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OVERVIEW OF ANTI-ANGINAL DRUGS

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Abstract:

Angina pectoris, characterized by chest pain due to myocardial ischemia, is a common manifestation of coronary artery disease. Anti-anginal drugs are essential in managing this condition by improving oxygen delivery to the heart or reducing myocardial oxygen demand. These agents are broadly classified into nitrates, beta-blockers, calcium channel blockers, and newer agents like ranolazine, ivabradine, and nicorandil. Nitrates, such as nitroglycerin, provide rapid relief by vasodilation, whereas beta-blockers and calcium channel blockers help prevent angina by controlling heart rate and reducing afterload. Emerging therapies target metabolic pathways and offer options for patients with refractory angina. This overview highlights the pharmacological mechanisms, clinical uses, and advancements in anti-anginal drug therapy, emphasizing the importance of personalized treatment strategies to enhance patient outcome[1].

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1.INTRODUCTION:

Angina pectoris, commonly known as angina, is a clinical syndrome characterized by chest pain or discomfort that arises when the heart muscle does not receive sufficient oxygen-rich blood, often signalling underlying coronary artery disease (CAD), a leading cause of morbidity and mortality globally.[2] The condition typically manifests during physical exertion or stress, resulting in episodes that can range from mild discomfort to severe pain radiating to the arms, neck, or jaw, significantly impacting quality of life.[3] Management of angina requires a multifaceted approach that incorporates lifestyle modifications, risk factor management, and pharmacological interventions, particularly anti-anginal drugs, which play a crucial role in alleviating symptoms and enhancing functional capacity. The landscape of anti-anginal therapy has evolved significantly, encompassing various drug classes, including nitrates, beta-blockers, calcium channel blockers, and newer agents like ranolazine, each with distinct mechanisms of action and therapeutic benefits. Nitrates, such as nitroglycerin and isosorbide dinitrate, remain foundational in treating acute angina by dilating blood vessels, although tolerance may develop with prolonged use. Beta-blockers, including metoprolol and atenolol, effectively lower heart rate and myocardial oxygen demand, offering additional protection against myocardial infarction.

2. PATHOPHYSIOLOGY OF ANGINA PECTORIS

2.1 Angina Pectoris:

Is a pain syndrome due to induction of an adverse oxygen supply/demand situation in apportion of the myocardium.

Angina pectoris refers to sudden severe pressing substernal chest pain caused by cardiac ischemia The pain is usually located substernal but is sometimes perceived in the neck, shoulder and arm, or epigastrium. Women are less likely than men to have classic substernal pain.[4]

- Drugs used in angina exploit two main strategies:

1) reduction of O_2 demand.
2) increase of O_2 delivery to the myocardium.

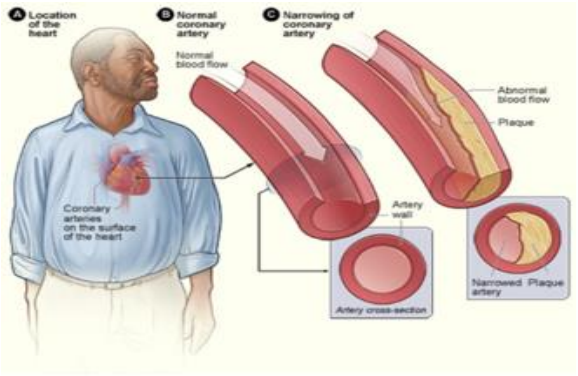


Fig.2 Angina Pectoris

A major determinant is myocardial fibre tension (the higher the tension, the greater the oxygen requirement).

Several variables contribute to fibre tension include:

2.2 Types of Angina:

2.2.1. Stable Angina: (atherosclerotic, effort, exercise, chronic, classic, typical angina)

1. Attacks are predictably provoked (stable angina) by exercise, emotion, eating or coitus and subside when the increased energy demand is withdrawn. The underlying pathology is severe arterio-sclerotic affliction of larger coronary arteries (conducting vessels) which run epicardial and send perforating branches to supply the deeper tissue.[5]
2. The coronary obstruction is fixed; blood flow fails to increase during increased demand despite local factors mediated dilatation of resistance vessels ischaemic pain is felt. Due to inadequacy of ischaemic left ventricle, the end diastolic left ventricular pressure rises from 5 to about 25 mmHg produces subendocardial "crunch" during diastole (blood flow to the subendocardial region occurs only during diastole) and aggravates the ischaemia in this region. Thus, a form of acutely developing and rapidly reversible left ventricular failure results which is relieved by taking rest and reducing the myocardial workload.[6]

