ESTIMATING CV RISK IN ASIAN AMERICANS AND PREVENTION OF CVD

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DISCLOSURES

Consultant: RubiconMD
Research: Amgen, NHLBI

OBJECTIVES

• Review current CV risk assessment tools
• Recognize limitations of CV risk tools for Asians
• Understand how to treat Asian patients and reduce CV risk

OUTLINE

• Clinical cases
  • CV risk assessment
  • How to reduce CV risk in Asian patients
• Opportunities to improve CV risk assessment
• Take Home Points
CASE #1: CV RISK ASSESSMENT

Mr. L is a 56 year old Chinese man with a past medical history of hypertension who presents to your clinic for establishment of care. No history of diabetes or tobacco use.

Current Medications:
- Losartan 50 mg daily

Exam: Healthy appearing man in no distress. BP 128/77 mm Hg, BMI 28.5

Labs: TC 215, LDL 132, HDL 41, Hba1c 5.5%

CASE #1: WHAT IS HIS 10 YEAR CV RISK?

- <5%
- 5-7.5%
- >7.5%
- >10%
10 YEAR CV RISK CALCULATOR

CASE #1: CV RISK ASSESSMENT

Treatment Advice Summary

- Treatment Advice for This Patient
  - LDL-C: Moderate-high intensity statin recommended
  - Smoking: Address smoking cessation if needed

ACC 2013 LIPID GUIDELINE SCOPE

- Focus on treatment of blood cholesterol to reduce atherosclerotic cardiovascular disease (ASCVD) risk in adults
- Emphasize adherence to a heart healthy lifestyle as foundation of ASCVD risk reduction
- Identify individuals most likely to benefit from cholesterol-lowering therapy
  - 4 statin benefit groups
- Identify safety issues

4 STATIN BENEFIT GROUPS

- Known ASCVD (Level A, strong): defined as acute coronary syndromes, or a history of MI, stable or unstable angina, coronary or other arterial revascularization, stroke, TIA, or peripheral arterial disease presumed to be of atherosclerotic origin
  - LDL ≥ 190 mg/dL, Age ≥ 21 (Level B, moderate)
  - Diabetics age 40-75 years, LDL-C 70-189 mg/dL (Level A, strong)
  - Age 40-75 years and 10-year risk ≥7.5%, LDL-C 70-189 mg/dL (Level A, strong)
**PARADIGM SHIFT: NO LDL-C TARGETS**

- "The expert panel was unable to find RCT evidence to support treatment targets"
- Appropriate intensity statin therapy should be used for ASCVD risk reduction in those most likely to benefit (i.e. at-risk populations)
- Targets result in undertreatment with statin intensity, or overtreatment with non-statin therapies
- Mainstay of treatment to reduce ASCVD is statin therapy; no strong clinical evidence for most non-statin therapies

**RELATIONSHIP BETWEEN LDL-C AND ASCVD**

- Statins are the most effective treatment to lower LDL-C levels
- In secondary prevention trials, cardiovascular event rates were proportional to LDL-C lowering
- LDL-C levels are causally related to ASCVD risk
- Treatments lowering LDL-C appear to decrease events proportional to LDL lowering?

**CONTOVERSY: OVERESTIMATION OF RISK?**

*Doctors at odds on heart-disease risk calculator*

Method defended after Brigham specialists criticize

Cholesterol Controversy Shows Medicine Needs Big Data, Not Old Data

Risk Calculator for Cholesterol Appears Flawed

**ASCVD RISK CALCULATOR: DEVELOPMENT**

- Risk Assessment Work Group judged new risk tool was needed:
  - Inclusive of African Americans and with expanded endpoint including stroke
- Sought cohorts representative of the U.S. population as a whole:
  - Community or population-based
  - Whites and African Americans (at a minimum)
  - Recent follow-up data of at least 10 years
  - Reflect more contemporary risk factor trends and event rates, ideally without significant downstream uptake of statins/revascularization
### ASCVD Risk Calculator: Development

