The Art of Cardiovascular Risk Assessment

Laurence S. Sperling, M.D., FACC, FACP, FAHA, FASPC
Professor of Medicine (Cardiology)
Professor of Global Health
Director- Center for Heart Disease Prevention
Emory University
Immediate Past President, American Society for Preventive Cardiology
Chairman of ACC Cardiometabolic Working Group
Chairman of The U.S. National Cardiometabolic Alliance
About the Presenter

Laurence S. Sperling, MD, FACC,FACP,FAHA
Professor of Medicine
Director of The Center for Heart Disease Prevention
Emory University School of Medicine
Atlanta, GA

DISCLOSURES

No potential conflicts related to this presentation
Best Assess CV Risk?

- Case
- Discussion CV Risk Assessment
Case:
A 58 yo Southeast Asian female wants your opinion on heart attack & stroke prevention.

Moderately active, Asx. Has worked hard to make lifestyle changes for 6 mo.

BMI of 29
BP 144/78 mmHg
TC 210, HDL 32, TG 180, LDL 152
No Hx of Tob or DM
Fasting BG 110 (family Hx of DM)
QUESTION:

She is worried about her risk of diabetes. In addition, she heard statins can hurt your muscles & liver.

How do I best assess CV Risk?
Identifying those at increased risk…….
“In 1961 with just two words, Bill (Kannel) helped to change our understanding of the underlying causes of heart disease and stroke, and with two words, the entire field of preventive cardiology was born.”

Daniel Levy
Current Framingham Heart Study Director

Wong N., Sperling L., Baum S. The ASPC: Our 30 Year Legacy, Clinical Cardiology, 2016
Concept of cardiovascular “risk factors”

Factors of Risk in the Development of Coronary Heart Disease—Six-Year Follow-up Experience

The Framingham Study

Framingham, Massachusetts

Age, sex, hypertension, hyperlipidemia, smoking, diabetes, (family history), (obesity)

FIGURE 1. Risk of CHD according to elevated blood pressure (BP), elevated cholesterol, and left ventricular hypertrophy: Framingham cohort 6-year follow-up. Elevated BP = $\geq 160/95$; elevated cholesterol = $\geq 260$ mg/dl.

Framingham Heart Study: Kannel et al., 1961
Why Use Risk Scores?

1) Dr. Kannel noted risk functions provide an “economic and efficient method of identifying persons at high cardiovascular risk who need preventive treatment,” (AJC 1976)

2) The ACC Bethesda Conf. noted intensity of treatment should match a person’s risk (Califf RM, JACC 1996).

3) A physician’s estimate is only accurate 24% of the time (Pignone et al, BMC health Serv Res 2003).

4) Routine use of global risk scores leads to greater use of guideline-based therapy and modest improvements in intermediate outcomes with no harm identified (Sheridan et al. BMC Health Serv Res 2008).
Preventive cardiology efforts begin with assessment of cardiovascular disease risk

Recommendation- begin with global risk assessment using Pooled Cohort Equations to estimate 10-year ASCVD Risk
Risk Stratification

Figure 1. Implementation of Risk Assessment Work Group Recommendations

Does the patient have existing clinical ASCVD?
- Yes: See AHA/ACC Secondary Prevention Guideline
- No:
  - Is the patient <20 y or >79 y of age?
    - Yes: See Pediatric Guidelines and ACC/AHA Adult Primary Prevention Guidelines
      - Blood Cholesterol
      - Obesity
    - No: Assess traditional risk factors every 4-6 y in patients 20-79 y of age; estimate 10-y risk in those 40-79 y of age using Pooled Cohort Equations
      - Elevated 10-y risk (≥7.5%):
        - Communicate risk data and refer to AHA/ACC Prevention Guidelines
          - Blood Cholesterol
          - Obesity
        - Low 10-y risk (<7.5%):
          - Assess 30-y or lifetime risk in those 20-59 y of age; Communicate risk data regardless of age and refer to AHA/ACC Lifestyle Guideline
Pooled Cohort Equations for ASCVD Risk

predict 10-year risk of both CHD and stroke (ASCVD) vs. CHD (focus of 2001 ATP III)

predict nonfatal MI, CHD death, or nonfatal or fatal stroke ONLY; do not include (PCI, CABG, UA requiring hospitalization, PAD) - Risk will be higher for total CVD

Clincalc; omnibus risk estimator; AHA; ACC Cardiosource
Pooled ASCVD RS- How used?

incorporate 4 cohorts: Framingham (original and offspring), ARIC, CARDIA, and CHS

used as starting point to help identify those most likely to benefit from a statin; other tests may help refine the treatment decision if uncertain

should be an impetus for a “risk discussion” between the clinician and patient
The ACC and the American Heart Association (AHA), in collaboration with the National Heart, Lung, and Blood Institute and other specialty societies, have released four guidelines focused on the assessment of cardiovascular risk, lifestyle modifications to reduce cardiovascular risk and management of elevated blood cholesterol and body weight in adults.

