Hypertension and dyslipidemia (LIPITENSION)

KCS – BOMA ELDORET
AKWANALO C
Cardiologist
Outline

- Introduction
- Definitions
- Prevalence
- Interplay: Lipitension and atherosclerosis
  - Dyslipidemia
  - Hypertension
    - Microalbuminuria
- Management
- Conclusions
Introduction

• Cardiovascular diseases: leading cause of mortality

• Hypertension and dyslipidemia: 2 major risk factors: adverse effects are additive

• Prevalence of co-existence: 15 - 31%
Leading causes of death for all males and females
(United States: 2004).

Source: NCHS and NHLBI.
Percentage breakdown of deaths from cardiovascular diseases (United States: 2004)

Source: NCHS and NHLBI.
Definitions

- Dyslipidemic hypertension (DH)
  - Familial DH: Genetic syndrome
    - 12% of patients with essential hypertension
    - 48% of hypertension sibships

- Lipitension: ease of identification
Levels of Risk Associated with Smoking, Hypertension and Hypercholesterolaemia

Hypertension
(SBP 195 mmHg)

Smoking

Serum cholesterol level
(8.5 mmol/L, 330 mg/dL)

Adapted from Poulter N et al., 1993
Prevalence

- Increases with age
  - < 40 years, < 2%
  - > 40 years, 31 – 56%
- Women > men (20 vs. 16 %)
- Racial variation
  - Lowest in Hispanics (9.6%)
  - Highest in African Americans (22%)
- Increases with increasing risk factor burden
  - Highest in CVD + DM
  - Metabolic syndrome
Interplay: Lipitension and atherosclerosis

• Dyslipidemia
  – Endothelial injury
    • Manifest as ASCVD
  – Physiologic vasomotor dysfunction
    • Manifest as hypertension**
  – Direct relation between hypertension and CV events
HDL-C vs LDL-C
as a predictor of CHD risk

Risk of CAD over 4 years of follow-up*

CHD RR

CHD Risk According to HDL-C Levels

Framingham Study

Kannel WB. *Am J Cardiol* 1983;52:9B–12B
Relative risks of MI

The Physicians Health Study

# Risk of Coronary Heart Disease by Serum Cholesterol

30-Year Follow-up, The Framingham Study

**Age-Adjusted Annual Rate per 1000**

<table>
<thead>
<tr>
<th>Serum Cholesterol</th>
<th>Age: 35-64*</th>
<th></th>
<th>Age: 65-94</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
<td>Men</td>
<td>Women</td>
</tr>
<tr>
<td>84-204</td>
<td>8</td>
<td>4</td>
<td>22</td>
<td>11</td>
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<tr>
<td>205-234</td>
<td>13</td>
<td>5</td>
<td>24</td>
<td>15</td>
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<tr>
<td>235-264</td>
<td>14</td>
<td>4</td>
<td>26</td>
<td>17</td>
</tr>
<tr>
<td>265-294</td>
<td>15</td>
<td>7</td>
<td>23</td>
<td>17</td>
</tr>
<tr>
<td>295-1124</td>
<td>26</td>
<td>10</td>
<td>38</td>
<td>32</td>
</tr>
</tbody>
</table>

Lifetime Risk of CHD Increases with Serum Cholesterol

Framingham Study: Subjects age 40 years

Effects of ↑ TC Levels on the Risk for CHD in the Presence of Other Risk Factors

Schaefer EJ, adapted from the Framingham Heart Study
Association of increasing plasma cholesterol and coronary risk
Relation between plasma cholesterol concentration and six-year coronary heart disease risk in 361,662 men (ages 35 to 57) screened during the MRFIT study. There is a continuous, positive, graded correlation between the plasma cholesterol concentration and coronary risk. To convert plasma cholesterol to mmol/L, divide by 38.5. (Data from Stamler, J, Wentworth, D, Neaton, JD, JAMA 1986; 256:2823.)
Correlation Between Serum Cholesterol and CVD Mortality