- **Pooled Cohort Equations**
  - Atherosclerosis Risk in Communities (ARIC)
  - Cardiovascular Health Study (CHS)
  - Coronary Artery Risk Development in Young Adults (CARDIA)
  - Framingham Original and Offspring
- **Hard ASCVD**
  - CHD death, nonfatal MI, fatal/nonfatal stroke
- **Models tested using traditional RFs + newer markers when possible**
- **Internal and external validation**

### Calculator Controversy

- **Pros:**
  - Derived from multiple and more diverse cohorts (only sufficient numbers of whites and blacks)
  - More clinically relevant endpoints (e.g., CVA)
- **Cons:**
  - No peer review evaluation prior to incorporation
  - Lack of specific risk calculator for Asians/Hispanics
  - Overestimates risk
  - Threshold lowered to 10-year risk ≥ 7.5%
CARDIOVASCULAR DISEASE STILL #1

- Despite lower risk than other ethnic groups, cardiovascular disease is still the most common cause of death among Asian Americans

ARE ALL ASIAN AMERICANS THE SAME?

MORTALITY DIFFERENCES: ASIAN SUBGROUPS

HOW ABOUT MULTIETHNIC PATIENTS?
CASE #1: CV RISK ASSESSMENT

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- Current Medications:
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- Exam: Healthy appearing man in no distress. BP 128/77 mm Hg, BMI 28.5

- Labs: TC 215, LDL 132, HDL 41, Hba1c 5.5%

CASE #2: REDUCING CV RISK

- Ms. I is a 67 year old Japanese woman with history of CAD s/p PCI of LAD in 2014, dyslipidemia, hypertension who presents to clinic for establishment of care. She is asymptomatic and walks 3 miles a day.

- Current Meds:
  - Aspirin 81 mg
  - Losartan 25 mg a day
  - Rosuvastatin 10 mg a day

- Exam:
  - Well appearing woman in no distress
  - BP 126/77 mm Hg, BMI 23.2

- Labs: BMP normal, TC 142, LDL 46, HDL 62

CASE #1: CV RISK ASSESSMENT

- Focus on diet and lifestyle modification
  - Weight not in optimal range (optimal BMI 18.5-23, obese >27)

- Exercise
  - 40 minutes of aerobic exercise 3-4x a week, moderate-high intensity activity

- Repeat fasting lipids 6-12 months to recalculate risk
**BASED ON CURRENT LIPID GUIDELINES YOU SHOULD RECOMMEND:**

- Reduce rosuvastatin to 5 mg a day
- No change in therapy
- Increase rosuvastatin to 20 mg a day
- Add ezetimibe 10 mg a day

**BASED ON CURRENT ACC LIPID GUIDELINES YOU SHOULD RECOMMEND:**

- Reduce rosuvastatin to 5 mg a day
- No change in therapy
- **Increase rosuvastatin to 20 mg a day**
- Add ezetimibe 10 mg a day

**TREATMENT FOR PATIENTS WITH ASCVD**

- ASCVD is defined as acute coronary syndromes, or a history of MI, stable or unstable angina, coronary or other arterial revascularization, stroke, TIA, or peripheral arterial disease presumed to be of atherosclerotic origin
  - ≤ 75 years old
    - High intensity statin or moderate intensity statin (if not candidate for high intensity statin)
  - > 75 years old or not candidate for high intensity statin
    - Moderate intensity statin

**ASIAN AMERICANS AND STATIN THERAPY**

- “None of the landmark statin clinical trials differentiated their patient populations on the basis of Asian ethnicity...”
- “Most studies assessing the efficacy and safety of statin therapy in Asians have been carried out in Asia”
- Differences in drug metabolism may reduce dosage requirements in Asians
STATIN THERAPY TRIALS IN ASIANS

<table>
<thead>
<tr>
<th>Table 1: Characteristics of statin trials in Asian patients</th>
<th>Lipid lowering efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statistic</td>
<td>No.</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>435</td>
</tr>
<tr>
<td></td>
<td>760</td>
</tr>
<tr>
<td></td>
<td>805</td>
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<td>252</td>
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</tbody>
</table>

CONSIDER LOWER DOSES OF STATINS?

