Population-Based Lipid Screening in the Era of a Childhood Obesity Epidemic: The Importance of Non-HDL Cholesterol Assessment

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Disclosures

• No disclosures

Background

• Lipid abnormalities contribute to accelerated atherosclerosis in youth.
• Original guidelines were aimed primarily at detecting familial dyslipidemias through screening based on family history.

Background

• Newer lipid guidelines have attempted to address the impact of the childhood obesity epidemic and to acknowledge pediatric clinical trials of more effective medications for treatment.


Background

• Obesity-related lipid abnormalities consist of a lipid triad:
  - High triglycerides
  - Low HDL
  - Small, dense LDL
  (High non-HDL, apolipoprotein B)

Background

Cardiometabolic Syndrome
- Dyslipidemia
- Insulin resistance
- Type 2 diabetes
- Hypertension
- Inflammation

Association Between Multiple Cardiovascular Risk Factors and Atherosclerosis in Children and Young Adults, Berenson et al. NEJM 1998

Intimal Surface Involvement (%)

Fibrous Plaques

- None
- 1
- 2
- 3 or 4

Background

- An imperative exists for universal lipid screening.
- Clinical practice-based screening with fasting lipid profiles may not be feasible or cost-effective.
- Non-fasting assessment does not allow accurate calculation of LDL due to post-prandial hypertriglyceridemia.
Background

- School-based screening is more likely to achieve universal assessment.
- Non-fasting fingerstick (capillary) assessment of total cholesterol and HDL allows calculation of non-HDL levels.
- Non-HDL = Total cholesterol - HDL

Background

- Non-HDL levels accurately reflect levels of both LDL and VLDL (apolipoprotein B containing particles).
- Non-HDL is elevated in both familial and obesity-related dyslipidemias, and has been shown to be an important correlate with cardiometabolic risk and accelerated atherosclerosis.

Non-HDL cholesterol concentration is associated with the metabolic syndrome among US youth aged 12-19 years. Li et al. J Pediatr 2011; 158:201-7
Background

• New NIH Integrated Pediatric CV Risk Guidelines will recommend universal lipid screening, which may include non-fasting non-HDL assessment.
• These guidelines will specify the contribution of other risk factors / risk conditions to decision-making regarding interventions, including use of lipid-lowering medication.

Objectives

• To determine:
  • The prevalence of lipid abnormalities in a population-based universal screening of adolescents.
  • To determine associations of lipid values with measures of adiposity, family history and blood pressure.
  • To determine the proportion of adolescents who would meet criteria for lipid-lowering drug therapy.

Methods

• Heart Niagara Inc. Heart Healthy Schools’ Program:
  • Curriculum enrichment program that targets the entire population of adolescents in grade 9 physical education class in Niagara Region, Ontario.
  • Provides personalized information regarding cardiometabolic risk and lifestyle.
  • Identifies adolescents and their families at increased risk for premature CV disease.
Methods

• Measurements:
  • Standardized questionnaire
  • Height, weight, waist circumference:
    • BMI (WHO) – %ile class, z score
    • WC (NHANES) – %ile class, WC / height
  • Blood pressure – 4th Report classification
  • Fingerstick (capillary) total cholesterol and HDL
    • Non-HDL
    • Total cholesterol / HDL

Methods

• Data analysis:
  • Means with standard deviations, frequencies
  • General linear regression modeling

Results
Participants

• 4104 (84%) of 4884 Grade 9 students participated in the 2009-2010 school year
  • 51% males
  • Mean age 14.6 ± 0.5 years
  • Positive family history of premature CV disease in 33%
  • Diabetes in 0.4%
  • Current smoker in 2.8%
Results
Adiposity

WHO Body Mass Index Category

Prevalence

100%
80%
60%
40%
20%
0%

Male
Female

97%+
95-96%
95-94%
<95%

Results
Lipid values

- 3283 (80%) of 4104 participants had lipids assessed.
  - Total cholesterol: 3.86 ± 0.75 mmol/L
  - HDL cholesterol: 1.22 ± 0.33 mmol/L
  - Non-HDL cholesterol: 2.64 ± 0.73 mmol/L
  - Total / non-HDL ratio: 3.38 ± 1.21
  - No relation to age
  - Significant gender differences

Results
Lipid abnormalities

Total Cholesterol (mmol/L)

Prevalence

100%
80%
60%
40%
20%
0%

Male
Female

5.20 +
4.40-5.19
<4.40

*p<0.001
Results
Lipid abnormalities

Lipid abnormalities

Results
Lipid values

• Total cholesterol: HDL ratio:
  • Males 3.50 ± 1.30
  • Females 3.25 ± 1.09  p<0.001
Results

Blood pressure

• 3968 (97%) of 4104 participants had blood pressure assessed.
• Blood pressure category:
  • Normal <90th ile 91.4%
  • Pre-HTN 90-94th ile 5.1%
  • Stage 1 HTN 95-98th ile 2.8%
  • Stage 2 HTN >99th ile 0.7%
• No significant gender differences

Results: Relation to family history

• There was no significant relationship between a positive family history of premature CV disease and any lipid variable.