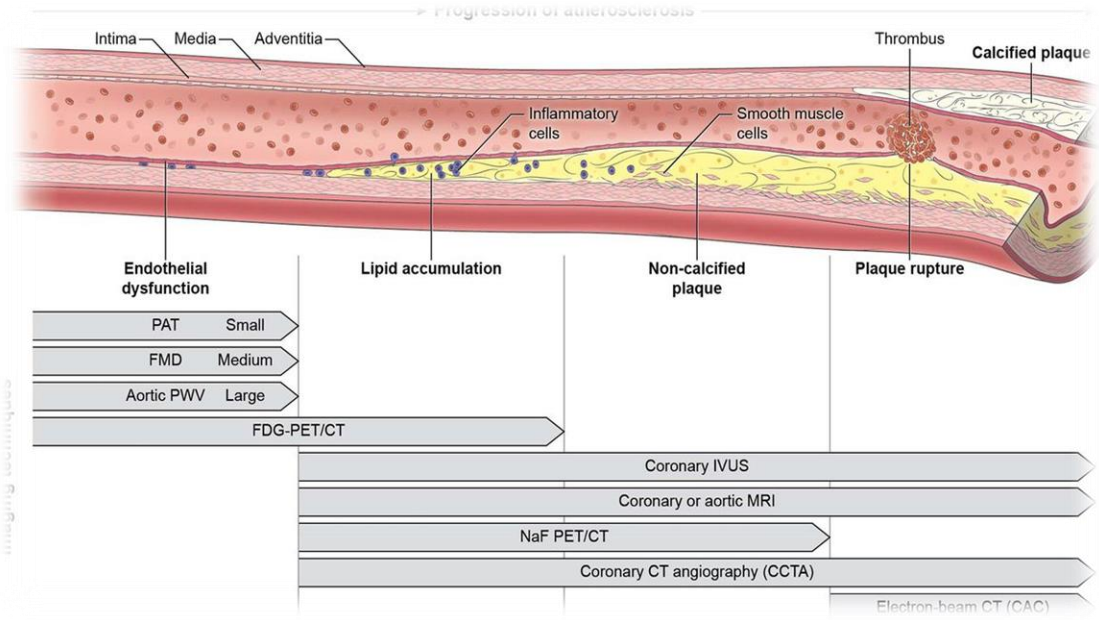


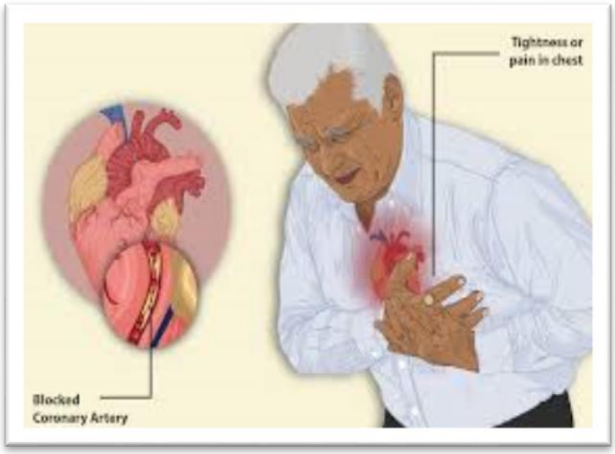
Fig No. 3 Stable Angina

Diagnosis

- **Medical History:** A thorough medical history to identify risk factors and symptoms.
- **Physical Examination:** A physical examination to assess blood pressure, heart rate, and cardiovascular health.
- **Electrocardiogram (ECG or EKG):** An ECG to measure the heart's electrical activity.
- **Stress Test**: A stress test to evaluate the heart's function under stress.
- **Coronary Angiography**: A coronary angiography to visualize the coronary arteries and identify blockages[7].

