Ischemic Heart Disease: Angina Pectoris

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Learning Objectives

☞ Contrast and compare chronic stable angina, with acute coronary syndromes unstable angina with respect to presentation, pathophysiology and approach to treatment

☞ Describe the role and clinical effects of agents used in the management of patients with chronic stable angina (ASA, anti-platelets, nitrates, beta-blockers, and CCBA's, ACE inhibitors, lipid lowering agents)

☞ Given a patient case, construct a treatment plan including selection of appropriate medication, sequencing of medications, dose, monitoring parameters and patient instructions.

Angina: Introduction

☞ Ischemic heart disease accounts for a substantial portion of death, disability and economic loss in most industrialized nations

☞ Coronary Artery Disease (CAD) is the leading cause of death in the U.S.

☞ Estimated 6.6M Americans have Angina

☞ 400,000 new cases diagnosed per year

☞ 27% of men and 14% of women will develop angina within 6 years of AMI

Angina Defined

☞ Angina pectoris is a <u>clinical syndrome</u> typically characterized by <u>discomfort</u> in the chest, jaw, shoulder, back or arm. Typically aggravated by exertion or emotional stress and relieved by nitroglycerine

☞ Typically occurs in patients with CAD involving at least one large epicardial artery

AHA/ACC Guideline Update for the Management of patients with Chronic Stable Angina R. Gibbons Nov 17, 2002

(www.americanheart.org)

Angina General

☞ **Angina pectoris is the development of chest pain due to myocardial ischemia**
- **coronary blood flow is inadequate to supply the heart with the needed oxygen and nutrients**
- **patients often have underlying coronary artery obstruction**
- **diagnosis of angina and its subclassification requires evaluation of the nature of the chest pain and circumstances surrounding its development**

Angina Types

☞ **Chronic Stable Angina: - a chronic and predictable development of chest pain upon exertion**

☞ **Unstable Angina: - a critical condition characterized by the unpredictable development of chest pain at rest or during minimal exertion. It is either accompanied by an increase in frequency and/or severity of pain within the recent (weeks to 1 or 2 months) past**

☞ **Vasospastic Angina or Prinzmetal's Angina: - is characterized by the unprovoked coronary artery spasm resulting in chest pain.**

Angina Types

☞**Chronic Stable Angina: - a chronic and predictable development of chest pain upon exertion**

- **Patients rely on antianginal medication throughout the day to perform various degrees of activity however, may prophylax with sublingual nitrates based on anticipated exertions**

Angina Types

☞**Unstable Angina (UA): - a critical condition characterized by the unpredictable development of chest pain at rest or during minimal exertion. It is either accompanied by an increase in frequency and/or severity of pain within the recent (weeks to 1 or 2 months) past.**

- **Patients with unstable angina are admitted to an acute care setting and managed aggressively with nitrates, beta-blockers, CCBA's, antiplatelets and anticoagulants.**
- **UA is part of the spectrum of acute coronary syndromes (ACS, see ACS lectures)**

Angina Types

☞ **Vasospastic Angina or Prinzmetal's Angina: -
is characterized by the unprovoked coronary
artery spasm resulting in chest pain.**

- **Patients with this angina may be relatively
young and have few or even no cardiac risk
factors**
- **the chest pain is often unpredictable and
cyclical in nature, sometimes reverting
spontaneously into remission.**

