Assessment and Primary Prevention of CAD

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Objectives

• Identify risk factors for CV disease
• Identify *populations* that likely benefit from cholesterol lowering medications *and* assess treatment goals
• Select appropriate therapies for lipid lowering
• Identify additional risk stratification tools
• “Power slide”
BMI <25

<130/80

HbA1c < 6.5-7%

PLANT-based
Low sugar, salt
Low saturated fat

40”, 3-4x/week
Weight training

1-800-QUIT-NOW

Hypercholesterolemia
2018 ACC/AHA Guideline

21+ yo

Screen CV risk factors, check lipids (LDL)

Clinical CVD (Secondary Prevention)

High intensity statin (<75 y.o.)

LDL 190+ (+FH)

High intensity statin

Non-DM (PRIMARY PREVENTION)

Age 40-75, LDL 70-189

DM-1/2

10-yr Risk calculation

7.5 - 20%: Shared decision-making; Mod intensity statin (IIb)
>20%: High intensity statin (I)

5-7.5%: Shared decision-making;
*Consider add’l testing

*LDL >160 mg/dL
*hs-CRP > 2 mg/L, High Lp(a), Apo B > 130 mg/dL
*ABI < 0.9
*+FHx (M<65, F<55)
*Southern Asian ancestry
*Comorbidities (Metabolic sx, CKD, HIV, Rheumatologic d/o, premature menopause
**CAC >100 or 75th %tile
Age: Male Female
Race: White or Other African American
Total Cholesterol: mg/dL
LDL: mg/dL
HDL: mg/dL
Systolic BP: mmHg
Treated: No Yes
Smoker: No Yes
Diabetes: No Yes

Calculate Risk Clear

10-year risk:
10-year risk for an individual with optimal risk factors:

Statin needed:
List of Statins
Other populations

- No formal recommendations:
  - ESRD (maintenance HD)
  - Non-Ischemic CHF (NYHA II-IV)
  - Primary prevention patients age > 75 (no clinical ASCVD)
Lipid management

- Focus on heart-healthy habits across life-course
- Shared decision-making process
Lipid management

• Secondary causes of elevated LDL
  • Diet: Saturated or trans fats
  • Drugs: Thiazide diuretics, BBl, cyclosporine, Amiodarone, Gluco- and androgenic steroids, protease inhibitors
  • Diseases: Nephrotic syndrome, Biliary obstruction, hypothyroidism, obesity, pregnancy
Lipid management

• Continued focus on use of HMG Co-A reductase inhibitors (aka – statins)
  • High intensity: Lowers LDL 50%+
    – Rosuvastatin (Crestor) 20-40 mg
    – Atorvastatin (Lipitor) 40-80 mg
  • Moderate intensity statin: Lowers LDL 30-50%
    – Simvastatin 20-40 mg
    – Pravastatin 40-80 mg
Caveats

• If unable to tolerate high intensity
  • Examples
    – Previous statin intolerance
    – Severe comorbidities: Severe hepatic or renal impairment
    – Asian population
    – Unexplained LFTS > 3x ULN
    – Concomitant use of drugs (Cyt P450) effecting statin metabolism
    – >75 y.o.
  • Default to moderate intensity or lowest tolerable dose
Non-statin medications

• Lower is better: CTT data
  – Ezetimibe [Zetia]
    • Additional 20% reduction in LDL (-16 mg dL)
    • *Within 30 days of ACS
      – Modest benefit in CV event reduction (MI, CVA)
      – No change in 10 yr all-cause mortality
  – Used in combination with –statins (unclear utility as mono-therapy)

• PCSK-9 Monoclonal Abs

*IMPROVE-IT
PCSK-9 Inhibitors

• Monoclonal Abs against PCSK-9 protein
  – Alirocumab [Praluent] or Evolocumab [Repatha]: SC injection
    • No dose adjustment in mild-moderate renal/hepatic impairment
  – Adverse reactions: Local injection site reaction
    • No muscle or hepatic toxicity (ie: myalgias)
• Clinical benefit
  • PCSK-9 inhibitor + statin: Additional 60% reduction in LDL vs. statin alone
  • Statistically significant reduction in MI and CVA
  • Mortality benefit suggested by meta-analysis
Non-statin medications

• Complete statin intolerance
• Combination Rx in patients with inadequate response
  – High risk (secondary prevention): If LDL >70 mg/dL
  – +FH: If LDL >100

• Not clinically beneficial
  – ^Niacin: No CV event risk reduction
    • Trend toward MSK/GI events, infection, ischemic CVA, bleeding
  – *Fibrates: No mortality benefit

