Virtual Histology Intravascular Ultrasound Analysis of Non-culprit Attenuated Plaques Detected by Grayscale Intravascular Ultrasound in Patients with Acute Coronary Syndromes

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Cardiovascular Research Foundation and Columbia University Medical Center, New York.
Disclosure

Gary S. Mintz
A member of the speakers bureau, serves as a consultant, has received research/grant support, and a stockholder with Volcano Corporation

Takashi Kubo
Has received research-grant support from Volcano Corporation

Martin B. Leon and Gregg W. Stone
Serve as consultants for Volcano Corporation

Bernard De Bruyne

Patrick W. Serruys

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NO relationships to disclosure
Attenuated plaque & Histopathology

- Attenuated plaque is defined as hypoechoic or mixed atheroma with ultrasound attenuation without evidence of calcification in grayscale IVUS.
- Histopathologically, attenuated plaque contains microcalcifications and cholesterol crystals.

[Image showing ultrasound attenuation behind plaque, cholesterol cleft with hematoxylin and eosin staining, and microcalcification with Von Kossa staining.]
Attenuated plaque & No-reflow

- Attenuated plaques are often seen in ACS
- Attenuated plaques are associated with no-reflow and CK-MB elevation after PCI

Post-PCI decrease from baseline in final TIMI flow grade <2 without identified mechanical obstruction
†Deteriorated post-PCI coronary blood flow
The overall predictive accuracies of VH were 93.5% for Fibrous, 94.1% for fibro-fatty, 95.8% for necrotic core and 96.7% for dense-calcium when used to identify different atherosclerotic plaque elements.

Reproducibility of VH-IVUS analyses

The presence and size of the VH-IVUS necrotic core are related to liberation of small embolic particles during coronary stenting in ACS.

* Nair A et al Euro Intervention 2007;3:113-20
‡ Kawamoto T et al J Am Coll Cardiol 2007;50:1635-40
¶ Kawaguchi R et al J Am Coll Cardiol 2007;50:1641-6
Hypothesis

Attenuated plaques contain large amounts of necrotic core that would also explain the unstable nature of such lesions.
The PROSPECT Trial

700 pts with ACS
UA (with ECGΔ) or NSTEMI or STEMI >24hrs
1-2 vessel CAD undergoing PCI
at up to 40 sites in U.S., Europe

Metabolic S.
- Waist circum
- Fast lipids
- Fast glu
- HgbA1C
- Fast insulin
- Creatinine

Biomarkers
- Hs CRP
- IL-6
- sCD40L
- MPO
- TNFα
- MMP9
- Lp-PLA2
- others

PCI of culprit lesion(s)
Successful and uncomplicated
Formally enrolled

PI: Gregg W. Stone
Sponsor: Abbott Vascular; Partner: Volcano
3-vessel imaging post PCI

Culprit artery, followed by non-culprit arteries

Angiography (QCA of entire coronary tree)

IVUS

Virtual histology

Palpography (n=~350)

Meds rec
Aspirin
Plavix 1yr
Statin
Repeat biomarkers @ 30 days, 6 months

F/U: 1 mo, 6 mo, 1 yr, 2 yr, ±3-5 yrs

Repeat imaging in pts with events

MSCT Substudy N=50-100

Proximal 6-8 cm of each coronary artery
Methods

Study Population

124 vessels / 64 patients

111 vessels / 64 patients

13 vessels were excluded
4 had severe calcification
9 without a $\geq 40\%$ plaque burden

Grayscale analysis

Attenuated plaque group
maximum attenuation arc site
50 lesions / 46 vessels / 34 patients

Non-attenuated plaque group
MLA site
65 lesions / 65 vessels / 30 patients

VH analysis

Attenuated plaque group
maximum attenuation arc site
47 lesions / 43 vessels / 34 patients

Non-attenuated plaque group
MLA site
65 lesions / 65 vessels / 30 patients

3 vessels with attenuated plaques were excluded due to without $\geq 3$ frames of matched VH images
Methods - II
- Lesion site -

Attenuated plaque
Maximum attenuation arc site, >40% plaque burden,
Separate = if >5mm far each other