In order to support the implementation of these guidelines the ACC and AHA have jointly published a new mobile application (app).

The ASCVD Risk Estimator application helps health care providers and patients estimate 10-year and lifetime risks for atherosclerotic cardiovascular disease (ASCVD) using the Pooled Cohort Equations and lifetime risk prediction tools. The ASCVD Risk Estimator provides easy access to recommendations specific to calculated risk estimates. Additionally, the app includes readily accessible guideline reference information for both providers and patients related to therapy, monitoring, and lifestyle.

The app is available on both iTunes (iPhones, iPads) and Google Play (Galaxy, Nexus, other Android devices). Use the links below from your mobile device to download the app.

Available at www.cardiosource.com or www.clincalc.com
ASCVD Risk Estimator

- 10 year ASCVD Risk
- For those 20-59 risk estimator provides lifetime risk estimate
- Intended to drive discussions of greater adherence to heart-healthy lifestyle
- Part of risk discussion
Our case……
A 58 yo Southeast Asian female wants your opinion on heart attack & stroke prevention.

Moderately active, Asx. Has worked hard to make lifestyle changes for 6 mo.
BMI of 29
BP  144/ 78  mmHg
TC 210 , HDL 32 , TG 180 , LDL 152
No Hx of Tob or DM
Fasting BG 110  (family Hx of DM)
Her 10 yr ACC/AHA ASCVD risk is 5.3% (optimal risk 1.9%)

Remember……she is worried about her risk of diabetes. In addition, she heard statins can hurt your muscles & liver.

Discussion & implementation of treatment recommendations?
Lifetime Risk for CVD (Age 50) – LOE C

Men

Women

Adjusted Cumulative Incidence

Attained Age

≥2 Major RFs
1 Major RF
≥1 Elevated RF
≥1 Not Optimal RF
Optimal RFs

Lloyd-Jones, Circulation 2006
Her Lifetime ACC/ AHA ASCVD risk is 39% (optimal risk 8%)

Impact discussion & treatment recommendations?
From: Clinician-Patient Risk Discussion for Atherosclerotic Cardiovascular Disease Prevention: Importance to Implementation of the 2013 ACC/AHA Guidelines

A. Relative risk of experiencing a cardiac event or death by diabetes status (for a near 40 mg/dL reduction in LDL cholesterol) from a meta-analysis of 14 clinical trials of statin therapy.

B. Should I start a statin in my patient?

What is the underlying patient-specific risk of a cardiac event? (by conventional risk algorithms, e.g., Framingham score; primary vs. secondary prevention)

Ravi V. Shah, and Allison B. Goldfine Circulation. 2012;126:e282-e284
Efficacy & Safety of Statins

• Atorva 40 mg in 10K with ASCVD / High Risk
  – Prevent 1K events with ASCVD (10% absolute RR)
  – Prevent 500 events in high risk population (5% RR)
  – 5 cases myopathy / 50-100 myalgias
  – 50-100 new cases of diabetes

“Evidence-Based” Not “Evidence-Bound”

Three Key Dimensions

Scientific evidence

Patient preference

Clinical Judgment
Receiver Operating Characteristic Curves and Disease Prediction

![Graph showing ROC curves for different tests with sensitivity (true positives) on the y-axis and 1-specificity (false positives) on the x-axis. The graph compares a better test, a good test, and a chance line.]
Comparison of Novel Risk Markers for Improvement in Cardiovascular Risk Assessment in Intermediate-Risk Individuals

Intermediate Risk MESA Subjects
(n=1330)

C-statistics:
FRS alone 0.623
FRS+CAC 0.784 (p<0.001)
FRS+CIMT 0.652 (p=0.01)
FRS+FMD 0.639 (p=0.06)
FRS+CRP 0.640 (p=0.03)
FRS+FamHx 0.675 (p=0.001)
FRS+ABI 0.650 (p=0.01)

Yeboah J et al, JAMA 2012
“…risk estimation is based on group averages...applied to individual patients in practice. This process is admittedly imperfect..”