^AIM-HIGH, HPS-2-THRIVE
*VA-HIT, Helsinki Heart, FIELD, ACCORD-Lipid
Beyond LDL

• **Hypertriglyceridemia**
  – Secondary target in CV risk prevention
    • *Treat secondary causes*
      – DM/metabolic syndrome
      – EtOH abuse
      – CKD/ESRD/nephrotic syndrome
      – Hypothyroid
      – Meds (similar to LDL medication culprits)

• **Primary prevention**
  – 500+ mg/dL ➔ Treat to prevent Pancreatitis before use of LDL lowering medication (Ic)
  – *>150-199: O-3 Fish oil

• **Secondary prevention**
  – >150-199 ➔ O-3 Fish oil (Pure EPA; Vascepa)
  – Reduction of MACE

*REDUCE-IT*
Beyond LDL

• Low HDL: M <40 mg/dL, F < 50 mg/dL
  – Strongly determined by genetics
  – *No clinical benefit to raising HDL with existing pharmacotherapies
    • Cholesteryl ester transfer protein (CETP) inhibitors
    • Niacin

*Heartwire (Medscape), 7/2014
Beyond LDL

• Low HDL ➔ *Lifestyle Rx!
  – Diet
    • Olive oil (polyphenols higher in EVOO)
    • Coconut oil (2T daily; incorporated in diet)
    • Red/purple vegetables (anthocyanins and anti-oxidants in eggplant, red cabbage, blueberries/blackberries)
    • Fatty fish (Omega-3 fa with 4x/wk consumption: Salmon, herring, sardines, mackerel)
    • Lower carbohydrate diet (“Ketogenic” particularly in pre-existing DM, Obese, and Metabolic syndrome)
    • AVOID artificial trans-fats (“partially hydrogenated”)
  – Exercise (particularly high intensity exercise)
  – Quit tobacco (potential benefit of simply switching to vapor cigarettes)
  – Weight loss (via several methods of wt loss)

*Heartwire (Medscape), 7/2014
Follow-up

• Recheck FLP 4-12 weeks following initiation
  – Routine q3-12 month reassessment

• Follow-up visits
  – Assess effectiveness of treatment
    – Assess compliance/adherence
    – Reinforcement tool
    – Up-titration if necessary
    – Assess/address other secondary causes/lifestyle changes
  – Assess side effects
Follow-up

• Check LFT’s at baseline
  – No routine check thereafter (unless signs of hepatic dysfunction)

• CK not routinely checked (unless muscle symptoms)
Statin safety

- **MAIN concern:** Drug-drug interactions
  - NOT metabolized by Cyt P450
    - Pravastatin
    - Pitavastatin [Livalo]
  - Simva, Atorva, Lova-statin: CYP 3A4
    - Avoid with:
      - Try to avoid / LOW dose with Diltiazem, Verapamil (non-DHP)
      - HIV PI
      - -azole (antifungals)
      - -mycin (Macrolide Abx)
      - Gemfibrozil
      - Grapefruit juice
  - **Simvastatin**
    - Max dose 10 mg: Non-DHP CCB (Diltiazem, Verapamil)
    - Max dose 20 mg: Amiodarone, Ranolazine
Statin safety

- **Safety in pregnancy**
  - Category X: Recommend discontinuation prior to conception
  - Not recommended during breast-feeding
- **Myopathy***
  - Myalgias reported: 5-29%%
  - Myositis 0.5%
  - Rhabdomyolysis <0.1%
  - Highest risk: Renal dysfunction, hypothyroidism, liver dysfunction, concomitant meds
  - Measurement of CK (if muscle symptoms)
- **Hepatic dysfunction**
  - 0.5% - 3%
  - Dose dependent, and usually within first 4 months
  - Hepatic failure: Incidence no different from general population
  - 2012 FDA labeling: Baseline LFTs, with repeat monitoring only if clinically indicated (not routine)
  - If ALT > 3ULN, decrease dose or change statin
- **DM**
  - Accelerates development of DM in pre-diabetics
  - Assess risk: benefit (although overall benefit of vascular event reduction likely outweighs risk)
- **Cognition**
  - Data not definitive
  - Higher rates of concern with lipophilic statins (atorva, simva) compared to hydrophilic (prava, rosuva)
- **CA**
  - No data to support an increased risk

*Pravastatin and fluvastatin less intrinsic muscle toxicity

Pravastatin: Diminished DM risk

Source: Uptodate
Statin safety

- Statins associated with LOW risk of adverse effects
  - Serious muscle injury <0.1%
    - Myalgias 5-29%
    - 10% will discontinue
    - Incidence of muscle symptoms in statin v. placebo-treated: <1%
      - >50% pts also had sx w/ placebo*
  - Serious hepatotoxicity <0.001
  - Newly dx’d DM 0.2%/year
  - Potential increase in hemorrhagic CVA
  - NO causal relationship:
    - Cancer
    - Cognitive dysfxn
    - Cataracts, peripheral neuropathy, ED
- “…benefit of reducing CV risk with statin therapy far outweighs any safety concerns.”