Results: Relation to blood pressure

• Overall, significant though weak relationships (R² 0.0035 to 0.0154) between blood pressure category and lipid variables.
• Strongest relationship was with non-HDL > TChol/HDL ratio > TChol > HDL; stronger for systolic vs. diastolic BP.
• Blood pressure category: non-HDL
  • Normal <90th ile 3.84 mmol/L
  • Pre-HTN 90-94th ile 4.03 mmol/L
  • Stage 1+2 HTN 95th ile + 4.15 mmol/L
Overall, significant though weak relationships between adiposity variables and lipid variables.

- TChol $R^2$ 0.0124 to 0.0283
- HDL $R^2$ 0.0538 to 0.0880
- Non-HDL $R^2$ 0.0565 to 0.0794
- TC/HDL $R^2$ 0.0969 to 0.1195

Relationships with adiposity

- TC/HDL > non-HDL > HDL > TChol
- Waist measures > BMI
Results
Relation to adiposity

Results
Screening utility

• Application of NIH Integrated CV Risk Guidelines (not yet released)
• Explicit mechanisms for simultaneously considering multiple risk factors and risk conditions in clinical decision-making.
• Will recommend universal lipid screening at age 9-11 years.

Guidelines for Medication Use in Childhood and Adolescent Obesity

Risk Factors
Positive Family History
Premature CV disease in parent / grandparent:
<55 yrs males, <65 years females
Events: sudden cardiac death, angina, MI, stroke
Objectively diagnosed CV disease
Related procedures: angioplasty or stent, CABG
Guidelines for Medication Use in Childhood and Adolescent Obesity

Risk Factors

High Risk
- HTN requiring drug therapy (BP ≥99th%ile + 5 mmHg)
- Current smoker
- BMI >97th%ile

Moderate Risk
- HTN not requiring drug therapy
- BMI ≥95th%ile, <97th%ile
- HDL <1.0 mmol/L

Guidelines for Medication Use in Childhood and Adolescent Obesity

Risk Conditions

High Risk
- Kawasaki disease with current aneurysms
- Post heart transplantation
- Chronic renal disease
- Diabetes

Moderate Risk
- Kawasaki disease with regressed aneurysms
- Nephrotic syndrome
- HIV
- Chronic inflammatory disease (JRA, SLE)

Guidelines for Medication Use in Childhood and Adolescent Obesity

- Measure and average 2 fasting lipid profiles.
- Decision-making to start a statin is primarily based on the LDL level, but modified by other lipid abnormalities, family history, RF / RC.
- In the setting of obesity and higher triglycerides, cutpoints for non-HDL levels are also provided to guide decision-making.
BMI >97th percentile:
• LDL > 4.90 mmol/L (non-HDL > 5.30)
• LDL > 4.15 to 4.89 mmol/L (non-HDL 4.50-5.29)
• LDL > 3.35 to 4.14 mmol/L (non-HDL 3.75-4.49)
  with:
    • 1 high level RF/RC or
    • >2 or more moderate level RF/RC or
      clinical CVD

BMI >95th and <97th percentile:
• LDL > 4.90 mmol/L (non-HDL > 5.30)
• LDL > 4.15 to 4.89 mmol/L (non-HDL 4.50-5.29)
  with: positive family history or
    • 1 high or moderate level RF/RC
• LDL > 3.35 to 4.14 mmol/L (non-HDL 3.75-4.49)
  with:
    • >2 high level RF/RC or
    • 1 high + 1 moderate level RF/RC or
      clinical CVD

BMI <95th percentile:
• LDL ≥ 4.90 mmol/L (non-HDL ≥ 5.30)
• LDL ≥ 4.15 to 4.89 mmol/L (non-HDL 4.50-5.29)
  with: positive family history or
    • 1 high or ≥2 moderate level RF/RC
• LDL ≥ 3.35 to 4.14 mmol/L (non-HDL 3.75-4.49)
  with:
    • >2 high level RF/RC or
    • 1 high + ≥2 moderate level RF/RC or
      clinical CVD
**Results**

**Who needs a statin?**

- 35 (1.1%) of 3283 participants screened would meet criteria for lipid-lowering medication independent of adiposity.
- 56 (1.7%) would meet criteria for lipid-lowering medication when BMI is incorporated as a risk factor.
- No participant was taking lipid-lowering medication.

<table>
<thead>
<tr>
<th>BMI category</th>
<th>without BMI</th>
<th>with BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;85%ile</td>
<td>0.5%</td>
<td>0.5%</td>
</tr>
<tr>
<td>85-&lt;95%ile</td>
<td>1.2%</td>
<td>1.2%</td>
</tr>
<tr>
<td>95-&lt;97%ile</td>
<td>0%</td>
<td>2.3%</td>
</tr>
<tr>
<td>≥97%ile</td>
<td>4.0%</td>
<td>7.8%</td>
</tr>
</tbody>
</table>

**Limitations**

- Completion and results of further diagnostic evaluation of abnormalities noted on screening were not tracked.
Conclusions

• Non-fasting lipid screening in the school setting is feasible and identifies an important proportion of adolescents with abnormalities and increased cardiometabolic risk.
• Total cholesterol screening alone is inadequate; HDL assessment is required.
• Non-HDL, HDL and total cholesterol:HDL ratio discriminate risk in screening algorithms and new guidelines.

Conclusions

• In the general population, lipid abnormalities are related to adiposity, and waist measures further discriminate risk above BMI alone.
• Few adolescents, regardless of adiposity, will meet criteria for lipid-lowering medication.

Acknowledgements

www.obesityinyouth.org www.heartniagara.com