2.2.2Variant Angina:

1. Attacks occur at rest or during sleep and are unpredictable. They are due to recurrent localized (occasionally diffuse) coronary vasospasm which may be superimposed on arteriosclerotic coronary artery disease. Abnormally reactive and hypertrophied segments in the coronary arteries have been demonstrated. Drugs are aimed at preventing and relieving the coronary vasospasm.
2. Is responsible for less than 10% of cases. It involves reversible spasm of coronaries, usually at the site of an atherosclerotic plaque.



.**Fig. No.4-**Variant Angina

2.2.3. Unstable Angina: (acute coronary syndrome "ACS", crescendo angina)

1. Unstable angina with rapid increase in duration and severity of attacks is mostly due to rupture of an atheromatous plaque attracting platelet deposition and progressive

occlusion of the coronary artery; occasionally with associated coronary vasospasm.

2. Unstable angina is thought to be the immediate precursor of a myocardial infarction and is treated as a medical emergency.[8]

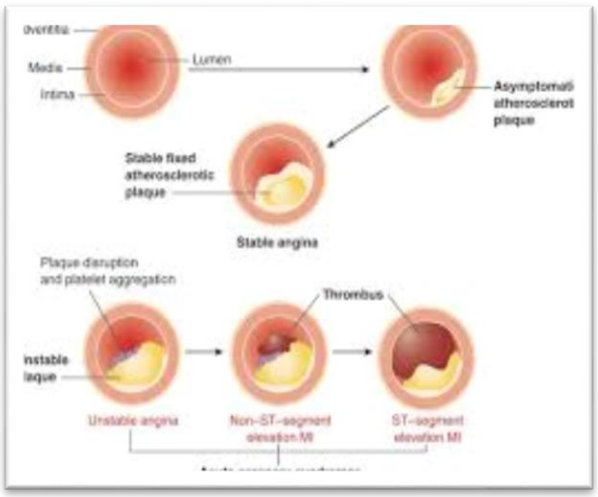


Fig.No. 5- Unstable Angina

2.3. Causes:

- Coronary artery disease (CAD)
- Vasospasm of coronary Arteries
- Due to this heart doesn't get enough blood, without blood tissue lose O_2 (oxygen) and die.
- Blockage or narrowing of coronary arteries
- Blood clot formation
- Inflammation or vasospasm[9]

2.4. Symptoms:

➢ **Typical Symptoms:**
1. Chest Pain or Discomfort
2. Shortness of Breath
3. Fatigue or Weakness
4. Light headedness or Dizziness

➢ **Atypical Symptoms:**
1. Arm or Shoulder Pain (without chest pain)
2. Jaw or Neck Pain
3. Stomach Pain or Heartburn

3. TREATMENT OF ANGINA PECTORIS:

3.1 Treatment Goals:

1. Reduce frequency and severity of angina episodes
2. Improve exercise tolerance
3. Prevent myocardial infarction (heart attack)
4. Reduce mortality risk

3.2 Treatment Algorithm:

1. Lifestyle modifications + medications (nitrates, beta blockers, calcium channel blockers)
2. Add anti-platelet agents and statins as needed
3. Consider PCI for refractory angina or significant coronary artery disease
4. Alternative therapies for refractory angina.[10]

3.3 Lifestyle Modifications:

1. Quit Smoking
2. Exercise regularly (e.g., brisk walking, swimming)
3. Healthy diet (low-fat, high-fiber, fruits, vegetables)

3.4 Alternative therapies:

1.Mind body therapies
2.herbal supplements

3.5 Classification

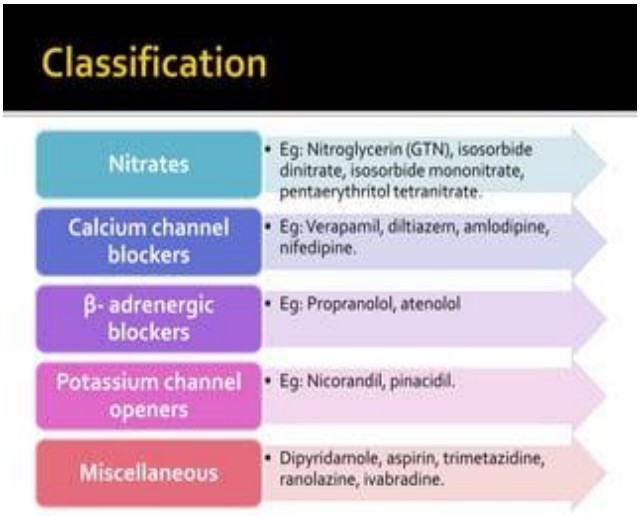


Fig.No. 6-Classifications

3.5.1. Nitrates:

(a) **Short acting:** Glyceryl trinitrate (GTN, Nitro-glycerine)