Other Forms of Ischemia

☞ **Silent Myocardial Ischemia: a phenomenon
experienced by a large percentage of patients
with ischemic heart disease who for various
reasons do not perceive chest pain despite
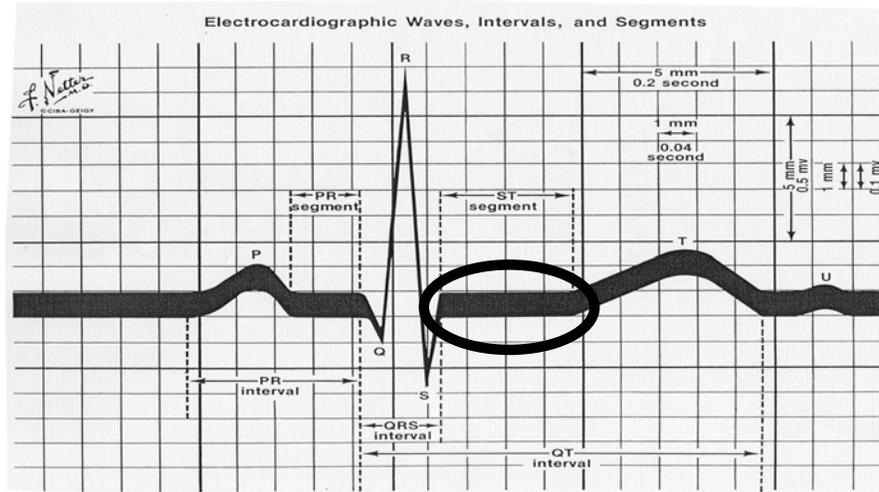EKG changes consistent with ischemic heart
disease.**

Events Associated with Ischemia
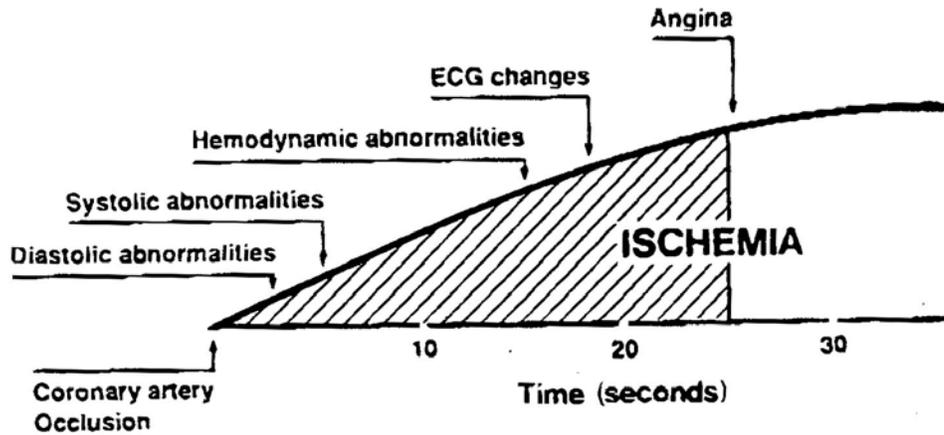
Exercise Provokes Ischemia
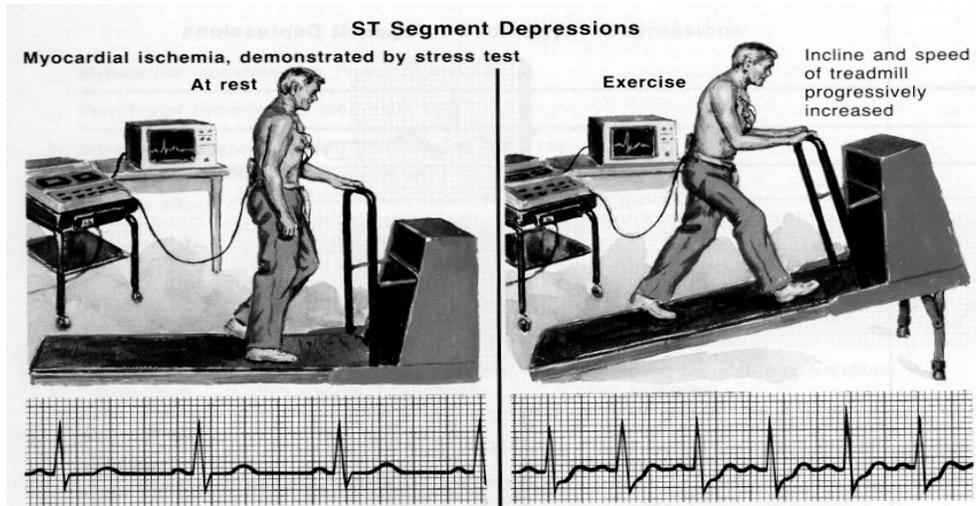
Typical ECG Complex and ST segment