Table 3: Recommended dose ranges for selected statins

<table>
<thead>
<tr>
<th>Statin</th>
<th>Dose Range (mg/d)</th>
<th>Japan</th>
<th>United States</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atorvastatin</td>
<td>10-40</td>
<td>10-40</td>
<td>20-80</td>
</tr>
<tr>
<td>Fluvastatin</td>
<td>20-80</td>
<td>20-80</td>
<td>20-80</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>10-20</td>
<td>10-20</td>
<td>10-20</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>2.5-20</td>
<td>5-20</td>
<td>5-20</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>5-20</td>
<td>5-20</td>
<td>5-20</td>
</tr>
</tbody>
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REDUCE CV RISK IN ASIANS WITH HYPERTENSION

- Canadian population based cohort study of hypertensive diabetics
- High proportion of Chinese and South Asians in Province of British Columbia
  - Total population ~4.6 million people, including 210,400 South Asian and 373,800 Chinese people
- Evaluated specific classes of antihypertensive therapies to see if associated with reduced CV events

DIFFERENCES BETWEEN CHINESE AND SOUTH ASIAN CV OUTCOMES

Table 5: Association between antihypertensive medications and cause-specific mortality, according to ethnicity

<table>
<thead>
<tr>
<th>Statin</th>
<th>South Asian</th>
<th>Chinese</th>
<th>Other</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARB</td>
<td>0.96 (0.91, 1.01)</td>
<td>0.47</td>
<td>0.34 (0.30, 0.39)</td>
<td>0.004</td>
</tr>
<tr>
<td>ACEI</td>
<td>0.99 (0.94, 1.05)</td>
<td>0.18</td>
<td>0.82 (0.74, 0.90)</td>
<td>0.002</td>
</tr>
<tr>
<td>GCS</td>
<td>1.15 (0.89, 1.48)</td>
<td>0.14</td>
<td>0.79 (0.72, 0.98)</td>
<td>0.08</td>
</tr>
<tr>
<td>Other</td>
<td>1.09 (0.95, 1.25)</td>
<td>0.22</td>
<td>1.03 (0.92, 1.16)</td>
<td>0.25</td>
</tr>
</tbody>
</table>

* Cox proportional hazards models were weighted using a propensity score model by the IPTW method adjusted for age, sex, SBP, cholesterol concentration and use of other medications (ACEI, ARB, beta-blockers, diuretics). AD, adjusted p-value; OR, odds ratio; CI, confidence interval; AKI, acute kidney injury; GCS, glomerular filtration rate; PTE, peripheral vascular disease; PTH, parathyroid hormone; TIA, transient ischemic attack; WBC, white blood cell count.
CASE #2: REDUCING CV RISK

• Ms. I is a 67 year old Japanese American woman with a history of CAD s/p PCI of LAD in 2014, dyslipidemia, hypertension who presents to clinic for establishment of care. She is asymptomatic and walks 3 miles a day.

• Current Meds:
  - Aspirin 81 mg
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  - Rosuvastatin 10 mg a day

• Exam:
  - Well appearing woman in no distress
  - BP 126/77 mm Hg, BMI 23.2

• Labs: BMP normal, TC 142, LDL 46, HDL 62

• Continue current dose of rosuvastatin (LDL is low)

• Repeat fasting lipids every 6-12 months

• Focus on diet and exercise

FUTURE DIRECTIONS

• Need to develop better infrastructure for research
  - Change data collection
  - Standard measurement tools (alternatives to BMI, e.g. body fat distribution), culturally-specific food surveys

• Increase participation of Asian-Americans in clinical trials

• Develop risk prediction models that account for differences in prevalence and relative importance of CV risk factors in Asian American subgroups

• Precision medicine
  - "an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person" (NIH Genetics Home Reference)
THERE IS HOPE!

• Cardiovascular disease remains the #1 cause of death among Asian Americans

• Current CV risk calculators may under- or overestimate CV risk in Asian American subgroups

• Studies to optimize CV risk factors are sparse in Asian Americans

• Need to increase awareness and conduct research on Asian American CV risk outcomes

TAKE HOME POINTS

THANKS!

SELECT REFERENCES