Multiple Risk Factor Intervention Trial (MRFIT)
N=325,346

Serum Cholesterol Quintile (mg/dL)

Q1 (<182)
Q2 (182-202)
Q3 (203-220)
Q4 (221-244)
Q5 (>244)

6-Year CVD Death Rate Per 1000

Untreated Patients
55-57 years
50-54 years
45-49 years
40-44 years
35-39 years

Q = serum cholesterol quintile.
**Plasma cholesterol and cardiovascular mortality**  Relation between the baseline plasma cholesterol concentration and ten-year cardiovascular death rate in patients without and with manifestations of coronary heart disease (CHD) in the Lipid Research Council study. Cumulative death rates were increased at higher plasma cholesterol levels in both groups, but the effect was more pronounced in patients with preexisting CHD. (Data from Pekannen, J, Linn, S, Heiss, G, et al, N Engl J Med 1990; 322:1700.)
Cholesterol and CHD: Seven Countries Study

TC mg/dL (mmol/L)

Northern Europe
United States
Southern Europe, Inland
Southern Europe, Mediterranean
Siberia
Japan

CHD mortality rates (%)

(2.60) (3.25) (3.90) (4.50) (5.15) (5.80) (6.45) (7.10) (7.75) (8.40) (9.05)

Lipitension and atherosclerosis

• Hypertension
  – Abnormal RAAS
    • Ag-II promotes atherogensis via AT-1 Receptor
      – Increased lipid uptake by cells
      – Vasoconstriction
      – Free radicals production
  – Altered shear stress and oxidative stress
    • Overproduction of collagen and fibronectin
    • Decreases NO-dependent vascular relaxation
    • Increased permeability of lipoproteins
    • Up-regulation of lipid oxidation enzymes
RISK OF CARDIOVASCULAR EVENTS BY LEVEL OF SYSTOLIC BLOOD PRESSURE


- % of Events in women
- % of Events in men
- Rate/1000 women
- Rate/1000 men

Age-Adj. Annual Rate

<table>
<thead>
<tr>
<th>Systolic Blood Pressure</th>
<th>% of Events in women</th>
<th>% of Events in men</th>
<th>Rate/1000 women</th>
<th>Rate/1000 men</th>
</tr>
</thead>
<tbody>
<tr>
<td>74-119</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>120-139</td>
<td></td>
<td></td>
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<tr>
<td>140-159</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>160-179</td>
<td></td>
<td></td>
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<tr>
<td>180-300</td>
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</tbody>
</table>

Persons Initially Free of CVD
Relation of Non-Hypertensive Blood Pressure to Cardiovascular Disease


10-year Age-Adjusted Cumulative Incidence

Framingham Study: Subjects Ages 35-90 yrs.

<table>
<thead>
<tr>
<th>SBP</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;120/80</td>
<td>1.9</td>
<td>1.0</td>
</tr>
<tr>
<td>120-129</td>
<td>2.8</td>
<td>1.3</td>
</tr>
<tr>
<td>130-139</td>
<td>4.4</td>
<td>2.5</td>
</tr>
<tr>
<td>140-149</td>
<td>5.8</td>
<td>7.6</td>
</tr>
<tr>
<td>150-159</td>
<td>7.6</td>
<td>10.1</td>
</tr>
</tbody>
</table>

Hazard Ratio* adjusted for age, BMI, Cholesterol, Diabetes and smoking *P<.001
Lipitension and atherosclerosis

• Hypertension
  – Micro-albuminuria
    • A marker glomerular function

• Predictor of CAD
  – Associated with dyslipidemia
    » Decreased HDL-C
    » Increased LDL-C
    » Increased lipoprotein (a)
Article: 8,029 subjects with hypertension and LV hypertrophy, mean age 66 years

- Normal albuminuria
- Microalbuminuria (Alb/Crea >3.5 mg/mmol)
- Macroalbuminuria (Alb/Crea >35 mg/mmol)

Diagram showing prevalence of various diseases associated with albuminuria.
Management

• Intuitive?
  – Treatment of two RF equates additive benefits?

