)		
Verapamil SR[b,c]	120-480 mg/day (divided qd-bid)		
Dihydropyridines			
Amlodipine[b,d]	2.5-10 mg qd		
Felodipine[b,d]	2.5-10 mg qd		
Nifedipine SR[b,c]	30-120 mg qd (manufacturer max=90 mg qd)		
Diuretics		• Hypokalemia, hyperuricemia, hypochloremic alkalosis, dilutional hyponatremia • Spironolactone: hyperkalemia, gynecomastia, GI intolerance, hyperchloremic metabolic acidosis	• Monitor potassium levels for diuretic induced hypokalemia • K+-sparing diuretics, K+ supplements may cause ↑ K+ • Diuretic-induced hyperuricemia does not require treatment in the absence of gout or kidney stones • Thiazide diuretics may ↑ TC and ↑ TG, although these effects may be transient • Thiazide diuretics may ↑ lithium reabsorption; ↓ lithium dose by 50%
Furosemide[b,c] (primarily for HF)	20-400 mg/day (consider dividing bid if dose > 160 mg/day)		
Chlorthalidone	12.5-25 mg qd (max=50 mg/day)		
Hydrochlorothiazide[b,c]	12.5-25 mg qd (max=50 mg/day)		
HCTZ/Triamterene[b,c]	25/37.5-50 mg/75mg qd		
Spironolactone[b,c] (primarily for HF)	12.5-25 mg qd (max 50 mg qd, use with caution due to hyperkalemia)		
Centrally Acting		• Drowsiness, dry mouth • May exacerbate depression	• Taper dose to discontinue • Clonidine patches are costly but may be useful in selected patients. Full effect of clonidine patch may not be evident until several days after it is first placed
Clonidine Tablet[b,c]	0.1-0.8 mg/day (divided bid-tid) (max can be up to 2.4 mg/d)		
Clonidine Patch[b]	0.1-0.6 mg patch weekly		
Methyldopa[b]	500 mg-3g/day (divided bid-qid doses)		

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DRUG[a]	ORAL DOSE	POTENTIAL SIDE EFFECTS	PRECAUTIONS/CONTRAINDICATIONS/COMMENTS
CARDIOVASCULAR			
Peripherally Acting Reserpine[b]	0.05-0.25 mg qd	• Sedation, nightmares, tremors, nasal congestion, activation of peptic ulcer • May exacerbate depression	• Active PUD, ulcerative colitis, history gallstones • Depression with suicidal tendencies • May cause a hypertensive reaction when initiated in patients on a MAOI
Vasodilators Minoxidil[b] Hydralazine[b,c]	5-40 mg/day (divided qd-bid) (max=100 mg/day) 30-200 mg/day (divided bid-qid)	• Hypertrichosis, edema, and pericardial effusions with minoxidil • Headache, edema and SLE (dose-related) with hydralazine	• Direct-acting vasodilators do not reduce LV hypertrophy • Should be used with a diuretic and β-blockers to reduce edema and reflex tachycardia • Hydralazine used in combination with ISDN for HF
Alpha-blockers Doxazosin[b,d] Prazosin[b,d] Terazosin[b,d]	1-4 mg qd (max=16 mg/d) 1-15 mg/day (divided bid-tid) (max=20 mg/d) 1-5 mg qd (max=20 mg/d)	• First-dose syncope, dizziness • Tachyphylaxis	• Initiate at low doses (1 mg) with 1st dose given at bedtime to avoid syncope
Nitrates Nitroglycerin SL tab[b,c] or spray[c] ISDN[b,c] ISDN ER ISMN conventional ISMN ER[b] Nitroglycerin patch[b] Nitroglycerin ointment[b]	0.4 mg tab (or 1-2 sprays) SL at time of chest pain (or prophylaxis), q 5 min up to 3 doses 10-120 mg (divided bid-tid) (up to 160 mg used in combination w/hydralazine for HF) 40 mg bid 10-20 mg bid 30-120 mg qd 2.5-20 mg/24 hrs topically qd (remove at hs) 1/2-5 inches topically q 8 hrs	• Persistent transient headache (may be severe) • Postural hypotension, syncope • Transient flushing • Allergic contact dermatitis is rare with topical preparations	• Allow nitrate-free interval of 10-12 hours to prevent tolerance (e.g., dose tid at 7am, 12pm, 5pm) • Use with caution in SBP < 90 mmHg • Contraindicated in conjunction with sildenafil • Contraindicated in severe anemia • Use with caution in patients with increased intracranial pressure • Avoid nitrates with right ventricular infarction
Digoxin Digoxin[b,c]	0.0625-0.375 mg qd (usual dose 0.125-0.25 mg qd to achieve goal of 0.5-1.0 ng/ml)	• Signs of toxicity include nausea, confusion, abdominal pain, diarrhea, visual disturbances, arrhythmias, bradycardia, fatigue, anorexia, headache	• Avoid in hypertrophic obstructive cardiomyopathy • Caution with AV block, ventricular arrhythmias • Verapamil/diltiazem may ↑ digoxin levels 20-70% • Telmisartan may ↑ peak and trough digoxin levels by 49% and 20%, respectively; monitor trough digoxin levels at steady-state • Diuretics may induce hypokalemia which may ↑ risk of digitalis toxicity
LIPID-LOWERING			
Statins Atorvastatin[d] Fluvastatin[b,d] Lovastatin[b] Pravastatin[d] Simvastatin[b,c]	10-80 mg qd 20-80 mg/day (divided qpm-bid) XL 80mg qpm 10-80 mg qpm with food (80 mg given as 40 mg bid) 10-80 mg qpm 5-80 mg qpm	• Abdominal pain, constipation, diarrhea, dyspepsia, nausea, myopathy (<0.2%; 5% in combination with gemfibrozil; 2% in combination with niacin), rhabdomyolysis • Increase in LFTs >3 x the upper limit, and CPKs >10 x the upper limit	• Hypersensitivity • Caution in hepatic disease • LFT monitoring is recommended by drug manufacturers - within 3 months of initiation or changing dose, and then periodically • Avoid in pregnant/lactating women • Caution in severe renal impairment, use lowest dose in moderate renal impairment • Evening/bedtime dosing may improve efficacy • Increased risk for myopathy when any statin is combined with fibrates or niacin (≥1 gm daily). The risk is also increased if combining atorvastatin, lovastatin or simvastatin with potent inhibitors of CYP 3A4 (azole antifungals, macrolide antibiotics, immunosuppressives, protease inhibitors or delavirdine, grapefruit juice, nefazodone, diltiazem, verapamil, or amiodarone).

