The Beat Goes on . . . Usually

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Summary

- Atherosclerosis starts in middle school & has been with us since antiquity
- Medical therapy as good as stents for angina
- Vytorin is OK
- Palpitations are almost always benign
Atherosclerosis in Children and Young Adults

You’re Older than You Think
The Prevalence of Fibrous-Plaque Lesions in the Aorta and Coronary Arteries in 204 Children and Young Adults, According to Age.
Prevalence of CAD by Age

IVUS of Donor Coronaries Circ 2001
Intracoronary US:
17 & 32 y/o

A
Left Anterior Descending
Maximum Atheroma Thickness - 0.71 mm

B
Left Circumflex
Ramus Branch
Risk Factors For CAD in Adolescence & Young Adults

- Cigarette smoking
- DM
- Hyperlipidemia
- HTN
- Truncal obesity
- Family history
- Inactivity
- Kawasaki’s disease, transplant, CKD, inflammation
The Bogalusa Heart Study data show that as the number of cardiovascular risk factors increases, so too does the extent of atherosclerosis detected by autopsy.

Figures give the percent of intimal surface covered with fatty streaks or fibrous plaques.

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Fatty Streaks*</th>
<th>Fibrous Plaques*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Aorta</td>
<td>Coronary Arteries</td>
</tr>
<tr>
<td>0</td>
<td>19.1</td>
<td>1.3</td>
</tr>
<tr>
<td>1</td>
<td>30.3</td>
<td>2.5</td>
</tr>
<tr>
<td>2</td>
<td>37.9</td>
<td>7.9</td>
</tr>
<tr>
<td>3 or 4</td>
<td>35.0</td>
<td>11.0</td>
</tr>
</tbody>
</table>

* Figures give the percent of intimal surface covered with fatty streaks or fibrous plaques.
Plaques Can Start in 7th Grade!

Arrows show fatty streaks in the aorta
Aorta with extensive atherosclerosis
Why Are Our Children Getting CVD?
Beaten, Mindless Herds Staring at Computer Screens

“How do I sign on KPHC with these hooves?”
Screening Kids for CAD

**Step 1. Risk stratification by disease process**
- **Tier I: high risk**
  - Homozygous FH
  - Diabetes mellitus type I
  - Chronic kidney disease/ESRD
  - After orthotopic heart transplantation
  - Kawasaki disease with current coronary artery aneurysms
- **Tier II: moderate risk**
  - Heterozygous FH
  - Chronic inflammatory disease
  - Kawasaki disease with regressed coronary aneurysms
  - Type 2 diabetes mellitus
- **Tier III: at risk**
  - Congenital heart disease
  - Kawasaki disease without detected coronary involvement
  - Cancer treatment survivors

**Step 2. Assess all CV risk factors**
- If ≥2 additional comorbidities:
  → Advance to next higher risk tier
- **Cardiovascular risk factors/comorbidities**
  - Fasting lipid profile
  - Smoking history
  - Family history of early CAD in expanded 1st-degree pedigree (male ≤55 years; female ≤65 years)
  - Blood pressure (3 separate occasions), interpreted for age/sex/height
  - BMI
  - Fasting glucose
  - Physical activity history

**Step 3. Tier-specific cutpoints/treatment goals**
- **Tier I: high risk**
  - BMI ≤85 percentile for age/sex
  - BP ≤90 percentile for age/sex
  - LDL cholesterol ≤100 mg/dL
  - FG <100 mg/dL, HgbA1c <7 percent
- **Tier II: moderate risk**
  - BMI ≤90 percentile for age/sex
  - BP ≤95 percentile for age/sex/height
  - LDL cholesterol ≤130 mg/dL
  - FG <100 mg/dL, HgbA1c <7 percent
- **Tier III: at risk**
  - BMI ≤95 percentile for age/sex
  - BP ≤95 percentile + 5 mmHg for age/sex/height
  - LDL cholesterol ≤160 mg/dL
  - FG <100 mg/dL, HgbA1c <7 percent

