Global Perspectives of CV Health
Aging / Disease to Youth / Health

VUS in Subclinical Disease

New York, June 15, 2017  No Disclosures
From Aging / Disease to Youth / Health

- Primordial
- Primary
- Secondary

2) TANSNIP AGING
3) HRP PESA AWHS
4) IIIP 50/50
5) SHE
6) HARLEM VILLAGE MEXICO

Additional text:

- Aging / Disease to Youth / Health
1. Feasibility: 2D/3D, Presence & Distribution

2. Prediction: Progression plaques & Events

3. Prevention: Lipid Aspects & Statins

4. Future: Technological & Clinical
From Aging / Disease to Youth / Health


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From Aging / Disease to Youth / Health
1). Subclinical Atherosclerotic Burden
Carotid 2D/3D-VUS  Coronary Calcification

The High Risk Plaque (HRP) or BioImage Study - Events
The High Risk Plaque (HRP) or BioImage Studym- Events
216 first MACE events were observed. Increasing cPB and cPTmax were both associated with increasing risk of disease & future MACE as compared to those without carotid disease. Fully adjusted for RFs, HR for cPTmax were for 1ary MACE 1.96, and for 2ary MACE 3.13. IMT did not improve risk prediction significantly. The simpler cPTmax predicted CV events similarly to the more comprehensive cPB whereas IMT did not
The Bioimage Study (N=5808)
Polyvascular Atherosclerosis & Framingham Risk

- Any Polyvascular Atherosclerosis (Tertile 1 or greater)
- Moderate Polyvascular Atherosclerosis (Tertile 2 or greater)
- Extensive Polyvascular Atherosclerosis (Tertile 3)

Prevalence (%)

- Entire Cohort (N=5,808): 58% Any, 31% Moderate, 11% Extensive
- Low Risk (N=3,829): 50% Any, 23% Moderate, 6% Extensive
- Intermediate Risk (N=1,527): 71% Any, 44% Moderate, 19% Extensive
- High Risk (N=452): 81% Any, 56% Moderate, 28% Extensive

The Bioimage Study (N=5808)
Cumulative 3-Year MACE 2ary Endpoints (N=216)
The Bioimage Study (N=5808)
Cumulative 3-Year MACE Primary Endpoints (N=82)

Reclassification: CAC 24% - cPB 18%
3). The Bioimage Study (N=5808)
Disease-Guided Primary Prevention With Statins

B. Clinical Implications in the BioImage Study

5,805 BioImage participants free of ASCVD at baseline

2013 ACC/AHA
86% Statin Eligible

CAC-guided
64% Statin Eligible

Net Reclassification Improvement
CHD: 20%
CVD: 14%
*NRI = ΔSensitivity + ΔSpecificity

70% Statin Eligible

cPB-guided

Net Reclassification Improvement
CHD: 9%
CVD: 6%

Improved Statin Allocation
The Bioimage Study (N=5808)
Disease-Guided Primary Prevention With Statins

A. Simple Disease-guided Reclassification Approach

<table>
<thead>
<tr>
<th>Individuals Free of ASCVD</th>
<th>ACC/AHA Statin Eligibility</th>
<th>Subclinical Atherosclerosis?</th>
<th>Disease-guided Reclassification</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Step 1</td>
<td>Step 2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Not eligible</td>
<td>Yes=Up-classify</td>
<td>Not eligible</td>
</tr>
<tr>
<td></td>
<td>Statin eligible</td>
<td>No=Down-classify</td>
<td>Statin eligible</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Improved statin allocation after clinician-patient discussion</td>
</tr>
</tbody>
</table>

A healthy life style score (7) and a polygenic score of DNA sequence polymorphisms (50), we quantified genetic risk for CAD in four prospective cohorts – 7814 participants in the Atherosclerosis Risk in Communities (ARIC) study, 21,222 in the Women’s Genome Health Study (WGHS), and 22,389 in the Malmö Diet and Cancer Study (MDCS) – and in 4260 participants in the cross-sectional BioImage Study. Across four studies involving 55,685 participants, lifestyle and genetic factors were independently associated with susceptibility to CAD. Among participants at high genetic risk, a favorable lifestyle was associated with a 50% lower relative risk of CAD.

