Current Treatment Of Ischemic Heart Disease In the United States: An Overview

By Dr Gary Mo
Ischemic Heart Disease in the US

1. Cardiovascular disease remains the most common cause of death and is responsible for almost 1 million deaths per year in the US.

2. In 2005, the estimated direct and indirect costs of cardiovascular disease were 393.5 billion.

3. Ischemic heart disease is the most prevalent cardiovascular disease in the US.

4. Each year, 1.5 million people admitted to hospitals for unstable angina / NSTEMI, and half million will have MI.
Detection of Ischemic heart Disease

1. Clinical symptoms

2. Diagnostic Tests:
   a. Ultra fast Cat scan
   b. Treadmill exercise stress test
   c. Stress echocardiogram
   d. SPECT [Thallium/Cardiolite myocardial perfusion test]
   e. CAT scan angiogram [16-slices, 64-slices]
   f. Coronary angiogram
Treatment strategy for Ischemic Heart Disease

1. Identification and modification of risk factors
2. Life style change
3. Drug treatment
4. Interventional treatment [balloon angioplasty, coronary stents etc.]
5. Surgical treatment [Coronary artery bypass surgery]
Major Risk Factors for Ischemic Heart Disease [ IHD ]

1. Smoking
2. Hypertension  >140 / >90
3. Hyperlipidemia [Cholesterol, Triglyceride]
4. Diabetic
5. Family History of premature coronary artery disease [IHD in male first-degree relative < 55 years; IHD in female first-degree relative < 65 years]
Emerging Risk Factors for IHD

1. Lipoprotein(a)
   - Individual with increased level has increased IHD risk.
2. Homocystein level
   - Increased level with increased IHD risk.
3. Prothrombotic factors
   - Fibrinogen levels may correlate with coronary risk.
4. Proinflammatory factors
   - C-reactive protein correlate with coronary risk and ACS outcome.
5. Impaired fasting glucose
6. Post-menopausal state
   - Reduced HDL-C and increased LDL-C.
Hypertension Treatment

Goal: < 140 / < 90  Diabetic < 130 / < 80

1. Diet [ low salt ]
2. Life style change [ exercise etc. ]
3. Drugs:
   a. Diuretics
   b. B-Blockers
   c. Ca-Blockers
   d. ACE-Inhibitors and ARBs
   e. Alfa-Blockers
   f. Central-acting ( older meds. like Aldomet, clonidine )
ASCOT (Anglo-Scandinavian Cardiac Outcome Trials)

19000 patients
Trial prematurely stopped.
BP arm: Amlodipine + Perindopril Vs Atenolol + Diuretics
Result: 10% RR all cause mortality, fatal / nonfatal MI, CHD, new on-set DM.
Hyperlipidemia Trials

1% reduction LDL-C level equals 1% reduction of major coronary heart disease events.

Major Lipid Trials: Decrease Events (%)

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<th>Study</th>
<th>All cause mortality</th>
<th>CV events</th>
<th>Need for PTCA or CABG</th>
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<td>30</td>
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<td>HPS</td>
<td>RR coronary deaths</td>
<td>18%</td>
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Hyperlipidemia Treatment: NCEP - ATP III Guideline

Risk factors: cigarette smoking, hypertension, low HDL-C (< 40 mg/dl), DM, FH, Age (man > 45 yr women > 55 yr) Obesity, Physical inactivity, atherogenic diet.

1. Less than 2 risk factors LDL-C goal: < 160
2. 2 or more risk factors LDL-C goal: < 130
3. 2 or more risk factors + established atherosclerosis / DM LDL-C goal: < 100
4. High risk (prior MI, CABG, PTCA, severe DM etc) LDL-C goal: < 70
Drug Treatment for Hyperlipidemia

1. HMG-CoA Reductase Inhibitors "Statins"
   a. Lipoprotein effects. Decrease LDL-C (30-50%), Increase HDL-C (5-15%), Decrease TG (15-35%)
   b. Pleiotropic effect. Improve endothelial dysfunction, stabilize plaques, decrease platelet aggregates, decrease inflammation and cardiovascular event.