VA/DoD Medications Used in the Management of Cardiovascular Diseases in Primary Care

DRUG[a]	DOSE	POTENTIAL SIDE EFFECTS	PRECAUTIONS/CONTRAINDICATIONS/COMMENTS
LIPID-LOWERING			
Bile Acid Resins Colestipol powder[b] Colestipol tablets[b,c]	5-30 gm/day (divided qd-tid) 2-16 gm/day (divided qd-tid)	• Nausea, bloating, constipation, flatulence • May ↑ TG	• Complete billiary obstruction • Caution if active PUD due to GI irritation • Best tolerated 2-5 gm bid; usual effective dose 8-10 gm/d • Take other medications 1 hr prior or 4 hr after resin
Fibrates Gemfibrozil[b,c]	600 mg bid AC	• GI symptoms, nausea, vomiting, diarrhea, rash, hepatitis, gallstones, and myositis	• Gallbladder disease • Monitor ALTs throughout therapy; contraindicated in hepatic disease • Reduce dose in modest renal insufficiency; contraindicated in severe renal dysfunction • Risk of myopathy with statin • Monitor INR; may need to adjust warfarin dosage to prevent bleeding complications
Niacin Niacin ER[b,c] Niacin IR[b]	500 mg-2 gm qd hs (use titration pack) 1.5-3 gm/day (divided tid) Start IR 50-100 mg bid-tid, ↑ dose by 300 mg/day per week	• Flushing, blurred vision, GI distress, itching, headache, hepatotoxicity, hyperglycemia, hyperuricemia	• Hepatic disease; persistent elevation of LFTs • Monitor ALTs at baseline; 6 weeks after start or dosage change; monitor every 6-12 months thereafter • Active PUD • Arterial bleeding • Causes glucose intolerance; caution in established or borderline DM • Decreases urinary secretion of uric acid, caution with gout • If CrCl is 10-50 ml/min give 50% of dose; if <10 ml/min give 25% • Take with food to avoid flushing or GI upset

ACEI=angiotensin-converting enzyme inhibitors; ACS=acute coronary syndrome; ALT=alanine aminotransferase; ASA=aspirin; AST=aspartate aminotransferase; AV=atrioventricular; BPH=benign prostatic hyperplasia; CCB=calcium channel blocker; CPK=creatine phosphokinase; CrCl=creatinine clearance; CYP 3A4=cytochrome P450 3A4 isoenzyme; DHP=dihydropyridine; DM=diabetes mellitus; ECG=electrocardiogram; ER=extended release; GI=gastrointestinal; GU=genitourinary; HF=heart failure; HTN=hypertension; INR=internal normalized ratio; IR=immediate release; ISDN=isosorbide dinitrate; ISMN=isosorbide mononitrate; K+=potassium; LFT=liver function tests; LV=left ventricular; MAOI=monoamine oxidase inhibitor; MI=myocardial infarction; NNT=number needed to treat; NYHA=New York Heart Association; PUD=peptic ulcer disease; SBP=systolic blood pressure; sCr=serum creatinine; SL=sublingual; SLE=systemic lupus erythmatosus; SR=sustained-release; TC=total cholesterol; TG=triglycerides; UA/MI=unstable angina/myocardial infarction; XL=extended release

[a] Partial list
[b] VA National Formulary item
[c] DoD Basic Core Formulary item
[d] VA criteria for use (refer to www.vapbm.org)
[e] DoD Place In Therapy (PIT) guide (www.pec.ha.osd.mil)