• Control of CVD risk factors inadequate
  – Overall: target not achieved in 50.2% (NHANES-2001-2002)

• Multiple RF interventions?
  – Incongruent results!
2nd Prevention of Stroke: Percentage Prevented per Year

- Antihypertensives
- Clopidogrel vs. ASA
- Warfarin
- Statins
- Smoking Cessation
- Aspirin
- Carotid Endarterectomy

% of strokes prevented/yr
0 2 4 6 8 10 12 14 16 18

Key Statin Trials and Spectrum of Risk

Increasing absolute CHD risk

1. 4S
2. LIPID
3. HPS
4. CARE
5. ASCOT-LLA
6. WOSCOPS
7. AFCAPS/TexCAPS

- CHD/high cholesterol
- CHD/average to high cholesterol
- CHD*/average to high cholesterol
- CHD/average cholesterol
- Some patients with CHD/average cholesterol
- No MI/high cholesterol
- No CHD/average cholesterol

*CHD or CHD risk equivalent, e.g. diabetes
This improvement in survival is accounted for by the 42% reduction in coronary death.

The differential benefit of LDLc lowering in patients with diabetes has been evident from the earliest statin trials and is more evidence that higher risk=greater benefit: 4S study: Major Coronary Events

WOSCOPS: Non-fatal MI and CHD Death

Benefits of Cholesterol Lowering

Meta-analysis of 38 primary and secondary intervention trials

Mortality log odds ratio vs. % in cholesterol reduction

- Total mortality ($p=0.004$)
- CHD mortality ($p=0.012$)

Adapted from Gould AL et al. Circulation. 1998;97:946–952
Change In Age-Adjusted Mortality
1979 - 1995

Noncardiovascular Disease
Coronary Heart Disease
Stroke

National Center for Health Statistics.
Effects of lipid lowering on BP

• If on ACE-I, potentiation?
  – Pleotropic effects
  – Correction of dyslipidemia

• Not replicable
Effects BP lowering on dyslipidemia

- B-blockers: B-1 selective; little effect
- Thiazides: significant effect at high doses
- Preferred: CCB, A-blockers, RAAS blockers
Lowering your cholesterol is next to impossible with diet, and often dangerous with drugs—and it won’t make you live any longer

By Thomas J. Moore
Vascular Protection Checklist

✓ **A** • A1C – optimal glycemic control (usually ≤7%)
✓ **B** • BP – optimal blood pressure control (<130/80)
✓ **C** • Cholesterol – LDL ≤2.0 mmol/L if decided to treat
✓ **D** • Drugs to protect the heart (regardless of baseline BP or LDL)
  A – ACEi or ARB | S – Statin | A – ASA if indicated
✓ **E** • Exercise / Eating healthily – regular physical activity, achieve and maintain healthy body weight
✓ **S** • Smoking cessation
Pooled Cohort Risk Assessment Equations

Predicts 10-year risk for a first atherosclerotic cardiovascular disease (ASCVD) event

Risk Factors for ASCVD

- Gender: Male, Female
- Age: [ ] years
- Race: [ ] White or other
- Systolic BP: [ ] mmHg
- Receiving treatment for high blood pressure (if SBP > 120 mmHg): [ ] No, [ ] Yes
- Diabetes: [ ] No, [ ] Yes
- Smoker: [ ] No, [ ] Yes
- Total Cholesterol: [ ] mg/dL
- HDL Cholesterol: [ ] mg/dL

[Reset] [Calculate]

http://clincalc.com/Cardiology/ASCVD/PooledCohort.aspx
Conclusions

• Lipitension: important RF for CVD

• LDL < 70 mg/dl and SBP < 120 mmHg is associated with % progress in atheroma

• Interplay mainly at vascular endothelial level

• Global risk assessment mandatory
It is time for Questions