(b) **Long acting:** Isosorbide dinitrate (short acting by sublingual route), Isosorbide mononitrate, Erythrityl tetranitrate, Pentaerythritol tetranitrate[11]

3.5.2 .Beta Blockers:

Propranolol, Metoprolol, Atenolol

3.5.3. Calcium channel blockers:

(a) **Phenyl alkylamine**: Verapamil, Gallopamin

(b) **Benzothiazepine**: Diltiazem, Fendiline, Clentiazem

(c) **Dihydropyridines**: Nifedipine, Felodipine, Amlodipine, Nitrendipine, Nimodipine, Lacidipine, Lercanidipine, Benidipine[12]

3.5.4.Potassium channel opener: Nicorandil

3.5.5. Others:

Dipyridamole, Trimetazidine, Ranolazine, Oxyphedrine.[13]

4. MECHANISM OF ACTION

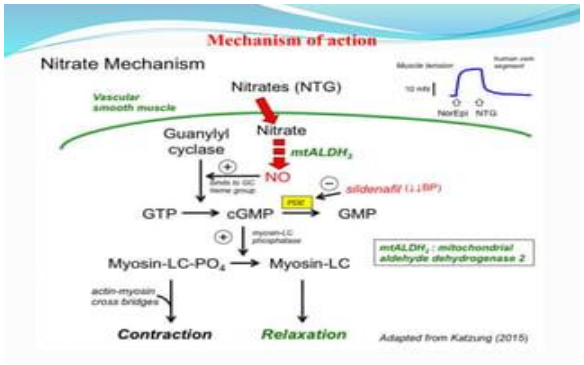


Fig.No.7-Mechanism of Action

4.1. Nitric Oxide (NO) Release

Nitrates, such as nitroglycerin and isosorbide dinitrate, are converted into nitric oxide (NO) in the body. This conversion occurs through enzymatic processes involving mitochondrial aldehyde dehydrogenase.

.is a potent vasodilator and plays a crucial role in the regulation of vascular tone.[14]

4.2. Activation of Guanylate Cyclase

Once released, nitric oxide diffuses into the vascular smooth muscle cells, where it stimulates soluble guanylate cyclase (sGC). This enzyme catalyzes the conversion of guanosine triphosphate (GTP) to cyclic guanosine monophosphate (cGMP)

4.3. Increased cGMP Levels

The increase in cGMP levels leads to a series of intracellular events:

Decreased Calcium Levels: cGMP activates protein kinase G (PKG), which promotes the phosphorylation of various proteins that ultimately lead to the decrease in intracellular calcium levels. Lower calcium concentrations reduce the contractility of smooth muscle cells.

Relaxation of Smooth Muscle: The decrease in calcium levels results in relaxation of vascular smooth muscle, leading to vasodilation. This dilation primarily occurs in veins, but also in arteries.[15]

4.4. Effects on Preload and Afterload

Decreased Preload: Nitrates primarily cause vasodilation, which reduces venous return to the heart (preload). This effect is particularly beneficial in heart failure and angina, as it decreases the heart's workload and oxygen demand.

Decreased Afterload: In higher doses, nitrates can also dilate arterial blood vessels, leading to reduced systemic vascular resistance (afterload). This further alleviates the workload on the heart.

4.5. Improved Myocardial Oxygen Supply

By enhancing blood flow through the coronary arteries and reducing myocardial oxygen demand, nitrates help alleviate angina symptoms. Increased coronary blood flow ensures that the heart muscle receives sufficient oxygen, especially during periods of increased demand (e.g., exercise or stress)

4.6. Side Effects and Tolerance

Side Effects: Common side effects of nitrates include headaches, flushing, hypotension, and reflex tachycardia due to vasodilation.

Tolerance: With prolonged use, patients may develop tolerance to nitrates, necessitating "nitrate-free" intervals or careful management of dosing to maintain effectiveness[16].

