

Ischemic Heart Disease (IHD)

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Objectives

Describe

- Describe the classic symptoms of angina

Discuss

- Discuss the characteristics of CP

List

- List the risk factors for ischemic heart disease

Distinguish

- Distinguish risk factors as modifiable or non-modifiable

Objectives

Explain

- Explain non-pharm therapies for IHD

Describe

- Describe the effects of nitrates, beta blockers, and calcium channel blockers on myocardial oxygen supply and demand

Outline

- Outline the goals in treating angina, which medications are used, and the interventions that may be necessary

Key Concepts

IHD is primarily caused by coronary atherosclerotic plaque formation that leads to an imbalance between O₂ supply and demand.



Chest pain is the cardinal symptom of myocardial ischemia due to CAD.



Risk factor identification and modification are important interventions for patients with IHD.

Key Concepts

Statins, aspirin, and ACE inhibitors reduce the risk of acute coronary events and death in patients with ischemic heart disease.

Sublingual NTG is indicated to relieve acute ischemic symptoms.

β -Blockers or long acting CCBs are first-line therapy for preventing ischemic symptoms; long-acting nitrates may be added for refractory symptoms or substituted if a other therapies are not tolerated.

Desired outcomes with treatment

prevent
progression
of disease,
ACS, and
death

alleviate
acute
symptoms
of
myocardial
ischemia

prevent
recurrent
symptoms
of
myocardial
ischemia,

avoid or
minimize
adverse
treatment
effects.

Definitions

Coronary Heart Disease (CHD): atherosclerotic narrowing of major coronary arteries



Ischemic Heart Disease (IHD): imbalance between myocardial O₂ supply and demand

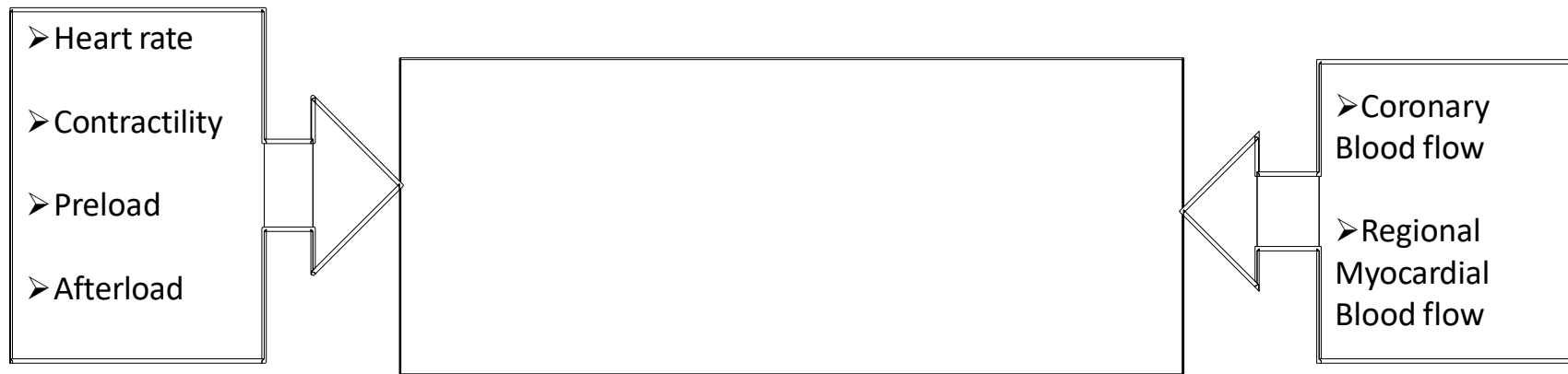


Manifestations include CSA and ACS (UA, STEMI, NSTEMI)