2013 ACC / AHA Guidelines on the Assessment of CV Risk
Biomarkers & Noninvasive Testing that Can Inform Treatment Decision (when Uncertain Based on RA)

1) Primary LDL-C $\geq 160$ mg/dl or other genetic evidence of hyperlipidemia
2) Family history of premature ASCVD with onset $< 65$ in a female first degree or $< 55$ years of age in a male first degree relative
3) C-reactive protein $\geq 2$ mg/L
4) CAC score $\geq 300$ or $\geq 75^{th}$ percentile for age and sex
5) ABI $< 0.9$ indicative of peripheral arterial disease
6) Elevated lifetime risk of CVD
Contribution to RA is uncertain at present

1) ApoB
2) CKD
3) Albuminuria
4) Cardiorespiratory fitness
The Detection Gap in CHD

“Despite available RA approaches substantial gap in detection of asymptomatic individuals who develop CHD”

Current risk scores… “emphasize classic risk factors…. only moderately accurate for prediction of short- and long-term risk of major events…”

Pasternak and Abrams et al. 34th Bethesda conf. JACC 2003; 41: 1855-1917
Predicting ASCVD Risk?

Arterial imaging/function

Biomarkers

Metabolic syndrome

Family history

Pooled 10 yr ASCVD Risk Equation

Identification of the Metabolic Syndrome

- Abdominal obesity (waist circumference)
  - Men >40 in
  - Women >35 in
- Triglycerides >150 mg/dL
- HDL-cholesterol
  - Men <40 mg/dL
  - Women <50 mg/dL
- Blood pressure >130/85 mm Hg
- Fasting glucose >100 mg/dL
Affirmed Concepts

• MetS associated with risk for DM & ASCVD
• MetS cluster of under-recognized causally inter-related RFs
• Risk increases with # of components
• Ectopic and visceral adiposity central
• Treatment-prioritize TLC / focus on specific components

Sperling LS, et al. JACC 2015;66(9):1050-1067
Staging system for MetS- A Framework
Sperling LS et al., JACC 2015;66(9):1050-67

• Identify
• Risk-stratify
• Apply evidence-based therapeutic interventions
  – **imperative that Rx decisions incorporated within context of absolute risk
Stages in Evolution of MetS
(Therapy by Stage)
Sperling LS et al., JACC 2015;66(9):1050-67
Spectrum / Lifecourse of Health

Optimal Window at 3-5 years

Promotion of CV Health

Subclinical CVD

Stable CVD

Acute CV Events

Secondary Prevention

Primary Prevention

Adapted from Fuster V., JACC 2015; 66(4):482.
Biomarkers and Noninvasive Testing Can Inform Treatment Decision (when Uncertain Based on Risk Assessment)

1) Primary LDL-C >160 mg/dl or other genetic evidence of hyperlipidemia
2) Family history of premature ASCVD with onset <65 in a female first degree or <55 years of age in a male first degree relative
3) C-reactive protein >=2 mg/L
4) CAC score >=300 or >=75th%tile for age and sex
5) ABI <0.9 indicative of PAD
6) Elevated lifetime risk of CVD
Non-traditional CV Risk Factors

- Autoinflammatory diseases
- XRT
- X-plant recipients
- Stress / Anxiety / depression
- Pregnancy-related disorders
  - Gest DM, preeclampsia
- Drugs / Toxins
  - Cocaine, HRT, ? NSAIDS
Criteria for Marker of CV Risk

- Proof of concept
- Prospective validation
- Incremental value
- Clinical utility
- Clinical outcomes
- Cost-effectiveness

- AHA Scientific Statement, Hlatky MA et al., Circulation, 2009;119
Use All Available Information

- Contemporary Risk Score Calculators
- Clinical Markers of ASCVD
- Advanced Measures of Subclinical Atherosclerosis (CAC) For Difficult Cases

### Table. Clinical Markers of Coronary Heart Disease Risk

<table>
<thead>
<tr>
<th>Category</th>
<th>Markers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Historical markers</td>
<td>Family history, Transient ischemic attack, Claudication, Erectile dysfunction, Physical inactivity</td>
</tr>
<tr>
<td>Physical examination markers</td>
<td>Widened pulse pressure, Ankle–brachial index, Increased waist circumference, Retinal arteriolar narrowing, Aortic aortic murmur, Carotid bruit, Femoral bruit, Absent lower extremity pulses</td>
</tr>
<tr>
<td>Radiologic markers</td>
<td>Aortic knob calcification, Abdominal aortic calcification, Breast arterial calcification (mammogram), Laboratory/electrocardiographic markers</td>
</tr>
<tr>
<td>Fasting blood glucose</td>
<td></td>
</tr>
<tr>
<td>Serum creatinine/microalbuminuria</td>
<td></td>
</tr>
<tr>
<td>Left ventricular hypertrophy</td>
<td></td>
</tr>
</tbody>
</table>

DeFilippis A, Sperling LS. Prev Card 2007
Art of CV Risk Assessment - Summary

• RA begins with population-based risk score
• Importance of
  – Clinician-patient risk discussion
  – Net clinical benefit
• Consider select use
  – Biomarkers
  – Measures of subclinical atherosclerosis
• GLs are a starting point