2. Cholesterol Absorption Inhibitors "Ezetimibe/Zetia"
   10 mg/day brings 18% reduction LDL-C / 4% increase in HDL-C

3. Nicotinic Acid/Niacin. Decrease LDL-C (10-25%), increase HDL-C (dose-dependent 10-30%) "most effective". Decrease TG (20-35%)

4. Fibrates "fenofibrate etc". Decrease TG primarily (25-50%). Increase HDL-C. Increase LDL-C in Hypertriglyceridemia.

5. Bile acid sequestrants. "cholestyramine" Decrease LDL-C 10-25%. Increase TG.
Omega-3 Fatty Acids

- Source: seafood, fatty fish, oils (flaxseed, canola, soybean oils)
- Mortality from MI in the Eskimo population in Greenland was significantly lower than in Danish population.
- Eskimo diet rich in Omega-3 / monounsaturated fatty acids (EPA i.e Eicosapentaenoic acid and DHA i.e Docosahexaenoic acid).
- 4 gm / day Omega-3 fatty acids decrease serum TG by 25-30%; raised LDL_C by 5% to 10%; HDL-C by 1-3%.
- EPA: anti-thrombotic, anti-inflammatory, endothelial relaxation, decrease susceptibility of ventricular arrhythmia.
Chronic stable IHD

1. Modification and treatment of risk factors: Hypertension, Hyperlipidemia, DM etc.
2. Exercise and life style changes
3. Drugs: ASA
   Clopidogrel if ASA intolerant
   Nitrates
   B-blockers
   Ca-blockers
   Ace-inhibitors
ASA

1. Remains a cornerstone of therapy for IHD.
2. Effective, inexpensive, well-tolerated
3. It irreversibly acetylates cyclooxgenase I, preventing synthesis of Thromboxane A2 (one of agonists activating platelets).
4. Weak antiplatelet potency since ASA inhibits only one mechanism through which platelet activation can occur.
5. ASA--resistance occurs between 5% and 8% patients.
Indications for ASA

1. All patients with stable coronary heart disease
2. All patients with Non-ST elevation Acute Coronary Syndromes
3. All patients with ST-Elevation Myocardial Infarction
4. All patients undergoing PCI (Percutaneous Coronary Interventions)
5. Also used in Primary prevention of Coronary Heart Disease in women, controversial in men because of increased risk of hemorrhagic strokes.
6. Used in secondary prevention of CHD in both men and women.
Clopidogrel (Plavix)

1. Irreversibly inhibits Adenosine Diphosphate (ADP) from binding to its Platelet P2Y12 receptor, resulting in potent inhibition of platelet activation, degranulation, and aggregation.

2. Clopidogrel Vs Aspirin in Patients at risk of Ischemic Events (CAPRIE) Trials for secondary prevention of ischemic events: Established Clopidogrel as a safe and at least equally effective alternatives for secondary preventions in patients with Vascular disease who are intolerant of ASA.
Indications for Clopidogrel

1. All patients with stable Coronary Heart Disease intolerant of ASA.
2. All patients with Non-ST Elevation Acute Coronary Syndromes ( in combination with ASA : CURE Trial showed RR of 20% in MI )
3. Patients with ST-Elevation Myocardial Infarction presenting <12 Hrs. after symptom onset treated medically
4. All patients undergoing PCI
5. Post- Coronary stent insertion ( up to 12 months )
GP IIb/IIIa antagonists (Abciximab, Eptifibatide etc.)

1. Prevent fibrinogen / Von Willibrand factor from binding to platelet GP IIb/IIIa receptors and subsequently cross-linking with adjacent platelets, significantly reducing platelet aggregation.

2. Indications:
   a. High-risk patients (elevated Troponin level, ischemic ST-segment deviations or ongoing ischemia) with Non-ST elevation Acute Coronary Syndromes.
   b. High-risk patients undergoing PCI.
Non-ST Elevation Acute Coronary Syndromes Treatments

A. Anti-ischemic treatment:
1. Bed rest and Telemetry
2. Oxygen to maintain O2 saturation > 90%
3. Nitrates (sublingual, then oral / tropical, then IV for ongoing pain)
4. Morphine (IV for pain, CHF)
5. B-blocker (first dose IV for ongoing pain, then oral)
6. Non-dihydropyridine Ca-blocker IF B-blocker contraindicated. (Diltiazem, Verapamil, Bepridil)
7. Ace-Inhibitor for patients with Hypertension, Decreased LVEF, CHF or DM
Non-ST Elevation Acute Coronary Syndromes Treatments