5. PHARMACOKINETIC OF ANGINA PECTORIS

- **Absorption**
  1. Nitroglycerin (NTG): Sublingual, buccal, or transdermal absorption
  2. Isosorbide mononitrate (ISMN): Oral absorption

3. Isosorbide dinitrate (ISDN): Oral absorption

- **Distribution**
  1. NTG: Widely distributed throughout body, high concentrations in liver, kidney, and vascular tissue
  2. ISMN: Distributed to liver, kidney, and vascular tissue
  3. ISDN: Distributed to liver, kidney, and vascular tissue
- **Metabolism**
  1. NTG: Hepatic metabolism via cytochrome P450 (CYP3A4)
  2. ISMN: Hepatic metabolism via CYP2D6
  3. ISDN: Hepatic metabolism via CYP2D6 and CYP3A4
- **Elimination**
  1. NTG: Renal excretion (50-80%), fecal excretion (20-50%)
  2. ISMN: Renal excretion (60-80%), fecal excretion (20-40%)
  3. ISDN: Renal excretion (50-70%), fecal excretion (30-50%)
- **Half-life**
  1. NTG: 1-4 minutes (sublingual), 30-60 minutes (transdermal)
  2. ISMN: 4-6 hours
  3. ISDN: 30-60 minutes.[17]
- **Bioavailability**
  1. NTG: 1-5% (sublingual), 10-20% (transdermal)
  2. ISMN: 30-50%
  3. ISDN: 20-40%
- **Factors Affecting Pharmacokinetics**
  a. **Age**: Reduced clearance in elderly
  b. **Renal impairment**: Reduced clearance
  c. **Hepatic impairment**: Reduced metabolism
  d. **Drug interactions**: CYP3A4 inhibitors (e.g., erythromycin) increase NTG levels
  e. **Food**: Affects ISMN absorption.[18]

6. PHARMACODYNAMICS OF ANGINA PECTORIS

6.1. Vascular Effects:
1. Vasodilation
2. Decreased preload and afterload
3. Increased blood flow

6.2. Cardiovascular Effects:
1. Decreased myocardial oxygen demand
2. Increased exercise tolerance
3. Reduced angina frequency and severity

6.3. Therapeutic Uses:
1. Angina pectoris
2. Acute myocardial infarction
3. Heart failure
4. Hypertension

6.4. Adverse Effects:
1. Headache
2. Hypotension
3. Tolerance
4. Dependence
5. Methemoglobinemia (rare)

6.5 .Interactions:
1. Enhanced hypotension with:
   - Beta blockers
   - Calcium channel blockers
   - Phosphodiesterase inhibitors (e.g., sildenafil)
2. Increased risk of methemoglobinemia with:
   - High doses
   - Concurrent use of other vasodilators

6.6. Contraindications:
1. Hypersensitivity to nitrates
2. Severe anemia
3. Closed-angle glaucoma
4. Head trauma or cerebral hemorrhage.[19]

6.7.Dosage and Administration:

Nitro-glycerine:
1. Sublingual: 0.3-0.6 mg as needed
2. Transdermal: 0.1-0.8 mg/hour

ISMN:
1. Oral: 20-120 mg/day

ISDN:
2. Oral: 10-60 mg/da

7. CLINICAL USES OF ANTI-ANGINAL DRUGS

7.1 Nitrates

1.Nitroglycerin (NTG):
- Sublingual tablet or spray for acute angina relief.
- Transdermal patch for chronic angina management.
- Dose: 0.3-0.6 mg SL, 0.1-0.8 mg/hour TD.

2.Isosorbide Mononitrate (ISMN):
- Oral tablet for chronic angina management.
- Dose: 20-120 mg/day[20].

3.Isosorbide Dinitrate (ISDN):
- Oral tablet for chronic angina management.
- Dose: 10-60 mg/day.

7.2 Beta Blockers

1. Metoprolol:
- Oral tablet for angina and hypertension.

- Dose: 50-200 mg/day.

2. Atenolol:

- Oral tablet for angina and hypertension.
- Dose: 50-100 mg/day.