AV Khera, V Fuster, PM Ridker et al., NEJM 2016; 375:2349
Standardized Coronary Events Rates, Genetic and Lifestyle Risk

Atherosclerosis Risk in Communities

Genetic Risk
- High; hazard ratio, 1.75 (1.46–2.10)
- Intermediate; hazard ratio, 1.27 (1.09–1.49)
- Low (reference)

Lifestyle Risk
- Unfavorable; hazard ratio, 1.71 (1.47–1.98)
- Intermediate; hazard ratio, 1.18 (1.02–1.36)
- Favorable (reference)

Temporal Sequence & Functions of Leukocytes in the CAs

Thrombosis promoting factors
Thrombosis resisting factors
Vascular Thrombosis/ACS
Asymptomatic Plaque Healing

High Risk Plaque Study Participants Who Underwent Carotid Ultrasound (Chicago, Florida)

Additional data:
- Coronary Calcium Biomarkers
- Genomic markers
- MRI
- PET-CT

3-D Carotid Plaque Volume Ultrasound

CV Risk assessment

Events and long-term Follow up

Sept 1, 2017

8 yrs

4b)
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1). The PESA Study (N=4184) – 2D/3D & 3D-VUS Atherosclerosis Assessment (mm$^3$)

2). The PESA Study (N=4184)
Presence/Extend Subclinical Atherosclerosis

L Fernandez-Friera, A Fernandez-Ortiz, V Fuster et.al
Circulation 2015;131:2104
The PESA Study (N=3860)
Femoral And Carotid 3D-VUS Plaque Volume

The PESA Study (N=3860)
Predicting (OR) Carotid / Femoral 3D Plaque Burden

The PESA Study (N=4184)
Subclinical Atherosclerosis & Framingham Risk Score

L Fernández-Friera, V Fuster et al., Circulation 2015; 131:2104
The PESA Study (N=4184)
Subclinical Atherosclerosis & 10 yr European Risk Score

L Fernández-Friera, V Fuster et al., Circulation 2015; 131:2104
3). The PESA Study (N=4184) Subclinical Atherosclerosis & AHA/ACC Criteria for Statins

L Fernández-Friera, V Fuster et al., Circulation 2015; 131:2104
Expected rate of cardiovascular events in PESA participants

≈ 600 events by 9 years of follow-up
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2). The AWHS Study (N=1423)
Subclinical Atherosclerosis & FRS Equations

![Graph showing ASCVD 10-year risk and subclinical atherosclerosis]

- Low Risk (<5%) (n=591)
- Moderate Risk (5-7.5%) (n=375)
- High Risk (≥7.5%) (n=457)

M Laclaustra, V Fuster et al. J Am Coll Cardiol 2016;67:1263
The AWHS Study (N=1423) - 3D-VUS Subclinical Disease Distribution

Age-adjusted prevalence of atherosclerosis estimated for 50-year-old males

Prevalence (%)

<table>
<thead>
<tr>
<th>Territory</th>
<th>None</th>
<th>One</th>
<th>Two</th>
<th>Three or More</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carotid</td>
<td>23.1%</td>
<td>28.6%</td>
<td>35.5%</td>
<td>44.7%</td>
</tr>
<tr>
<td>Femoral</td>
<td>34.1%</td>
<td>46.6%</td>
<td>63.7%</td>
<td>84.0%</td>
</tr>
<tr>
<td>Coronary</td>
<td>21.0%</td>
<td>34.1%</td>
<td>41.7%</td>
<td>45.1%</td>
</tr>
</tbody>
</table>

Any territory

Any territory

Any territory

Any territory

M Laclaustra, V Fuster et. al. J Am Coll Cardiol 2016;67:1263
3). Ideal CV Health Score (ICH, AHA) & Fuster-BEWAT Scores (FBS)
4). The AWHS Study (N=1423) Framingham, CACS & Ultrasound

