Lipid Management for the Primary Care Physician

Deepak Kumar Honuganahalli MD, MPH, FNLA
Diplomate, American Board of Clinical Lipidology
Assistant Clinical Professor, Dept of Medicine
University of Colorado School of Medicine
Internist and Clinical Lipidologist
University of Colorado Health Medical Group

Conflict of Interest Disclosure

I have no conflicts and nothing to disclose

Objectives

• Evaluation of lipid panel and discuss evidence-based management of individual component
• Discuss evaluation and management of risk enhancers
• Summarize non-pharmacological and pharmacological therapeutic approaches
### Lipid Panel

<table>
<thead>
<tr>
<th>Final Result</th>
<th>Reference Range</th>
<th>Resulted Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol</td>
<td>100-199</td>
<td>215</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>0-149</td>
<td>159</td>
</tr>
<tr>
<td>HDL Cholesterol</td>
<td>&gt;39</td>
<td>45</td>
</tr>
<tr>
<td>VLDL Cholesterol</td>
<td>5-40</td>
<td>41</td>
</tr>
<tr>
<td>LDL</td>
<td>0 - 99</td>
<td>170</td>
</tr>
</tbody>
</table>

#### Lipoprotein Structure

- **Surface Monolayer of Phospholipids and Free Cholesterol**
- **Hydrophobic Core of Triglyceride and Cholesteryl Esters**


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Lipoprotein Classification

Apo lipoprotein B

Low Density Lipoprotein
- LDL

Non-High Density Lipoprotein
- CM, VLDL, Remnants, Lp(a)

Low Density Lipoprotein
ACC/AHA Cholesterol Treatment Guidelines

Secondary Prevention: Primary Prevention:
• ASCVD • DM
• LDL >190 • LDL >190
• Pooled ASCVD risk of >7.5

Secondary Prevention

• Identify ASCVD
• Recent ACS (within the past 12 mo)
• History of MI (other than recent ACS)
• History of Ischemic Stroke
• Symptomatic peripheral arterial disease (history of claudication with ABI <0.85, or previous revascularization or amputation)

Secondary Prevention

High-Risk Conditions
• Age ≥65 years
• Heterozygous familial hypercholesterolemia
• History of prior coronary artery bypass surgery or percutaneous coronary intervention
• Diabetes mellitus
• Hypertension
• CKD (eGFR 15-59 mL/min/1.73 m2)
• Current smoking
• Persistently elevated LDL-C (LDL-C ≥100 mg/dL despite maximally tolerated statin therapy and ezetimibe
• History of congestive HF


Primary Prevention

Primary Prevention:
- DM
- LDL >190
- Pooled ASCVD risk of >7.5

Diabetes

Diabetes Mellitus: Type 1 or Type 2

Diabetes mellitus and age 40-75 y
Moderate-intensity statin (Class I)

Diabetes mellitus and age 40-75 y
Risk assessment to consider high-intensity statin (Class IIa)

Age >75 y
Clinical assessment, Risk discussion

Physiological Mechanisms

Increased production of ApoB Lipoprotein

Decreased clearance of LDL particle:
  - Defective LDL receptor
  - Decreased number of LDL receptor
  - Increased production of PCSK9 (Gain in function mutation)
  - Defective LDLRAP1 (LDL receptor adaptor protein)
LDL: > 190

- Simone Brome Criteria
- Dutch Lipid Clinic Criteria
- US MedPed Criteria

- History
- Physical Examination
- Laboratory measures

Cascade Screening

ASCVD Risk

Pooled ACC/AHA Risk Calculator based on age
Risk Categories:
- Low: <5%
- Borderline: 5 – 7.5%
- Intermediate: 7.5 – 20%
- High: >20%
Estimated average 10-year cardiovascular disease risk in adults 50 to 54 years of age according to levels of various risk factors

2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease

ASCVD Risk

• Pooled ACC/AHA Risk Score
• Framingham Risk Score
• Reynolds Risk Score
• MESA Risk Score
Treatment