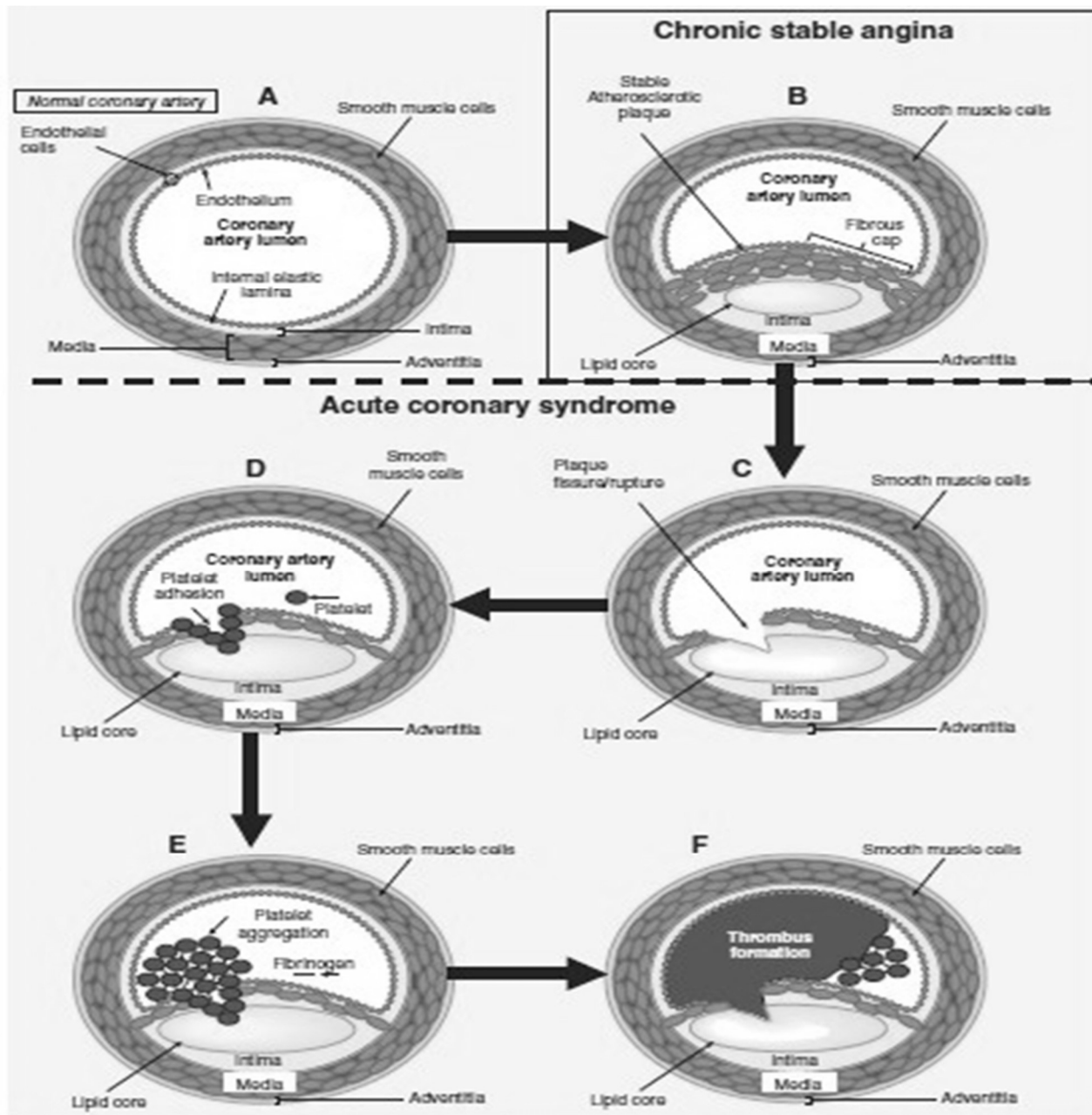


Angina pectoris: discomfort in the chest that occurs when the blood supply to the myocardium is compromised

IHD Pathophysiology



Ischemic heart disease refers to an imbalance in myocardial oxygen demand and coronary blood flow.