Electrocardiographic Waves, Intervals, and Segments

Unstable Angina: Prognosis

☞ **Risk of death or ischemic complications is lower than with MI but higher than with stable angina.**

☞ **Prolonged episodes of severe chest pain are important markers of high-risk unstable angina**

Angina Therapy: General

☞ Ranges from intensive medical management (unstable angina) to conservative medical management with the goal of preventing progression to MI or death to

☞ Drug therapy may include

- Antiplatelets: ASA, GPIIb/IIIa and ADP inhibitors)
- beta-blockers
- calcium channel blockers
- nitrates
- Anticoagulants: (UFH/LMWH) heparin
- Lipid lowering agents
- ACE inhibitors
- analgesics (morphine)

Angina Therapy: General

☞ Therapy may require cardiac catheterization and myocardial revascularization: (usually unstable angina or advanced stable angina)

- Goal: to risk stratify and place in context the need for CABG or PTCA or stents

Angina Therapy: General

☞ **Therapy may require cardiac catheterization and myocardial revascularization:**

☞ **Indications may include**

- **failure to stabilize with adequate medical therapy**
- **recurrent unstable angina**
- **high-risk result from a non-invasive test**
- **prior revascularization procedure**
- **diagnosis or exclusion of significant CAD with multiple clinical episodes without objective documentation of ischemia**

Pharmacologic Therapy Angina

☞ **ASA in absence of contraindications**

☞ **B-blockers in pts. With prior MI or without prior MI**

☞ **ACE Inhibitors to pts with CAD who also have diabetes and/or LV systolic dysfunction**

☞ **LDL-C lowering therapy (target<100mg/dL)**

☞ **SI or nitroglycerin spray for immediate relieve of angina**

☞ **CCBA or long-acting nitrates for reduction in symptoms (when b-blockers contraindicated)**

☞ **CCBA or long-acting nitrates with b-blockers (when b-blockers not successful)**

☞ **CCBA and long-acting Nitrates as a substitute for b-blockers if b-blockers leads to unacceptable SEs**

Beta-Blockers for Angina

☞ Beta-Blockers should be started in the absence of contraindications (IV for high-risk patients) or oral for intermediate and low-risk patients for pts with prior MI

☞ Consider pt. intolerance due to pulmonary disease, especially asthma, LV dysfunction, risk of hypotension or severe bradycardia, diabetes, lipid disorders.

Nitrates for Angina

☞ Mechanism: reduce cardiac work afterload and preload reduction as well as coronary dilitation and possibly antiplatelet effects.

☞ Pharmacologic Issues: Variable bioavailability, short half-life, tolerance

☞ Monitor: SE's are extension of pharmacologic effects, hypotension, headache, especially post withdrawal

☞ Other Issues: multiple dosage forms, durations of action, cost, compliance

Nitrates for Angina

☞ **Outpatient only-** take one sl NTG in response to chest pain if already prescribed NTG, and if pain not relieved in 5 " call 911 (2004, STEMI Guidelines AHA page e96)

☞ **In patient only-** If symptoms not relieved with 3 sl NTG tablets each taken 5" apart and initiation of B-Blocker therapy (when possible), IV NTG is recommended.