Prevention is better than Cure
Promote Healthy Lifestyle Throughout life

Healthy Lifestyle

- Diet
- Caloric restriction and weight loss
- Physical Activity
- Smoking cessation
- Social determinants of health

Pharmacological Therapy

**Established agents:**
- HMG CoA inhibitors
- Dietary cholesterol absorption inhibitor
- Human monoclonal antibodies
- Fish Oils
- Bile acid sequestrants
- PPAR inhibitors

**Novel agents**
STATIN

- 4S
- AFCAPS/TEXCAPS
- ALLHAT-LLT
- ASCOT-LLA
- ARBITER
- ASCOT
- ASTEROID
- CARDS
- CTT
- CORONA
- HPS
- JUPITER
- LIPID
- METEOR
- PROSPER
- PROVE-IT
- REGRESS
- REVERSAL
- TNT
- WOSCOPS

**STATIN**

High Intensity Statin:
- Clinical ASCVD + Very high risk ASCVD
- Clinical ASCVD + Not at very high risk + <75 or >75 years
- LDL >190
- DM, 40-75 years + Risk Assessment
- <19 years + diagnosis of FH

Moderate Intensity Statin:
- Clinical ASCVD + Not at very high risk + >75 years
- DM + 40-75 years
- Borderline + Intermediate risk + 40-75 years + Risk Enhancers
- High Risk + 40-75 years
- 20-39 years + FH of premature ASCVD + LDL >160

Non Statin Therapies

Adjunctive Therapies for High and Very High Risk Patients

**Mod or High Intensity Statin** → **Acute Coronary Syndrome Event within 10 Days** → **Ezetimibe**

**IMPROVE-IT Trial**

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Adjunctive Therapies for High and Very High Risk Patients

**Mod or High Intensity Statin** → **Stable ASCVD + Risk Factors Or Acute Coronary Syndrome Within 1-12 Months** → **PCSK9 Inhibitor**

**FOURIER Trial**
**ODYSSEY-Outcomes Trial**

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Adjunctive Therapies for High and Very High Risk Patients

**Mod or High Intensity Statin** → **Stable ASCVD or Diabetes + Additional Risk Factors and TG 135 to 499 mg/dL** → **Icosapent Ethyl**

**REDUCE – IT Trial**

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Non HDL Cholesterol

- Chylomicrons: Formed in gut, ApoB48, least dense
- VLDL: De novo synthesis in Liver, ApoB100, more dense
- Remnants
- Lipoprotein (a)

Non HDL Cholesterol

- Secondary Goal
- Non HDL Cholesterol Goal: <30mg/dl of LDL goal
Elevated Non-HDL Cholesterol

**Life Style:**
- Diet
- Exercise
- Overweight/Obesity
- Alcohol
- Smoking

**Diseases:**
- Diabetes Mellitus
- Metabolic Syndrome
- Hypothyroidism
- CKD
- Nephrotic Syndrome
- HIV
- Autoimmune disorders
- Pregnancy
- PCOS

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Elevated Non-HDL Cholesterol

**Drugs:**
- Beta Blockers
- Thiazide Diuretics
- Glucocorticoids
- Rosiglitazone
- Bile acid sequestrants
- Oral estrogen
- SERMs

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Primary Disorders of Non HDL Cholesterol

**Hypertriglyceridemia: Pancreatitis**
- Lipoprotein Lipase Deficiency: FCS
- ApoC-II Deficiency: FCS
- LMF1 Deficiency: FCS
- GPIHBP1 Deficiency: FCS/FHTG
- ApoA-5 Deficiency: FCS/FHTG
Primary Disorders of Non HDL Cholesterol

Combined Hyperlipidemia: Pancreatitis and CHD

- Familial Combined Dyslipidemia: Hepatic Lipase Deficiency: LDL and VLDL
- Familial Hyperapobetalipoproteinemia: Over production of ApoB
- Familial Dysbetalipoproteinemia: ApoE Defect: Chylomicron and VLDL remnants