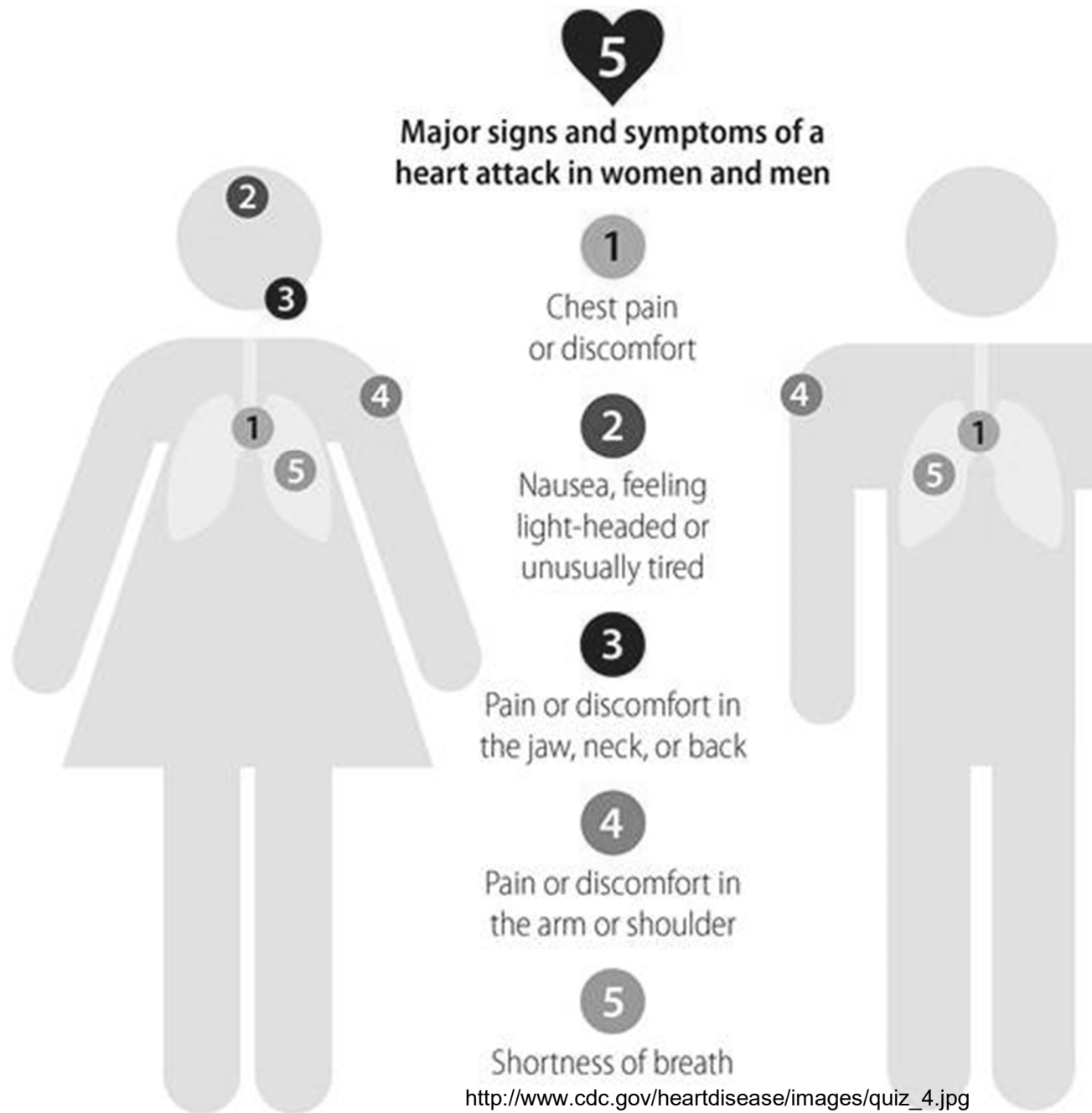


Clinical Presentation

Symptoms of angina pectoris

- Quality of pain: pressure, heaviness, tightness, squeezing
- Location of pain: anterior chest area; may radiate to neck, jaw, shoulder, back, arm
- Duration: several mins
- Factors that provoke symptoms: exertion, emotional stress
- Factors that relieve pain: Rest, sublingual NTG

May be accompanied by dyspnea, N/V, diaphoresis



http://www.cdc.gov/heartdisease/images/quiz_4.jpg

Symptoms of Angina



Angina can spread anywhere between the belly button and the jaw, including to the shoulder, arm, elbow or hand- usually on the left side.

Typical

- Sub-sternal
- Left sided (chest & jaw)
- Radiate down left arm

- Atypical
 - Epigastric

Duration

Stable Angina

- 30 seconds - 10 minutes
- relieved by rest or NTG

Unstable Angina

- 10 - 20 minutes
- may or may not be relieved by NTG

Myocardial Infarction

- > 30 minutes
- unrelieved by rest or NTG

Classification of angina



Several classification systems used



Most common is The Canadian Cardiovascular Society Classification System (CCS Angina Grading Scale)



Class 0: asymptomatic angina



Class I: angina only with strenuous exertion



Class II: angina with moderate exertion



Class III: angina with mild exertion



Stage IV: angina at rest

Diagnostic Tests

Laboratory tests

- Cardiac enzymes are normal in (chronic stable angina) CSA
- Other labs should be determined to assess risk factors

Electrocardiogram (ECG)

- ST-segment or T-wave changes in two or more contiguous leads during symptoms of angina support the diagnosis of IHD.
- Exercise ECG considered positive if shows ≥ 1 mm ST-segment deviation
- Echocardiography
- Electron beam CT (EBCT) (none invasive method .
- Coronary angiography (cardiac cath)

Catheterization and Angiogram

Definitive test for CAD

Angiography

- Injecting contrast dye into coronary vessels
- Identifies locations and extent of disease

Indications:

- Positive stress test
- Unresolved angina
- Urgent diagnosis

What are the main risk factors for IHD?

Risk Factors

Non-modifiable

- Age (M>45, F>55)
- Male gender
- Family history of premature disease
- MI or sudden death
 - < 55 yrs in male 1st-degree relative
 - < 65 yrs of in female 1st-degree relative

Risk Factors

Modifiable

- Physical inactivity
- Obesity
- Cigarette smoking
- Diabetes
- Dyslipidemia
- Hypertension

NEGATIVE Risk Factor: HDL > 60 (good thing!)