**Step 4. Lifestyle change**
- **Therapeutic lifestyle change - (TLC) table 2**
  → PLUS
  - **Disease-specific management - table 3**
  → If goals not met, consider medication - table 2
- **Therapeutic lifestyle change - (TLC) table 2**
  → If goals not met, consider medication - table 2
- **Therapeutic lifestyle change - (TLC) table 2**
  → If goals not met, consider medication - table 2
Atherosclerosis in Antiquity
Atherosclerosis in Mummies

Calcified patches in an aorta.

Pelvic and thigh arteries completely calcified
Atherosclerosis in Animals (Other than Human)

- Monkeys, baboons
- Deer
- Dogs
- Turkeys
- Rabbits
- Birds - Maca, pigeons
Primary Care Management of Patients with Intracoronary Stents
Medical Therapy vs. Stents for CAD

• Stents clearly beneficial in STEMI & acute coronary syndromes

• Stents not so beneficial in stable CAD
COURAGE Trial: Medical Therapy vs. PCI for Stable CAD

Death or MI
(HR 1.05, p = 0.62)

Freedom From Angina at 5 Years
(p = 0.35)

<table>
<thead>
<tr>
<th></th>
<th>Optimal Medical Therapy + PCI</th>
<th>Optimal Medical Therapy Alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death or MI (%)</td>
<td>19.0</td>
<td>18.5</td>
</tr>
<tr>
<td>Freedom From Angina</td>
<td>74</td>
<td>72</td>
</tr>
</tbody>
</table>
Drug Eluting Stents Don’t Endothelialize

Endothelium on BMS

Exposed Taxus stent
Management After Stents

- Do not stop Plavix & ASA for at least 1 year after drug eluting stent
- Chest pain common for a few weeks
- Control Risk factors
- LDL < 70 - 80
- Routine F/U or stress testing not required
Outpatient Care after MI

- Mediterranean diet & exercise
- Aggressive control RF’s
  - LDL < 70
  - BP 130/80
- ASA 325 mg daily (post stent) 162 mg thereafter
- Plavix 75 mg daily (post stent)
- Statin
- B-blocker
- ACE inhibitor or ARB
- Spironolactone if EF < 40%
- Warfarin for Anterior MI with CHF or AF
Outpatient Care after MI: Follow Up

- Minimal F/U for uncomplicated MI
- Target risk factors & compliance
- Address depression / anxiety
- Complicated MI to cardiology
  - CHF
  - Arrhythmias
  - Multivessel CAD
What’s a Myocardial Infarction?

• Elevation of Troponin I
  – Above 3 SD’s of normal, rise & fall
  – Tnl > 0.5 – 1.0
• Symptoms
• ECG
  – ST elevations or depressions
  – New LBBB
  – Q-waves

JACC 2007
Ezetimibe, a cholesterol-absorption inhibitor, reduces levels of LDL-c when added to statin treatment.

However, the effect of Ezetimibe on the progression of atherosclerosis is unknown.
ENHANCE Study Design

Pre-randomization Phase
- FH: LDL-c ≥ 210 mg/dL
- Screening and Fibrate Washout
- Placebo Lead-In/Drug Washout

RANDOMIZATION
- Ezetimibe 10 mg-Simvastatin 80 mg
- Simvastatin 80 mg

IMT assessment
- Weeks 0, 3, 6, 9, 12, 15, 18, 21, 24
ENHANCE cIMT Methodology

Carotid Intima-Media thickness (cIMT) measurements

- Measurements were made at a predefined angle of insonation
- Only the far-walls of all segments were imaged
- Images were stored in DICOM for offline image analyses

LDL-cholesterol

Percentage change from baseline

P<0.01

-16.5 % incremental reduction

<table>
<thead>
<tr>
<th></th>
<th>Baseline (mg/dL)</th>
<th>24 months (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simva</td>
<td>318 ± 66</td>
<td>193 ± 60</td>
</tr>
<tr>
<td>Eze-Simva</td>
<td>319 ± 65</td>
<td>141 ± 53</td>
</tr>
</tbody>
</table>