B. Anti-platelet Treatment:
1. ASA
2. Clopidogrel in combination with ASA
3. GP IIb/IIIa IF invasive procedure planned

C. Anti-thrombin Treatment:
1. SQ LMWH or IV Heparin in addition to anti-platelet treatment.

D. Invasive Vs Conservative treatment.
Invasive Strategy

1. Recurrent angina / ischemia at rest or with low-level activity despite medical treatment.
2. Elevated Troponin
3. New ST-segment depression
4. Recurrent ischemia with CHF, S3, Pulmonary edema, MR
5. High risk finding on stress test
6. LVEF <40% on non-invasive study
7. Hemodynamic instability
8. Sustained VT
9. PCI within 6 months
10. Prior CABG
11. In absence of above findings, either early conservative or early invasive strategy may be offered in patients without contraindication for revascularization.
Acute ST-Elevation Myocardial Infarction

Reperfusion Therapy:

A. Lysis (Thrombolytic Therapy)
   Adjunctive therapies

B. Primary Percutaneous Coronary Interventions (PCI)
   Adjunctive therapies

C. Rescue PCI
Current Short-fall in the United States

1. 70% of eligible patients in the US receive Reperfusion Therapy.

2. Door-to-needle time > 30 minutes

3. Door-to-balloon time > 115 minutes

4. Average delay to Emergency Department is 120 minutes
Fibrinolysis

Definitely Helpful
1. ST elevation (&gt; 0.1 mv in 2 or more contiguous or adjacent leads); &lt; 12 hours
2. New LBBB + History suggestive of AMI.

Probably Helpful
1. ST elevation, 12-24 hrs. with ongoing ischemia.

Probably Not Helpful
1. ST elevation, &gt; 24 hrs, pain resolved.
2. ST depressions only.
Tenecteplase

1. TNK-tPA
2. Triple combination mutant of tPA
3. t\( \frac{1}{2} \) 20 minutes ; single bolus ( weight adjusted )
4. Clot lysis
5. Safe
Adjunctives for Fibrinolysis

A. Heparin
   1. 60 U/kg bolus, If >70 kg, maxi. bolus 4000 U
   2. 12 U/kg/hr infusion, If >70kg, maxi. infusion 1000 U/hr.
   3. Target aPTT 50-60 sec.

B. GP IIb/IIIa inhibitors
   1. No role in ST-Elevation Myocardial Infarction as either
      a. substitute for lysis or
      b. adjunctive therapy with full dose lysis.

C. Clopidogrel
   1. Improved patency, survival, and decrease re-infarction
   2. No excessive bleeding.
Primary PCI (Percutaneous Coronary Interventions)

1. Preferred method of early Reperfusion when AVAILABLE.
   a. Expertise: Individuals performed 75 PCI / yr
   b. Local logistics: Centers done >200 PCI / yr + 36 Primary PCI / yr
   c. Surgical back-up

2. Door-to-ballon time < 90 minutes
2004 ACC /AHA Guidelines for Primary PCI

A. Definitely indicated :
   1. MI < 12 hours. ( ST elevation, new LBBB, true Posterior MI )
   2. In Shock with ST Elevation or new LBBB
      a. <18 hours of shock ( <36 hrs of MI )
      b. < 75 yr. old

B. Probably indicated :
   1. Shock in >75 yrs. within 36 hrs. of MI

C. Probably Not indicated :
   1. > 12 hrs. with No evidence of ischemia
   2. Elective PCI of Non-IRA ( infarct-related artery ) at time of Primary PCI.
Rescue PCI

A. Performed for failed lysis (90 + minutes)
   1. Shock and severe CHF (definitely indicated)
   2. Persistent ischemia (probably indicated)
   3. Blood Pressure, Electrical instability (probably indicated)

B. Limitations:
   1. Fails in 10-20%
   2. Complication rate higher
   3. Role of microvascular injury
Post-MI maintenance meds

1. ASA and/or Clopidogrel
2. B-blockers
3. Statins
4. Ace-Inhibitors
5. Others such as treatments for Hypertension, DM, CHF etc.
The End