☞ **Inpatient only-** IV NTG should start at 5-10 mcg/min continuous infusion and titrated up by 10 mcg/min q 5-10 minutes until relief of symptoms or limiting side effects (headache /hypotension SBP <90) or dose exceeds 200 mcg/min
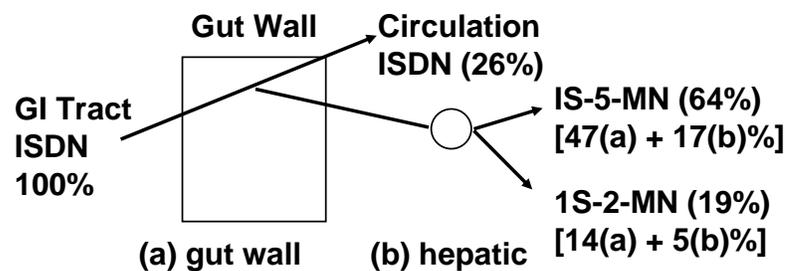 ● **Switch to oral nitrates within 24 hours when possible**

Nitrate Tolerance

☞ **Main limitation of long-term prophylactic nitrate therapy is the development of tolerance (both to hemodynamic effects on exercise capacity)**

☞ **Definition: decrease in response to a given amount of nitrate or the need of increased amounts of nitrate to maintain a continuous effect**

☞ **Tolerance can develop with all forms of nitrate therapy that maintain continuous blood levels of the drug**

☞ **Tolerance can develop after only a few doses**

☞ **Numerous trials, using exercise testing to assess the efficacy of nitrate therapy, have shown an attenuation of antianginal effect with chronic therapy**

Nitrates

☞ **Issues of Metabolism**
- **ISDN has a high first pass effect --> low blood levels of ISDN**
- **Approx. 26% (F = 26%) enters systemic circ. from po dose**
- **Majority of effect from ISDN is IS-5-MN**
- **ISMN (F=100%, t1/2 approx. 5 hrs, duration of effect 12 hrs, elimination- hepatic)**

Gut Wall   **Circulation**
ISDN (26%)

GI Tract
ISDN
100%

IS-5-MN (64%)
[47(a) + 17(b)%]

1S-2-MN (19%)
[14(a) + 5(b)%]

(a) gut wall   **(b) hepatic**

Patient Information: Nitrates

☞**Discuss issue of tolerance (rational ISDN-ISMN, importance of following instructions)**

☞**Do not crush or chew IMDUR tablets**

☞**Potential for hypotension and headache with all nitrates**

☞**ISMO or ISDN are not choice for immediate anti-anginal effect**

☞**Eccentric dosing (7 hour separation)**

☞**sl NTG -storage, dating, dosing,**

Angina Pectoris
"Guideline Review of Key Statements"

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Recommendations for Pharmacotherapy to Prevent MI and Death and to Reduce Symptoms

ACC/AHA 2002 Guideline Update for Chronic Stable Angina (www.americanheart.org)

➢ **Class I**
  - ➢ Aspirin in the absence of contraindications (Level of Evidence: A)
  - ➢ Beta-blockers as initial therapy in the absence of contraindications in patients with prior MI (Level of Evidence:A) or without prior MI. (Level of Evidence:B)
  - ➢ Angiotensin converting enzyme inhibitors in all patients with CAD who also have diabetes and/or LV systolic dysfunction (Level of Evidence:A)
  - ➢ Low-density lipoprotein-lowering therapy in patients with documented or suspected CAD and LDL cholesterol greater than 130 mg/dL, with a target LDL of less than 100 mg/dL (Level of Evidence: A)
  - ➢ Sublingual nitroglycerin or nitroglycerin spray for the immediate relief of angina (Level of Evidence:B)

Recommendations for Pharmacotherapy to Prevent MI and Death and to Reduce Symptoms

ACC/AHA 2002 Guideline Update for Chronic Stable Angina (www.americanheart.org)

➢ **Class I continued…**

☞   6. Calcium antagonists or long-acting nitrates as initial therapy for reduction of symptoms <u>when beta-blockers are contraindicated</u> (Level of Evidence:B)

