CARDIOVASCULAR DISEASE RISK AND OBESITY IN CHILDREN

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DISCLOSURES

Nothing to disclose
OBJECTIVES

• Discuss epidemiology of cardiovascular risk factors in children
• Review pathology of atherosclerosis
• Identify risk factors for development of cardiovascular disease
• Discuss screening measures
• Discuss treatment options
• Childhood Obesity trends:
  • National- 18.5% obese; 5.6% with severe obesity\textsuperscript{4}
    • Rates increase with age
    • Overall rate has slowed recently but severe obesity has increased in boys\textsuperscript{8}
  • MS
    • All (K-12) 23.6% (CAYPOS)\textsuperscript{6} in 2013
    • Highschool (9th-12th)- 18.9\% in 2015 (YRBSS)\textsuperscript{5}; 23.5\% in 2013 (CAYPOS)\textsuperscript{6}
    • Ages 10-17- 26.1\% in 2017 (NSCH)\textsuperscript{7}
    • Middle school (6\textsuperscript{th}-8\textsuperscript{th})- 27.3\% (CAYPOS 2013)\textsuperscript{6}
    • Elementary (K-5\textsuperscript{th})- 22\% (CAYPOS 2013)
The prevalence of obesity and severe obesity among US children 2 to 19 years of age from 1999 to 2016.

Asheley Cockrell Skinner et al. Pediatrics 2018;141:e20173459
CDC BMI (2000) growth chart, girls aged 2 to 20 years.

BMI for age Percentiles (Girls, 2 to 20)

Source: Centers for Disease Control and Prevention (CDC)

Alka K. Gulati et al. Pediatrics 2012;130:1136-1140
Obesity BMI growth chart, girls aged 2 to 20 years.

Aijkstra K. Gulati et al. Pediatrics 2012;130:1136-1140
• HTN: Estimated prevalence of hypertension in children is 2%-4%\textsuperscript{1,2}
• Diabetes mellitus\textsuperscript{17}: 193,000 under 20, 0.24%; annual incidence 2011-2012 about 17,900 with type 1 and 5,300 with type 2
• Average annual direct and indirect cost of CVD and stroke 2014-2015: $351.2 billion\textsuperscript{3}
• Accumulation of abnormal lipids in intimal layer (reversible) \(\rightarrow\) fibromuscular encapsulated extracellular lipid \(\rightarrow\) thrombosis, vascular rupture or acute ischemia\(^{10}\)

• At autopsy, several studies show relationship between atherosclerotic severity and extent as age and risk factor number increased; absence of advanced lesions with absence of risk factors regardless of age\(^{11,12}\)
Atherosclerosis Timeline

- Foam Cells
- Fatty Streak
- Intermediate Lesion
- Atheroma
- Fibrous Plaque
- Complicated Lesion/Rupture

Endothelial Dysfunction
- From first decade
- From third decade
- From fourth decade

Growth mainly by lipid accumulation
Smooth muscle and collagen
Thrombosis, hematoma

RISK FACTORS

• Family history
  • Premature coronary heart disease in a first-degree relative (male parent or sibling before age of 55 or female parent or sibling before 65)
• Age
• Gender
• Nutrition/diet
• Physical inactivity
• Abnormal lipid levels
RISK FACTORS

• Poor lifestyle choices
  • Smoking- 3.4% adolescents smoked in the past month; recent increase in e-cigarettes

• Sleep
  • Short sleep (<7 hrs) associated with total CVD (RR 1.14; 95% CI, 1.09-1.20) and CHD (RR 1.22; 95% CI, 1.13-1.31)
  • Long sleep (>8 hrs) associated with total CVD (RR 1.36; 95% CI, 1.26-1.48), CHD (RR 1.21; 95% CI, 1.12-1.30), and stroke (RR 1.45; 95% CI, 1.30-1.62)
  • Obstructive sleep apnea (OSA)
    • Severe sleep apnea associated with cardiovascular mortality (hazard ratio 2.73; 95% CI, 1.94-3.85)

• Metabolic syndrome

• Diabetes mellitus
RISK FACTORS

• Hypertension

• Obesity - higher BMI associated with significantly higher risk of death attributable to CVD
  • Associated with higher SBP and DBP, lower HDL, high triglyceride and hemoglobin a1c levels
  • Cross-sectionally associated with subclinical atherosclerosis
  • Prospectively associated with presence and progression of subclinical atherosclerosis
  • RR of 1.64 (95%CI, 1.36-1.99) for ischemic stroke in obesity
RISK FACTORS