Management Goals :Modify risk factors

Physical inactivity
→ Physical
Activity

Obesity → Weight
Management

Cigarette smoking
→ Smoking
Cessation

Diabetes →
Diabetes
Management

Dyslipidemia →
Lipid
Management

Hypertension →
Blood Pressure
Control

Goals of Therapy

Goal	General Strategy	Therapy
Prevent disease progression, ACS, and death	• Modify Risk Factors • Stabilize atherosclerotic plaques	• Lifestyle modifications • Vasculoprotective therapy (statins, ACE inhibitors) and aspirin
Alleviate acute symptoms	Improve balance b/w O2 demand and supply	Antianginal therapy (SL NTG)
Prevent recurrent symptoms	Improve balance b/w O2 demand and supply	Antianginal therapy (β -blockers, CCBs, nitrates, ranolazine) Coronary revascularization
Avoid/minimize ADE	• Avoid drug interactions • Avoid use of drugs with unfavorable effects on comorbid diseases	

Treatment IHD

Lifestyle modification

Pharmacotherapy

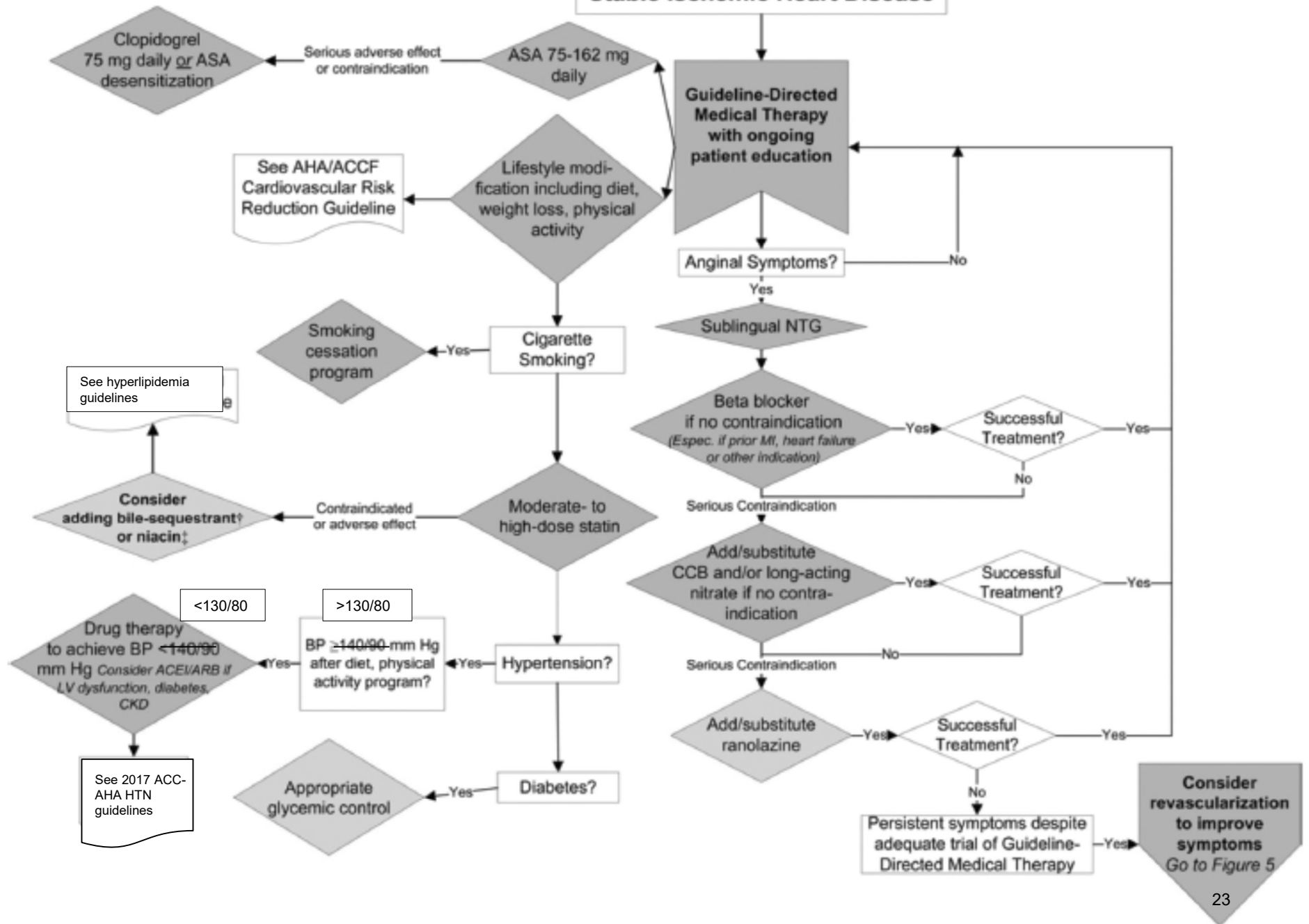
Revascularization

- CABG (coronary artery bypass grafting)
- PCI (percutaneous coronary intervention)
 - PTCA (percutaneous transluminal coronary angioplasty) with or without intracoronary stent placement