Variables included in the prediction model

- Risk Factors
- Risk Factors + Carotid Plaques
- Risk Factors + Femoral Plaques
- Risk Factors + Carotid Plaques + Femoral Plaques

CACS ≥ 1

- 0.665
- 0.689
- 0.706
- 0.719

CACS ≥ 300

- 0.743
- 0.778
- 0.810
- 0.827

M Laclaustra, V Fuster et. al. J Am Coll Cardiol 2016;67:1263
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4a). AMPATH Centers In Kenya
BP Control / Non MD / High Technology

R Vedanthan, V Fuster, NHLBI / Kenya Model (2012-2016)
4b). The Seven Community Study

N=552

Spain - E. Gomez, V Fuster et al JACC 2016; 67:476
Cardona Integral – “Fifty-fifty” - 2014
Global Demonstration Project – GHP – 2013
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AWHS

PESA
3. HW Querfurth et al NEJM 2010;362:329 - Ischemia 60-90% A’sD
5. CARDIA (K Yaffe et al) Circ 2014;129:1560 - CV RFrs, Cognitive
6. JI Friedman et al. JACC CV Imag. 2014;7:1039 - Imaging
7. FINGER (T Ngandu et al), Lancet 2015; 385:2255 - Intervention
Increasing evidence suggests that many lifestyle-related factors, including diabetes, obesity, physical and mental inactivity, depression, smoking, low educational attainment, and diet have a role in dementia, and the potential for primary prevention related to such modifiable risk factors is huge but yet to be fully explored. On the basis of the Rotterdam study, it has been modelled that elimination of the seven most important modifiable risk factors would lead to a 30% reduction in dementia incidence.

P Scheltens et al., The Lancet 2016; 388:507 - Dementia
Hypertension disrupts the structure and function of cerebral blood vessels, leads to ischemic damage of white matter regions critical for cognitive function, and may promote Alzheimer pathology. There is strong evidence of a deleterious influence of midlife hypertension on late-life cognitive function. Observational studies demonstrated a cumulative effect of hypertension on cerebrov. damage, but evidence from clinical trials that antihypertensive treatment improves cognition is not conclusive.

C Iadecola et al., Hypertension 2016; 68: e67-e94
10. **Cardiovascular Risk Factors From Childhood & Midlife Cognitive Performance**

*YFS (SP Rovio et al), J Am Coll Card 2017 (In Press)*
TANSNIP Pathway 1

STEP 1: Neurocognitive battery

Cognitive impaired N=50

Cognitive Normal N=50

CV Risk Assessment

CACS

3DVUS-Carotid Plaque Volume and ileo-femoral

PET for Amyloid

MRI- functional + Micro/ Macrovasculature

FAD

N=2750
TANSNIP Pathway 2

STEP 1:
CACS
Carotid Plaque w Volume

Continuous Scale
N=100

Source- MSH
Coronary CT Suites

CV Risk Assessment

3-D carotid and ileo-femoral ultrasound

PET for Amyloid

Neurocognitive Testing

MRI- functional + Micro/Macrovasculature
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Child’s Brain Development
Less Networking Brings Attention

Increasing Communications among Brain Regions over Time

JN Giedd. Scientific American 2015;312:32
CHILDREN’S – BOGOTA, SPAIN, NEW YORK – N = 50,000

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4. Future: Technological & Clinical (DBD, A’sD)
EDUCATION (7)

CARDONA - MEXICO - PERU

HARLEM

GRENA DA - SPAIN
KENYA
US - SPAIN

SPAIN
BOGOTA

Villages (3)
Family (1)
Adults (5)
Children (2)

CONCEPTS, SCIENTIFIC STUDIES, NPOs
GLOBAL HEALTH & THE FUTURE ROLE OF THE US

Report Conceptual Model

SECURING AGAINST GLOBAL THREATS

Global Health Security
Continuous Communicable Threats

ENHANCING PRODUCTIVITY AND ECONOMIC GROWTH

Saving and Improving the Lives of Women and Children
Promoting Cardiovascular Health and Preventing Cancer

Maximizing Returns
Catalyzing Innovation
Smart Financing
Global Health Leadership