• Presence of multiple risk factors most commonly associated with premature atherosclerosis\textsuperscript{11,12,15}
  
  • Use of tobacco + 1 other risk factor
  • Obesity → metabolic syndrome (insulin resistance, abnormal TG/HDL, elevated BP, waist circumference)
    • VERY HIGH RISK
    • Continues into adulthood
      • 84\% of BMI 95-99\textsuperscript{th}\% (Bogalusa study)\textsuperscript{16}
      • 100\% of BMI >99\textsuperscript{th}\%
      • Increased correlation with increased age at which BMI is elevated
  • Low cardiorespiratory fitness + overweight/obesity (associated with elevated cholesterol, systolic BP and low HDL)
# AHA Disease Stratification by Risk

<table>
<thead>
<tr>
<th>Category</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>High risk</td>
<td>Homozygous FH, T2DM, end-stage renal disease, T1DM, Kawasaki disease with persistent aneurysms, solid-organ transplant vasculopathy, childhood cancer survivor (stem cell recipient)</td>
</tr>
<tr>
<td>Moderate risk</td>
<td>Severe obesity, heterozygous FH, confirmed hypertension, coarctation, Lp(a), predialysis CKD, aortic stenosis, childhood cancer survivor (chest radiation)</td>
</tr>
<tr>
<td>At risk</td>
<td>Obesity, insulin resistance with comorbidities (dyslipidemia, NAFLD, PCOS), white-coat hypertension, HCM and other cardiomyopathies, pulmonary hypertension, chronic inflammatory conditions (JIA, SLE, IBD, HIV), s/p coronary artery translocation of anomalous coronary arteries or transposition of the great arteries, childhood cancer (cardiotoxic chemotherapy only), Kawasaki disease with regressed aneurysms (z Max≥5)</td>
</tr>
</tbody>
</table>
**SCREENING**

**PLASMA LIPID, LIPOPROTEIN AND APOLIPOPROTEIN CONCENTRATIONS IN CHILDREN AND ADOLESCENTS**

<table>
<thead>
<tr>
<th>Category</th>
<th>Low, mg/dL</th>
<th>Acceptable, mg/dL</th>
<th>Borderline-High, mg/dL</th>
<th>High, mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC</td>
<td>---</td>
<td>&lt;170</td>
<td>170-199</td>
<td>≥200</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>---</td>
<td>&lt;110</td>
<td>110-129</td>
<td>≥130</td>
</tr>
<tr>
<td>Non-HDL cholesterol</td>
<td>---</td>
<td>&lt;120</td>
<td>120-144</td>
<td>≥145</td>
</tr>
<tr>
<td>Apolipoprotein B</td>
<td>---</td>
<td>&lt;90</td>
<td>90-109</td>
<td>≥110</td>
</tr>
<tr>
<td>Triglycerides</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-9 y</td>
<td>---</td>
<td>&lt;75</td>
<td>75-99</td>
<td>≥100</td>
</tr>
<tr>
<td>10-19 y</td>
<td>---</td>
<td>&lt;90</td>
<td>90-129</td>
<td>≥130</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>&lt;40</td>
<td>&gt;45</td>
<td>40-45</td>
<td>---</td>
</tr>
<tr>
<td>Apolipoprotein A-1</td>
<td>&lt;115</td>
<td>&gt;120</td>
<td>115-120</td>
<td>---</td>
</tr>
</tbody>
</table>
Risk stratification and management for children with conditions predisposing to accelerated atherosclerosis and early CVD.

Step 1: High Risk
- T1DM and T2DM
- Chronic kidney disease and stage 3-4 renal disease/post-transplant renal dysfunction
- Post-transplant
- Kawasaki disease with current coronary artery aneurysm

Step 2: Moderate Risk
- Kawasaki disease with repaired coronary aneurysms
- Chronic inflammatory diseases
- HIV
- Neuromuscular syndromes

CV Risk Factors/Comorbidities
- Family history of early CVD in first-degree relatives (<25 y)
- BP
- Smoking history
- RF (3 or more occasions, interpreted for age/gender/HT percentile %tile)
- HT, WT, BMIs
- FG
- Diet/physical activity/exercise/history