Treatment Mnemonic for Stable Angina ACC/AHA/ACP- ASIM Guidelines

- A : Aspirin and Anti-anginals
- B : β-blocker and Blood pressure
- C : Cholesterol and Cigarettes
- D : Diet and Diabetes
- E : Education and Exercise

Stable Ischemic Heart Disease



Antiplatelet Therapy

- Antiplatelet therapy should be considered for all patients without contraindications, particularly if h/o myocardial infarction.
 - Aspirin 81 to 162 mg daily
 - Alternative antiplatelet (e.g. clopidogrel) if aspirin is contraindicated or not tolerated
 - Aspirin has been consistently shown to reduce the risk of major adverse cardiac events, particularly MI.
 - Clopidogrel shown to reduce the risk for adverse cardiovascular events in patients with previous MI, stroke, or symptomatic PAD (Lancet 1996;349-8:1329- 39)
 - Dual therapy with aspirin and clopidogrel beneficial in certain high-risk groups, such as after PCI

Aspirin

MOA

- Irreversibly Inhibits COX-1 & 2 enzymes (decreases prostaglandin precursors) and irreversibly inhibits formation of thromboxane A₂ (prostaglandin derivative)

Contraindications

- Allergy to salicylates or other NSAIDs, bleeding disorders

Cautions

- Peptic ulcer disease or erosive gastritis, heavy EtOH use (> 3 drinks/day)

Aspirin

Adverse reactions

- Bleeding, gastric discomfort

Drug Interactions

- Ketorlac, NSAIDs, Ticagrelor (if Aspirin dose is > 100 mg), anticoagulants

Monitoring

- Signs and symptoms (s/sx) bleeding, CBC (Hgb, Hct, Plt)

Clopidogrel (Plavix)

MOA:

- Irreversibly blocks the P2Y₁₂ component of the ADP receptor on the platelet surface, which prevents activation of GPIIb/IIIa receptor complex AND reduces platelet aggregation
- Requires transformation in vivo to active metabolite

Dosage

- 75 mg PO daily

Class:

- Antiplatelet, thienopyridine

Place in therapy

- Use instead of aspirin IF aspirin absolutely CI

Clopidogrel (Plavix)

Contraindications

- Active pathological bleeding (ex: peptic ulcer, intracranial hemorrhage)

Cautions

- Bleeding disorders, reduced CYP2C19 function

Adverse reactions

- Bleeding, bruising, rash, pruritis

Drug Interactions

- CYP2C19 inhibitors (strong) – controversial (PPIs, etc), anticoagulants due to bleeding risk

Monitoring

- S/sx bleeding, CBC (Hgb, Hct, Plt)

WARNING: DIMINISHED EFFECTIVENESS IN POOR METABOLIZERS

See full prescribing information for complete boxed warning.

- Effectiveness of Plavix depends on activation to an active metabolite by the cytochrome P450 (CYP) system, principally CYP2C19. (5.1)
- Poor metabolizers treated with Plavix at recommended doses exhibit higher cardiovascular event rates following acute coronary syndrome (ACS) or percutaneous coronary intervention (PCI) than patients with normal CYP2C19 function. (12.5)
- Tests are available to identify a patient's CYP2C19 genotype and can be used as an aid in determining therapeutic strategy. (12.5)
- Consider alternative treatment or treatment strategies in patients identified as CYP2C19 poor metabolizers. (2.3, 5.1)

Nitrates

Class:

- vasodilator, antianginal agent

MOA:

- Decreases myocardial oxygen demand
 - Venodilation & arterial-arteriolar dilation
- Increases myocardial oxygen supply
 - Dilates coronary arteries, collateral circulation, stenosed coronary arteries and relieves spasm

Nitrates

Contraindications

- Use with phosphodiesterase-5 inhibitors (sildenafil, tadalafil, vardenafil)

Caution

- Hypotension, Increased intracranial pressure

Adverse reactions

- Headaches (up to 35%) & flushing
- Postural hypotension
- Dizziness
- Reflex tachycardia

Nitrates

Drug Interactions –

- Sildenafil, Vardenafil, Tadalafil - AVOID USE!!

Monitoring Parameters

- ↓ chest pain
- ↓ # anginal episodes
- Amount of SL NTG used
- Resolution of ECG Δ s
- BP

Nitrates

Mechanisms of tolerance:

- Decreased availability of sulfhydryl radicals
- Activation of the RAAS system
- Increased intravascular volume
- Generation of free radicals with enhanced degradation of nitric oxide

Nitrate-free period of 8-14 hours

Nitrates

Acute chest pain

Sublingual nitroglycerin*

- 0.3 or 0.4 mg SL X 1 dose, If no relief after one dose, call 911, Repeat q 5 min up to 3 doses
- Sublingual tablets must be stored in original container
- Spray: 0.4 mg/spray – onto or under tongue
- Should be carried by all pts with angina
- May use prophylactically 5-10 min prior to activities that may provoke angina
- Take while seated Seal bottle tightly away from light