Non HDL Cholesterol

- TC – HDL-C = Non HDL-C
- TC: TG is > 1:8 (Chylomicrons)
- TG:VLDL = 1:5 (0.2 Normal) if > 0.3 then Elevated VLDL and Remnants
- TC – HDL – Direct VLDL = Remnants (Also includes Lp(a))

Non HDL Cholesterol

- Identify and Treat Secondary Cause
- Non Pharmacological Treatment
- Pharmacological Treatment
Non-Pharmacological Therapy

**VLDL:**
- Low Carbohydrate Diet
- Avoidance of alcohol
- Exercise
- Weight loss
- Strict and life long

**Chylomicrons:**
- Low Fat Diet
- Avoidance of alcohol
- Exercise
- Weight loss

**Lp (a):**

Pharmacological Therapy

**Statins:**
- HMG CoA inhibition
- Increase LDL hepatic receptors

**Fish oils:**
- Inhibition of DGAT
- LPL activity
- Decrease Hepatic TG synthesis

**Fibrates:**
- PPAR-A
- LPL activation
- Decrease VLDL synthesis

**Ezetimibe:**
- Inhibits Cholesterol absorption

Risk-Enhancing Factors
Risk-Enhancing Factors

**History:**
- Family history of premature ASCVD: Males <55 y; Females <65 y
- Primary hypercholesterolemia: LDL-C 160–189 mg/dl or non-HDL-C 180–219 mg/dl.
- Metabolic syndrome
- Chronic kidney disease: eGFR 15–59 with or without albuminuria
- Chronic inflammatory conditions: Psoriasis, RA, or HIV/AIDS
- History of premature menopause: before age 40 y
- History of pregnancy-associated conditions that increase later ASCVD risk such as preeclampsia
- High-risk race/ethnicities (e.g., South Asian ancestry)

**Lipid/biomarkers:**
- Persistently elevated, primary hypertriglyceridemia: ≥175 mg/dL
- Elevated high-sensitivity CRP: ≥2.0 mg/L
- Elevated Lp(a): ≥50 mg/dL
- Elevated apoB ≥130 mg/dL: A relative indication for its measurement would be triglyceride ≥200 mg/dL. A level ≥130 mg/dL corresponds to an LDL-C ≥160 mg/dL
- ABI <0.9

**Lp (a)**
- Level > 50mg/dl or 125 nmol/L
- ACS risk is tripled in patients <45 and doubled in age 45-60
- Consider guideline-based treatments for LDL
- Consider aggressive lowering of LDL in patients elevated with Lp (a) with statin
- Consider earlier use of PCSK9i

Lp (a)

- Relative indication with family history of premature ASCVD in first-degree relatives
- Premature ASCVD in the absence of traditional risk factors
- Individuals with very high ASCVD risk to define who could benefit from PCSK9i
- Intermediate and borderline risk in whom use of statin use is uncertain


Lp (a)

- Less than anticipated reduction in LDL level despite good statin adherence
- Family history of elevated Lp (a)
- Calcific Aortic Stenosis
- Recurrent or progressive ASCVD despite good adherence to Statin


Coronary Artery Calcium Score

Candidates Who Might Benefit from Knowing Their CAC Score is Zero

- Patients reluctant to initiate statin therapy who wish to understand their risk and potential for benefit more precisely
- Patients concerned about need to reinstitute statin therapy after discontinuation for statin-associated symptoms
- Older patients (men, 55-80 y of age; women, 60-80 y of age) with low burden of risk factors who question whether they would benefit from statin therapy
- Middle-aged adults (40-55 y of age) with PCE-calculated 10-year risk of ASCVD 5% to <7.5% with factors that increase their ASCVD risk, although they are in a borderline risk group

HDL

- Metabolic syndrome/Insulin resistance
- Quality vs. Quantity
- Secondary causes for low HDL
- Focus treatment on TLC and secondary causes
Summary

• Look beyond numbers
• Four categories for LDL management
• Use appropriate statin dose
• Escalation of pharmacotherapy
• Review Non-HDL
• Treat secondary causes for Non-HDL first
• Review Non-pharmacological and pharmacological treatment for Non-HDL
• Review Risk enhancers

Thank you