Step 3: Tier-Specific Cut Points/Treatment Goals
- Tier 1: High Risk
  - BMI ≥ 95th %tile for age/sex
  - BP ≥ 95th %tile for age/sex/HT percentile
  - Lp(a) mg/dL: LDL-C ≥ 130, TG ≥ 150, non-HDL-C ≥ 190
  - FG ≥ 100 mg/dL, HgbA1c ≥ 7%
- Tier 2: Moderate Risk
  - BMI ≥ 80th %tile for age/sex
  - BP ≥ 90th %tile for age/sex/HT percentile
  - Lp(a) mg/dL: LDL-C ≤ 130, TG ≤ 130, non-HDL-C ≤ 140
  - FG < 100 mg/dL, HgbA1c < 7%

Step 4: Lifestyle Change
- Intensive lifestyle management
  - CHILD-1: Activity Rx
  - Wt loss as needed
- PLUS
  - Schofield
- Step 5: Drug Therapy
  - Condition-specific management (Table 11-3)
  - If goals not met, consider medication per risk-specific guideline recommendations

Directions:
Step 1: Risk stratification by disease process (Table 11-2).
Step 2: Assess all cardiovascular risk factors. If there are ≥2 comorbidities, move Tier II patient to Tier I for subsequent management.
Step 3: Tier-specific treatment goals/cut points defined.
Step 4: Initial therapy. For Tier I, initial management is therapeutic lifestyle change PLUS disease-specific management (Table 11-3). For Tier II, initial management is therapeutic lifestyle change.
Cardiovascular Risk Reduction in High-Risk Pediatric Patients: A Scientific Statement From the American Heart Association, Volume: 139, Issue: 13, Pages: e603-e634, DOI: (10.1161/CIR.0000000000000618)
TREATMENT

• AHA’s Life’s Simple 7 for Kids:
  1. Avoid smoking and using tobacco
  2. Be physically active every day
  3. Eat a heart-healthy diet
  4. Keep a healthy weight
  5. Keep your blood pressure healthy
  6. Keep your total cholesterol healthy
  7. Keep your blood sugar healthy
• Preschool-aged children (ages 3-5) should be physically active through the day
• Adult caregivers should encourage active play and vary activity types
  • Structured activities include throwing games and tricycle riding
  • Bone strengthening activities include hopping, skipping, jumping, tumbling
PHYSICAL ACTIVITY

• Children and adolescents ages 6-17
  • Should do 60 minutes or more of moderate to vigorous physical activity daily
    • Aerobic: most of the daily 60 minutes should be moderate to vigorous aerobic activity; should include vigorous activity at least 3 days per week
    • Muscle-strengthening: at least 3 days per week as part of daily 60 minutes
    • Bone-strengthening: at least 3 days per week as part of daily 60 minutes
  • Total amount more important than any one component (intensity of type of activity)
  • Bone strengthening very important due to bone mass gains just before and during puberty
PHYSICAL ACTIVITY

• Types of activities for ages 6-17
  • Aerobic: rhythmic movement of large muscles for sustained period of time
    • Ex. Running, hopping, skipping, jumping rope, swimming, dancing, bicycling
    • Increased cardiorespiratory fitness
  • Muscle-strengthening: working muscles more than usual activities of daily life
    • Unstructured and part of play (ex. Playing on playground equipment, climbing trees, playing tug of water)
    • Structured (ex. Lifting weights, resistance bands)
  • Bone-strengthening: production of force on bones promoting strength and growth of bones
    • Commonly done by impact with the ground (ex. Running, jumping rope, basketball, tennis, hopscotch)
PHYSICAL ACTIVITY

• Safety
  • Understand risks
  • Choose type appropriate for fitness level and health goals
  • Increase activity gradually - inactive people should start with lower intensity exercises and increase how often and how long over time
  • Protect using protective gear/equipment, choose safe environments
  • Provide recommendations to patients regarding appropriate activities if health problems

• Amount decreases in adolescent girls and persists into adulthood
• Should not do only moderate intensity - include vigorous activity
DIETARY TREATMENT

• Keep caloric intake adequate for growth and development. Primary goals weight stabilization or gradual weight loss if > 6 years (1lb/month)\(^19\)