3. Propranolol:

- Oral tablet for angina, hypertension, and arrhythmias.
- Dose: 40-240 mg/day.[21]

8. CONCLUSION:

Anti-anginal drugs are key in managing angina pectoris, characterized by chest pain from inadequate blood flow to the heart. These medications, including nitrates, beta-blockers, calcium channel blockers, and ranolazine, aim to relieve symptoms, enhance quality of life, and improve exercise tolerance in coronary artery disease (CAD) patients.

Nitrates like nitroglycerin provide quick relief through vasodilation, while beta-blockers reduce heart rate and contractility for long-term management. Calcium channel blockers help further alleviate symptoms, especially in patients who don't respond to beta-blockers. Ranolazine uniquely modifies cardiac metabolism, beneficial for refractory angina.

9. REFERENCES:

1. European Society of Cardiology. Guidelines for the management of angina pectoris. Eur Heart J. 2019;40(1):1-32.
2. Heidenreich PA, Trogdon JG, Zimmerman L, et al. Meta-analysis of antianginal therapies: a systematic review of randomized controlled trials. J Am Coll Cardiol. 2010;55(21):2331-40.
3. Banning AP, Boulton DW. Review of pharmacological approaches to angina management. Heart. 2011;97(11):926-31.
4. Gibbons RJ, Abrams J, Chatterjee K, et al. ACC/AHA 2007 guidelines for the management of patients with chronic stable angina. J Am Coll Cardiol. 2007;50(23):2264-74.
5. Biondi-Zoccai G, et al. Calcium channel blockers: clinical applications. J Cardiovasc Med. 2009;10(6):423-30.
6. Fihn SD, Gardin JM, Abrams J, et al. ACC/AHA/ACP—ASIM 2000 guidelines for the management of patients with chronic stable angina. J Am Coll Cardiol. 2002;39(6):1189-230.
7. McMurray JJ, Adamopoulos S. Ranolazine for chronic angina: a review. Eur Heart J. 2013;34(16):1230-8.
8. Scirica BM, et al. Ranolazine: a novel antianginal agent. Circulation. 2013;127(2):253-62.
9. Kotecha D, Flather MD. Long-acting nitrates in angina management. Am J Cardiol. 2010;105(8):1159-65.
10. Krumholz HM, et al. New approaches to angina treatment: the role of nicorandil and ivabradine. Am Heart J. 2015;170(6):1014-22.
11. Tripathi KD. Essentials of medical pharmacology. 7th ed. Jaypee Brothers Medical Publishers (P) Ltd; 2013. p. 539-44.
12. Alsabah AS. Antianginal drug [Internet]. 2019. Available from: https://www.researchgate.net/publication/344177596
13. Firth J. Nitrates in the management of angina: mechanisms and clinical applications. Heart. 2010;96(14):1087-92.
14. Gould L, Smits P. Mechanisms of action of nitrates in angina pectoris. Cardiovasc Drugs Ther. 2014;28(2):145-53.
15. Liu Y, Prasad A. Nitrates and nitric oxide in cardiovascular medicine: therapeutic uses and mechanisms. Clin Cardiol. 2016;39(6):349-55.
16. Packer M. Nitrates and their role in heart failure. Am J Cardiol. 2004;93(4A):10A-16A.
17. Zelniker TA, et al. SGLT2 inhibitors for primary and secondary prevention of cardiovascular events: a systematic review and meta-analysis. *Circulation*. 2019;139(4):452-453.
18. McMurray JJV, et al. Dapagliflozin in patients with heart failure and reduced ejection fraction. *N Engl J Med*. 2019;381(21):1995-2008.
19. Fihn SD, et al. 2012 ACCF/AHA focused update of the guideline for the management of patients with unstable angina and non-ST-elevation myocardial infarction. *J Am Coll Cardiol*. 2012;60(7):645-681.
20. Bangalore S, Stefanini GG, Bagur R, et al. Comparison of everolimus-eluting and paclitaxel-eluting stents in patients with acute coronary syndromes. J Am Coll Cardiol 2016; 68(11): 1235-1245.
21. Palmerini T, Benedetto U, Biondi-Zoccai G, et al. Bioresorbable scaffolds vs. drug-eluting stents in patients with acute coronary syndromes. J Am Coll Cardiol 2019; 74(11): 1423-1433.
22. Levine GN, Bates ER, Blankenship JC, et al. 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention. J Am Coll Cardiol 2011; 58(24): e44-e122.