☞   7. Calcium antagonists or long-acting nitrates in combination with beta-blockers <u>when initial treatment with beta-blockers is not successful</u> (Level of Evidence: B)

☞   8. Calcium antagonists and long-acting nitrates as a substitute for beta-blocker <u>if initial treatment with beta-blockers leads to unacceptable side effects</u> (Level of Evidence:C)

Recommendations for Pharmacotherapy to Prevent MI and Death and to Reduce Symptoms

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➢ **Class IIa**
  - ➢ Clopidogrel when aspirin is absolutely contraindicated (Level of Evidence:B)
  - ➢ Long-acting nondihydropyridine calcium antagonists instead of beta-blockers as initial therapy (Level of Evidence:B)
  - ➢ In patients with documented or suspected CAD and LDL cholesterol 100 to 129 mg/dL, several therapeutic options are available: (Level of Evidence:B)
    - ➢ Lifestyle and/or drug therapies to lower LDL to less than 100 mg/dL
    - ➢ Weight reduction and increased physical activity in persons with the metabolic syndrome
    - ➢ Institution of treatment of other lipid or non-lipid risk factors: consider use of nicotinic acid or fibric acid for elevated triglycerides or low HDL cholesterol

Recommendations for Pharmacotherapy to Prevent MI and Death and to Reduce Symptoms

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- ➢ **Class IIa Continued…**
  - ➢ **4. Angiotensin converting enzyme inhibitor in patients with CAD or other vascular disease (Level of Evidence:B)**
- ➢ **Class IIb**
  - ➢ **Low-intensity anticoagulation with warfarin in addition to aspirin (Level of Evidence:B)**
- ➢ **Class III**
  - ➢ **Dipyridamole (Level of Evidence:B)**
  - ➢ **Chelation therapy (Level of Evidence:B)**

Choice of Pharmacologic Therapy in Chronic Stable Angina

- ➢ **Beta-blockers also reduce cardiac events when used as 2° prevention in post-infarction patients and reduce mortality and morbidity among patients with HTN. On these bases, beta-blockers should be strongly considered as initial therapy for chronic stable angina. Diabetes mellitus is not a contraindication to their use. Nitrates have not been shown to reduce mortality with acute MI or in patients with CAD. Short-acting dihydropyridine calcium antagonists have been reported to increase adverse cardiac events. Long-acting or slow-release dihydropyridines, or nondihydropyridines, have the potential to relieve symptoms in patients with chronic stable angina without enhancing the risk of adverse cardiac events.**

Asymptomatic Patients with CSA to Prevent MI and Death
ACC/AHA 2002 Guideline Update for Chronic Stable Angina
(www.americanheart.org)

- Class I
  - Aspirin in the absence of contraindication in patients with prior MI (Level of Evidence:A)
  - <u>Beta-blockers as initial therapy</u> in the absence of contraindications in patients with prior MI (Level of Evidence:B)
  - Lipid-lowering therapy in patients with documented CAD and LDL cholesterol > 130mg/dL, with a target LDL of <100mg/dL (Level of Evidence:A)
  - ACE inhibitor in patients with CAD who also have diabetes and/or systolic dysfunction (Level of Evidence:A)

Asymptomatic Patients with CSA to Prevent MI and Death
ACC/AHA 2002 Guideline Update for Chronic Stable Angina
(www.americanheart.org)

- Class IIa
  - Aspirin in the absence of contraindications in patients without prior MI (Level of Evidence:B)
  - Beta-blockers as initial therapy in the absence of contraindications in patients without prior MI (Level of Evidence:C)
  - Lipid-lowering therapy in patients with documented CAD and LDL cholesterol of 100-129mg/dL, with a target LDL of 100mg/dL (Level of Evidence:C)
  - Angiotensin converting enzyme inhibitor in all patients with diabetes who do not have contraindications due to severe renal disease (Level of Evidence:B)