Intravenous nitroglycerin

- 5 mcg/min & titrate q 5 minutes by 5-10 mcg/min

Nitrates Long acting nitrates

Place in therapy

- In place of BB (if CI, unacceptable SE)
- In combo with BB (initial tx unsuccessful)
- Should be added to baseline therapy with either BB or CCB or combination of the two

Products Available

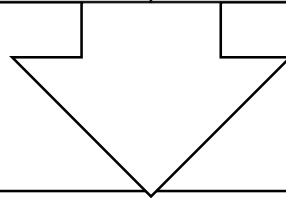
- ISMN – isosorbide mononitrate
 - Ismo – 20 mg BID (given 7 hours apart)
- ISMN – Extended release
 - Imdur – Starting dose 30 – 60 mg daily
 - Max dose: 240 mg daily
- ISDN – isosorbide dinitrate
 - Isordil – Starting 5 -20 mg q 6 hrs
 - Maintenance dose 40 – 80 mg

Nitrates Long acting nitrates

ISDN – Extended release

Dilatrate-SR – Initial dose
40 mg q 8 hrs

Maintenance dose 40 –
80 mg (Nitrate free 14hrs)



Transdermal patches (0.1, 0.2, 0.3, 0.4, 0.6
mg/hour)

Nitrate Product table 16-7

Product	Onset (min)	Duration	Initial Dose
Nitroglycerin			
IV	1-2	3-5 min	5 mcg/min
Sublingual/lingual	1-3	30-60 min	0.3 mg
Oral	40	3-6 h	2.5-9 mg tid
Ointment	20-60	2-8 h	0.5-1 in
Patch	40-60	>8 h	1 patch
Erythritol tetranitrate	5-30	4-6 h	5-10 mg tid
Pentaerythritol tetranitrate	30	4-8 h	10-20 mg tid
Isosorbide dinitrate			
Sublingual/chewable	2-5	1-2 h	2.5-5 mg tid
Oral	20-40	4-6 h	5-20 mg tid
Isosorbide mononitrate	30-60	6-8 h	20 mg daily, bid ^a

Beta Blocker

Mechanism of Action

- Decreases myocardial oxygen demand
- ↓ Heart rate
- ↓ Contractility
- ↓ Blood pressure
 - Do NOT improve oxygen supply

Place in therapy

- Beta blockers should be used as initial therapy (1st Line) for chronic angina requiring daily maintenance therapy
- improve exercise tolerance

Beta Blockers

- Use in all patients with LV dysfunction ($EF < 40\%$) with heart failure or prior myocardial infarction (MI), (unless CI)
 - **Metoprolol succinate, carvedilol, bisoprolol**
 - For patients after MI or acute coronary syndrome (ACS) Start at lower doses & titrate to goal slowly
 - Consider pharmacokinetics
 - Cardioselective agents preferred
 - Avoid agents with intrinsic sympathomimetic activity
 - Ace, Pin, Pen, Cart

Calcium channel blockers

Place in therapy

- As effective as β -blockers at preventing ischemic symptoms (may be more effective in preventing angina due to vasospasm).
- Verapamil and diltiazem are generally more effective than dihydropyridine CCBs.
- Avoid use of nondihydropyridine CCB with BB.

Nifedipine is a potent vasodilator that can cause baroreflex-mediated increases in sympathetic tone and HR

Calcium channel blockers

Decrease Myocardial O₂ demand)

- ↓ Wall tension
- ↓ HR (verapamil, diltiazem only)
- ↓ contractility (nonDHP and some DHP
 - (nifedipine > amlodipine > felodipine)

Increase Myocardial O₂ supply

- Dilating coronary arteries
- ↓ coronary vascular resistance and ↑ coronary blood flow = Reduction in vasospasm

Calcium Channel Blockers

Contraindications:

- Decompensated HF
- Bradycardia
- Sinus node dysfunction
- 2nd/3rd nodal block

Adverse Reactions:

- Hypotension
- Worsen heart failure
- Peripheral edema
- Constipation
- Headache, flushing, dizziness,
- Bradycardia
- AV block

Monitoring parameters

- HR, BP, peripheral edema

Drugs	Usual Dose	Duration of Action	Side Effects
Dihydropyridines			
<u>Amlodipine</u>	5–10 mg qd	Long	Headache, edema
<u>Felodipine</u>	5–10 mg qd	Long	Headache, edema
<u>Isradipine</u>	2.5–10 mg bid	Medium	Headache, fatigue
<u>Nicardipine</u>	20–40 mg tid	Short	Headache, dizziness, flushing, edema
<u>Nifedipine</u>	Immediate release:* 30–90 mg daily orally Slow release: 30–180 mg orally	Short	Hypotension, dizziness, flushing, nausea, constipation, edema
<u>Nisoldipine</u>	20–40 mg qd	Short	Similar to <u>nifedipine</u>
Nondihydropyridines			
<u>Diltiazem</u>	Immediate release: 30–80 mg 4 times daily Slow release: 120–320 mg qd	Short Long	Hypotension, dizziness, flushing, bradycardia, edema
<u>Verapamil</u>	Immediate release: 80–160 mg tid Slow release: 120–480 mg qd	Short Long	Hypotension, myocardial depression, heart failure, edema, bradycardia

