Imaging Modalities in Search of a Vulnerable Plaque

Nurse / Technologist Symposium

Jagat Narula MD, PhD, MACC
Philip J. and Harriet L. Goodhart Chair in Cardiology
Chief of Cardiology, St. Luke’s & Roosevelt Hospitals at Mount Sinai
Associate Dean, Arnhold Institute for Global Health at Mount Sinai
Editor-in-Chief, Journal of the American College of Cardiology- Imaging
Executive Editor, Journal of the American College of Cardiology

DISCLOSURES: NONE
Why Must A Clinician Understand Plaque Morphology?

NBC’s Tim Russert dies of heart attack at 58
Washington bureau chief, ‘Meet the Press’ moderator collapsed on job
NBC News and MSNBC; updated 4:07 a.m. PT, Sat., June 14, 2008
Histomorphological Characteristics of High-Risk Atherosclerotic Plaques

Morphology beyond geometry...

90-60/90 = 33%  
300-200/300 = 33%
Histopathological Characteristics of High-Risk Plaques
Picking Plaques that Pop! Narula & DeMaria, JACC [Editorial] 2005
[OCT in] Thin & Thick-Cap Fibroatheroma
Otsuka, Narula et al. Nature Reviews Cardiology 2014
Characterizing Plaques by CTA
2-Feature Positive & 2-Feature Negative Plaques

Motoyama, Narula, et al. JACC 2007
CTA Characteristics and Subsequent Coronary Events

*Motoyama, Narula et al. JACC 2009*

N = 1059

2 Feature-Positive PR(+), LAP(+)
45

1 Feature-Positive PR(+) or LAP(+)
27

2 Feature-Negative PR(-), LAP(-)
820

No Plaque
167

ACS(+)
10
ACS(-)
35
ACS(+)
1
ACS(-)
26
ACS(+)
4
ACS(-)
816
ACS(+)
0
ACS(-)
167
FDG-PET/CTA Imaging: Stable Angina

Tawakol et al. JACC-Imaging Apr 2010
Putting TCFA Into Clinical Perspective...

Narula [Editorial] JACC August 2014; data extracted from Kubo et al. 2010
Putting a High-Risk Plaque Into Clinical Perspective...

Lesion based analysis: number of ACS based on plaque characteristics

Kaplan-Meier Curve for ACS based on CTA-1 and CTA-2

Log-rank: \( p < 0.0001 \)

Median f/u, 3.1 years; \( n = 3158 \) (maximum, 10.5 years)

Motoyama, Narula et al. Presented at AHA 2013; submitted to JACC 2014
<table>
<thead>
<tr>
<th>RF</th>
<th>Lipid</th>
<th>Smoke</th>
<th>HTN</th>
<th>DM</th>
<th>obese</th>
<th>Psych</th>
<th>V&amp;F</th>
<th>Alc</th>
<th>PE</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR</td>
<td>3.25</td>
<td>2.37</td>
<td>1.91</td>
<td>2.37</td>
<td>1.12</td>
<td>2.67</td>
<td>-0.7</td>
<td>-0.86</td>
<td>-0.91</td>
</tr>
<tr>
<td>PAR</td>
<td>49.2</td>
<td>35.7</td>
<td>17.2</td>
<td>9.9</td>
<td>20.1</td>
<td>32.5</td>
<td>13.7</td>
<td>12.2</td>
<td>6.7</td>
</tr>
</tbody>
</table>

**INTER-HEART STUDY**

*52 Countries, 27K Subjects*

Yusuf et al. Lancet 2006
INTERHEART Apo B/A-1 and MI: Simplicity of Principles, Consistency of Observations

INTERHEART: ApoB/ApoA-1 ratio and MI (top quintile vs. lowest quintile)
Lady Rai - Nursemaid to Queen Amrose Nefertari who died in her 30’s during the early 18th Dynasty, 1570-1530 BC

Allam, et al. JACC-Imaging 2011
Vascular Calcification and Atherosclerosis In Egyptians

HORUS Study: Djeher, Male, 50-60 Years Ptolemaico Period - 304-30 BCE
Vascular Calcification and Atherosclerosis 10,000 Years Ago

Lima, Peru, May 2012
We LIVE in a world very DIFFERENT from that for which we are genetically adapted. Profound changes in our environment began with the introduction of agriculture and animal husbandry 10,000 years ago, too recent on an evolutionary time scale for the human genome to adjust.

As a result of this ever-worsening discordance between our ancient genetically determined biology and the nutritional, cultural, and activity patterns in modern populations, the so-called diseases of civilization, including atherosclerosis, have emerged.

<table>
<thead>
<tr>
<th>Hunter-Gatherer Humans:</th>
<th>LDL [mmol/L]</th>
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<tbody>
<tr>
<td>Hazda</td>
<td></td>
</tr>
<tr>
<td>Inuit</td>
<td></td>
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<tr>
<td>IKung</td>
<td></td>
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<tr>
<td>Pygmy</td>
<td></td>
</tr>
<tr>
<td>San</td>
<td></td>
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<tr>
<td>Wild Primates:</td>
<td></td>
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<tr>
<td>Baboon</td>
<td></td>
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<tr>
<td>Howler Monkey</td>
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<tr>
<td>Night Monkey</td>
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<tr>
<td>Wild Mammals:</td>
<td></td>
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<tr>
<td>Horse</td>
<td></td>
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<tr>
<td>Boar</td>
<td></td>
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<tr>
<td>Peccary</td>
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<tr>
<td>Black Rhinoceros</td>
<td></td>
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<tr>
<td>African Elephant</td>
<td></td>
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<tr>
<td>Modern Humans:</td>
<td></td>
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<tr>
<td>Adult Human</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Time (years)</th>
<th>Mean Total Cholesterol (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth</td>
<td>50</td>
</tr>
<tr>
<td>1</td>
<td>70</td>
</tr>
<tr>
<td>2</td>
<td>90</td>
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<tr>
<td>3</td>
<td>110</td>
</tr>
<tr>
<td>5</td>
<td>130</td>
</tr>
<tr>
<td>10</td>
<td>150</td>
</tr>
</tbody>
</table>

FAMILY Study Mean LDL- C at birth, 1, 3 and 5 years

![Graph showing LDL levels over time](image)

Courtesy: Salim Yusuf MD, Hamilton, ON
Predicted Probability of Acute MI at a Younger Age in S. Asians Compared with Individuals from Other Countries
EVOLUTION OF HUMANITY AND ANCESTROL MIGRATION: STORY OF 18 EVES

EVES: 3 African (L0-3, M, N), 6 Asians (A-D, F, G), 9 Europeans (H-K, T-X)

200,000 YBP

L0

20-300,000 YBP

ACD G

100,000 YBP

A, D

15,000 YBP

X

40-50,000 YBP

HIJKTUVWX

65,000 YBP

L3

6,500 YBP

M

N

A-F

F

20,000 YBP

L2

10,000 YBP

A-D

ACD

H

L1

0-20,000 YBP

0-300,000 YBP

ACD

X

Courtesy: Douglas C. Wallace, PhD
...THIS DAMN KREB CYCLE!

carbohydrate metabolism 6% lipid (fat) metabolism

Krebs' cycle

starve feed protein & amino acid metabolism
Deaths Attributable to Individual Risk Factors

Ezzati et al. NEJM 2013

The Death of Diseases

That our grand children will not know what CVD is, and ask us …” Granpa or Granma… it must have been a terrible time when there were all those nasty diseases….plague, small pox, polio and heart disease...Why did those diseases die?”

- Salim Yusuf 2012

I sincerely hope our children will live in a better world where the diseases would have died...