ENHANCE
Mean cIMT during 24 months of therapy
Longitudinal, repeated measures analysis

P=0.88
Possible explanations for the absence of an incremental reduction in cIMT

**Measurement Technique**
Technique not accurate enough to reflect changes in atherosclerotic burden?

**The Compound**
Ezetimibe lacks vascular benefit despite the observed LDL-c and hsCRP reduction

**The Population**
At too low a risk to detect changes, which would limit the ability to detect a differential response
ENHANCE in Perspective

- Vytorin is safe & effectively lowers LDL
- Small population w/ very high LDL followed for only 2 years
- Surrogate endpoint (CIMT) used
- Clinical outcomes and adverse events similar
- News media & competitors made alarmist statements
- **Is it the statin or the low LDL?**
Evaluation & Management of the Patient with Palpitations
Causes of Palpitations
Nonspecific Complaint

- **Cardiac** – arrhythmia, structural heart ds.
  - Alteration in rate, rhythm or stroke volume
- **Psychiatric** – panic, anxiety
- **Stimulants** - caffeine, drugs
- **Metabolic disorders** – thyrotoxicosis
- **High output states** – anemia, pregnancy
Clues by History

- Brief, Flip-flop, skipped beats – PVC’s
- Sudden off/on, prolonged – SVT or VT
- Anxiety – regular rate, gradual onset
- Irregular – AF
- Near syncope – VT, SVT
- Younger – SVT’s
- Older – AF, VT
Factors Predictive of Cardiac Cause

- Male
- Described as irregular heart beat
- H/O heart disease
- Lasts more than 5 minutes

AJM 1996
Prevalence of Palpitations & Arrhythmias

- Palpitations occur in up to 12% of elderly population
- Extrasystoles extremely common in patients referred for Holter monitor
- Correlation of extrasystoles or other brief arrhythmia with symptoms is poor
Outcomes of Patients with Palpitations

- About the same risk as age & sex matched controls
- Extremely low risk of death or stroke
- Malignant arrhythmias (VT) very unlikely
- Many patients remain symptomatic & anxious

Am J Med 1996
Arch Int Med 1995
Arrhythmias Causing Palpitations

- Extrasystoles - PVC’s, PAC’s
- PSVT
- PAT / PAF / Flutter
- VT
- Structural heart disease, CHF?
- Prior MI, Ischemia?
Evaluation of Palpitations

- **PE**
  - HOCM
  - Valve disease
  - CHF

- **ECG**
  - Old MI
  - LVH
  - QT Interval
  - WPW
Patients Who Require Further Evaluation

- Significant symptoms, syncope, near syncope, prolonged arrhythmia
- Suspect structural or ischemic heart disease
- Patients who can’t be reassured
Holter or Event Recorder?

- **Event recorder best**
  - Patient activated event recorder for 2 weeks has a much higher diagnostic yield than Holter for 24 hours
  - 80% for ER vs. 35% for Holter
Exclude Structural Heart Disease

- Stress Echo
  - Evaluate LV function & chamber sizes
  - R/O CAD
Management of Palpitations

- Reassurance & avoidance of precipitating factors
- Extrasystoles
  - B-blocker?
- Arrhythmia Specific therapy
  - PAF
  - PSVT
  - VT
Arrhythmias During Pregnancy

- Sinus tach common
- Higher rate of extrasystoles
- Atenolol should be avoided (IUGR)
- Verapamil, digoxin, quinidine, procainamide, flecainide, sotolol appear safe
Summary

- Atherosclerosis starts in middle school & has been with us since antiquity
- Medical therapy as good as stents for angina
- Vytorin is OK
- Palpitations are almost always benign
What if there were no hypothetical questions?

- George Carlin