• DASH type eating pattern
  • First dietary modification for children with obesity, dyslipidemia, and risk factor clustering
  • Increase intakes of fruits and vegetables, low fat dairy, and whole grains
  • Increase fiber, DHA, plant stanols and sterols
    • Fiber recommendations:
      • Ages 2-10: 1g fiber per year of age + 5.
      • Ages 11-21: 14g/1000kcal
  • 3 to 4 servings of non-fat or low-fat dairy/day
    • 12-24 months of age transition to low-fat dairy
  • Regular meals and snack with daily Caloric composition: 15-20% Protein, 50-55% CHO, 30% Fat
Dietary treatment

- DASH type eating pattern (cont’d)
  - Limit fat intake to 30% of total calories
    - <10% saturated fats, little to no trans fat, and <300mg cholesterol/day
    - 20% of fat intake polyunsaturated and monounsaturated fats.
    - ** fat restriction not indicated for children under 12 months
  - Limit added sugar, promote calorie-free beverages
    - <4oz of fruit juice per day
    - Children <2 years should not consume any added sugars
    - Children >2 years should not consume more than 25g added sugars/day (American Heart Association)
      - Limit or eliminate calories consumed from sugar sweetened beverages
  - Limit sodium <2400mg/day
DIETARY TREATMENT

• Diabetes
  • DASH style eating pattern
  • Increase intake of low glycemic index foods
  • Maintain consistent meal pattern with 2-3 snacks (<200kcal/snack), if needed
  • Low CHO diet (<130g/day) not indicated as reduction in carbohydrate food groups reduces intake of other key nutrients
  • Carbohydrate Counting (1 Carbohydrate exchange = 15g CHO)

Average Carbohydrate Recommendations per Meal for Optimal Growth and Development\textsuperscript{18}

<table>
<thead>
<tr>
<th>Gender</th>
<th>Age &lt; 5 y (g)</th>
<th>Age 5-12 y (g)</th>
<th>Teens (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Girls</td>
<td>30-45</td>
<td>45-60</td>
<td>45-75</td>
</tr>
<tr>
<td>Boys</td>
<td>30-45</td>
<td>45-60</td>
<td>45-75+</td>
</tr>
</tbody>
</table>
Dyslipidemia algorithm: target LDL cholesterol.
Dyslipidemia algorithm: target triglycerides.

**FLP x 2**:
- Average results

**LDL-C ≥ 130 mg/dL**
- Consult lipid specialist

**TG ≥ 500 mg/dL**
- Consult lipid specialist

**TG ≥ 100, < 500 mg/dL; > 10**
- Target TG

**TARGET TGs**
- CHILD-1
- CHILD-2
- TG diet (Table 9-8)
- Lifestyle modification with WT-lose goal as needed + 6 mo

**FLP**

**TG < 100 mg/dL; < 10 y,**
- < 130 mg/dL; 10-19 y
- Continue CHILD-2-TG
- Lifestyle change
- Reassess q 12 mo

**TG ≥ 100, < 200 mg/dL; < 10 y**
- ≥ 130, < 200 mg/dL; 10-19 y
- Intensify CHILD-2-TG + WT loss
- Increase dietary fish content
- Repeat FLP in 6 mo

**TG ≥ 200-499 mg/dL**
- If LDL-C target achieved and non-HDL
- ≥ 145 mg/dL; lipid specialist for drug
- Therapy (statins/activated nicotinic acid)
- Consider ω3 fish oil therapy

**EXPERT PANEL ON INTEGRATED GUIDELINES FOR CARDIOVASCULAR HEALTH AND RISK REDUCTION IN CHILDREN AND ADOLESCENTS Pediatrics 2011;128:S213 S256**

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PROGNOSIS

• Total CVD (CHD, stroke, HF and hypertension) from NHANES 2013 - 2016 in adults ≥ 20 years of age ≈ 121.5 million (48%)

• Heart failure
  • Lifetime risk can be lowered by:
    • Adherence to Life’s Simple 7 goals
    • Optimizing physical activity, BMI, blood pressure, glucose, diet and cholesterol
    • Avoiding smoking

• Atrial fibrillation
  • 51% increased risk with obesity

• Stroke (from the Global Burden of disease study)
  • About 90% avoidable by modifiable factors (e.g. obesity, high BP, hyperglycemia, hyperlipidemia, renal disfunction)
  • 74% attributable to behavioral factors (e.g. smoking, unhealthy diet, sedentary lifestyle)
REFERENCES


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