AHA Scientific Statement, 12/2018, Arteriosclerosis, Thrombosis, and Vascular Biology

* GAUSS-3 trial
CV Risk stratification

• Asymptomatic adult screening exams
  • For CAD (CHD risk stratification)
    – Resting 12-lead ECG
    – Calcium artery score CT (“Heart Healthy” CT)
    – ABI study (2nd line)
    – Hs-CRP (2nd line)
  • For AAA
    – Abdominal aortic U/S

*Stress testing (ETT, stress-echo, stress-Nuclear) NOT recommended screening tool in asymptomatic adults
Coronary artery calcium CT ("Heart Healthy" CT)

• M > 40 or F > 45 yo
  – 1 Framingham risk (HTN, HLD, *FHx)
  – 5-20% CV event risk by calculator

• Cash pay study
  – Widely available/accessible

*Family hx not included in risk calculators
Zero Calcium Score Provides 15-Year Mortality ‘Warranty’ for Asymptomatic Patients

Key Points:
- Cohort study looks link between CAC score, long-term prognosis for asymptomatic patients referred for testing
- CAC score of 0 predicts an annual mortality rate below 1% out to at least 15 years in those at low or intermediate risk
**Management of CV disease: Yes or No?**

<table>
<thead>
<tr>
<th>Treatment/Test</th>
<th>Primary Prevention</th>
<th>Secondary Prevention</th>
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</thead>
<tbody>
<tr>
<td>1. Diet, exercise</td>
<td>ABSOLUTELY YES</td>
<td>ABSOLUTELY YES</td>
</tr>
<tr>
<td>2. Lipid mgmt.</td>
<td>YES*</td>
<td>ABSOLUTELY YES*</td>
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<tr>
<td>3. HTN mgmt.</td>
<td>YES</td>
<td>YES; ACEi, +/- BBI</td>
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<tr>
<td>4. DM mgmt.</td>
<td>YES</td>
<td>YES#</td>
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<tr>
<td>5. Tobacco cess</td>
<td>ABSOLUTELY YES</td>
<td>ABSOLUTELY YES</td>
</tr>
<tr>
<td>6. Carotid doppler</td>
<td>NO</td>
<td>Symptom-driven</td>
</tr>
<tr>
<td>7. AAA screen</td>
<td>YES (&gt;65 y.o.^)</td>
<td>YES / symptom-driven</td>
</tr>
<tr>
<td>8. PAD screen (ABI)</td>
<td>YES (risk strat)</td>
<td>Symptom-driven</td>
</tr>
<tr>
<td>9. Calcium score</td>
<td>YES (risk strat)</td>
<td>NO</td>
</tr>
<tr>
<td>10. Lp(a), hs-CRP, apo-B</td>
<td>YES (risk strat)</td>
<td>NO</td>
</tr>
<tr>
<td>11. Stress testing</td>
<td>NO</td>
<td>Symptom-driven</td>
</tr>
<tr>
<td>12. Aspirin</td>
<td>??</td>
<td>YES; Rivaroxaban</td>
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</tbody>
</table>

*Ezetimibe, PCSK-9, O-3 fish oil (TG)  
^Males >65yo + smoked 100+ cigarettes  
Males or females >65yo with a +FHx of AAA  

# SGLT-2-I, GLP-1R-A  

**Seton Heart Institute**
Summary

• Modifiable CV risk factors and heart healthy habits
  – Assess early, often, and encourage/treat aggressively throughout life
• Identify the 4 patient groups that would benefit from lipid management
• Still focus on – statins as workhorse medication in lipid Rx
  – Ezetimibe, PCSK-9 inhibitors, O-3 fish oil
• Consider additional CV risk stratification tools in more ambiguous clinical scenarios (ie: CAC CT)
• Lipid management and CV risk management (similar to all therapeutic decisions) is never an absolutism ➔ “shared decision-making process”