Ranolazine (Ranexa™)

MOA: Not fully understood

- Inhibits the late phase of the inward Na⁺ channel in ischemic cardiac myocytes during cardiac repolarization, ↓ intracellular Na⁺ concentrations and thereby reducing Ca⁺⁺ influx via Na⁺-Ca²⁺ exchange.
- ↓ intracellular calcium reduces ventricular tension and myocardial oxygen consumption
- Does not reduce heart rate or blood pressure

Contraindications

- Hepatic cirrhosis, strong CYP3A4 inducers/inhibitors

Ranolazine (Ranexa™)

Class: Antianginal, miscellaneous

Place in Therapy

- Treatment of chronic angina
- Combination with amlodipine, beta- blockers and/or nitrates
- Reserve treatment for patients who have not achieved a satisfactory response to other antianginal drugs

Dose:

- Initiate at 500 mg PO BID
- Titrate to 1000 mg PO BID base on clinical symptoms

Ranolazine (Ranexa)

Caution

- Can prolong QT interval
 - Reserved for patients who have not achieved an adequate response with other antianginal drugs

Adverse reactions

- Constipation, headache, dizziness, peripheral edema

Drug interactions (MANY!)

- CYP3A4 inducers & inhibitors (azole antifungals, St. John's Wort, rifampin)
- NonDHP CCB, P-glycoprotein substrates (dabigatran, colchicine)
- Simvastatin

Monitoring

- EKG (for QT interval), BP (esp. if renal dysfunction)

ACE Inhibitors

Place In therapy

- ACE inhibitors should be considered in all patients with IHD, particularly those with HTN, DM, CKD, left ventricular dysfunction, and/or h/o MI
- Basis for this recommendation
- ACE inhibitors shown to reduce the risk of vascular events in patients with CSA or risk factors for IHD.

MOA/Therapeutic effects

- Vasodilation, ↓ sympathetic activity
- Plaque stabilization
- Reduced cardiovascular morbidity and mortality in pts with CAD

Blood Pressure Control

Specific medications will be based on patient specific characteristics

- ACEI, ARB, thiazide diuretics, CCB

2017 ACC-AHA Guidelines

Lipid Management

Moderate or high dose statin (unless CI)

For patients who don't tolerate statins:

- LDL-lowering therapy with bile acid sequestrants, niacin, or both is reasonable

Note:

- Dietary niacin must not be used as a substitute for prescription niacin
- Ability to initiate bile acid sequestrants is also dependent on patient's TG

Smoking Cessation

Smoking cessation

- Avoidance of exposure to tobacco smoke

Stepwise strategy

- Ask, Advise, Assess, Assist, Arrange, Avoid

Pharmacotherapy

- Nicotine replacement therapy
- Bupropion
- Varenicline

Diet

Reduced intake of saturated fats (<7% of total calories), trans fatty acids (to <1% of total calories), and cholesterol (to < 200 mg/day)

Increased amounts of fresh fruits, whole grains, and vegetables
low-fat dairy products

Increased amounts of low-fat dairy products

Reduced sodium intake

Diabetes Management

Blood glucose control

Goal HbA1C < 7 %

Education

Individualized education plan to optimize care and promote wellness

Importance of medication adherence for managing symptoms and slowing disease progression

Explanation of medication management and cardiovascular risk reduction strategies in manner that respects:

- Patient's level of understanding
- Reading comprehension
- Ethnicity

Education

Lipid management, BP control, Smoking cessation & avoidance of secondhand smoke exposure

Individualized medical, nutrition, and lifestyle changes for patients with diabetes mellitus to supplement diabetes treatment goals and education

Common symptoms of stress and depression to minimize stress-related angina symptoms (with comprehensive behavioral approaches for management of stress and depression)

Exercise

Increased physical activity

Moderate intensity exercise for 30 – 60 minutes/day for minimum of 5 days per week (7 days/week preferred)

Medically supervised programs (cardiac rehab) and physician-directed, home-based programs are recommended for at risk patients at first diagnosis

Complementary resistance training at least 2 days per week is reasonable

Weight management

Lifestyle physical activity, structured exercise, caloric intake, formal behavioral programs

Achieve (or maintain):

- BMI between 18.5 and 24.9 kg/m²
- Waist circumference
 - Men < 40 in (102 cm)
 - Women < 35 in (88 cm)
 - May be even less for certain racial groups

Initial goal of weight loss therapy: reduce body weight by 5-10% from baseline

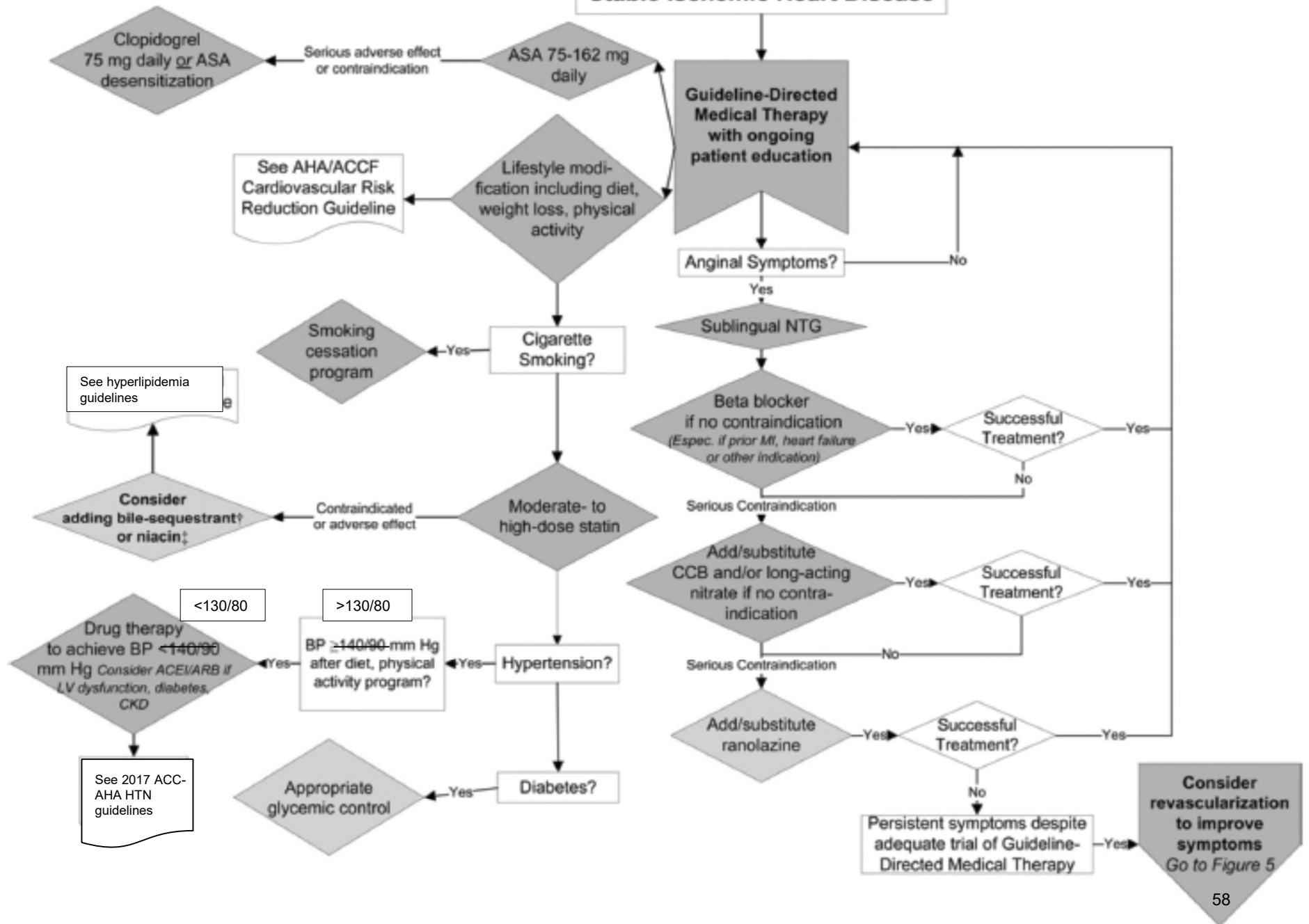
- With success, further weight loss can be attempted if indicated

Other Recommendations

Aldosterone antagonists for post-MI pts with EF < 40%, DM, or HF; as long as they don't have significant renal dysfunction or hyperkalemia; and they **MUST BE** already on therapeutic doses of ACEI and BB

An annual influenza vaccine is recommended for patients with SIHD

Stable Ischemic Heart Disease



Prinzmetal or Variant Angina

Vasospastic angina

Nitrates

- DOC for acute attacks
- High doses effective for preventing attacks

CCBs

- DOC for preventing attacks
- Nifedipine, diltiazem, verapamil

AVOID – BB

- Non-specific β Bs should be avoided 2/2 unopposed α -adrenergic stimulation

↑sympathetic tone & coronary vasospasm

Avoid alpha agonists (pseudoephedrine, oxymetazoline, etc.)

NOT recommended
for reducing CV risk or improving outcomes

Estrogen therapy

Vitamin E and C

Beta carotene

Vitamin B6 or B12, folate (for elevated homocysteine)

Chelation therapy

Garlic

Coenzyme Q10

Selenium

Chromium