Exclusion stent segment

Control
MLA site, >40% plaque burden
Methods - III

- IVUS-VH Imaging -

- IVUS system: phased-array, 20 MHz, catheters (Volcano)
- Automatic pullback at 0.5mm/sec
- Gray scale image=10 frame/second
- VH data=1 frame/beat at R-wave

- 4 color code
  - Necrotic Core
  - Fibrofatty
  - Fibrous tissue
  - Dense Calcium
VH-IVUS Classification

- Fibrothromboma: >10% confluent necrotic core
- VH-TCFA: 30° NC abutting to lumen

**VH-TCFA**
- >30° abutting
- Visible fibrotic cap
- >10% confluent NC

**ThFA**
- Visible fibrotic cap
- >15% FF
- <10% confluent NC

**PIT**
- Visible fibrotic cap
- >10% confluent NC

**Fibrotic**
- >10% confluent DC

**Fibrocalcific**
- >10% confluent DC
# Baseline Patients Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>52 (81%)</td>
</tr>
<tr>
<td>Age, yrs</td>
<td>59±12</td>
</tr>
<tr>
<td>ACS, n (%)</td>
<td></td>
</tr>
<tr>
<td>unstable angina</td>
<td>42 (39%)</td>
</tr>
<tr>
<td>NSTEMI</td>
<td>36 (23%)</td>
</tr>
<tr>
<td>STEMI (&gt;24hrs)</td>
<td>30 (28%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>42 (66%)</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>43 (67%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>11 (17%)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>29 (45%)</td>
</tr>
<tr>
<td>Previous myocardial infarction (MI)</td>
<td>3 (5%)</td>
</tr>
<tr>
<td>Culprit lesion</td>
<td></td>
</tr>
<tr>
<td>Left anterior descending</td>
<td>205 (46%)</td>
</tr>
<tr>
<td>Left circumflex</td>
<td>107 (24%)</td>
</tr>
<tr>
<td>Right</td>
<td>132 (30%)</td>
</tr>
</tbody>
</table>

Mean + SD or Number (percent)
Attenuated plaques identified by grayscale IVUS

47 attenuated plaque was present at 43 vessels in 34 patients

- Culprit vessel: 31 (52%) non-attenuated, 16 (34%) attenuated
- Non-culprit vessel: 34 (52%) non-attenuated, 17 (48%) attenuated

- LAD: 23 (53%) non-attenuated, 20 (47%) attenuated
- LCX: 24 (65%) non-attenuated, 13 (35%) attenuated
- RCA: 18 (56%) non-attenuated, 14 (44%) attenuated

P = 0.15 for culprit vs. non-culprit vessel
P = 0.6 for LAD vs. LCX vs. RCA
Distribution of attenuated plaques

39 (83%) attenuated plaques were located within 40mm proximal to the ostium of coronary arteries: 17 (85%), 12 (92%) and 10 (71%) in LAD, LCX and RCA, respectively.
# Gray-Scale IVUS Findings

<table>
<thead>
<tr>
<th>Lesion site</th>
<th>Attenuated plaque N=47</th>
<th>Non-attenuated plaque N=65</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EEM CSA, mm(^2)</td>
<td>16.5 ± 5.7</td>
<td>14.6 ± 4.6</td>
<td>0.12</td>
</tr>
<tr>
<td>Lumen CSA, mm(^2)</td>
<td>7.0 ± 3.9</td>
<td>5.6 ± 1.8</td>
<td>0.07</td>
</tr>
<tr>
<td>P&amp;M CSA, mm(^2)</td>
<td>9.5 ± 3.1</td>
<td>9.0 ± 3.5</td>
<td>0.53</td>
</tr>
<tr>
<td>Plaque burden, %</td>
<td>59.0 ± 11.4</td>
<td>60.8 ± 8.1</td>
<td>0.41</td>
</tr>
<tr>
<td>Eccentricity index</td>
<td>9.0 ± 8.7</td>
<td>5.9 ± 3.4</td>
<td>0.02</td>
</tr>
<tr>
<td>Positive remodeling, %</td>
<td>50.0</td>
<td>17.1</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td><strong>Proximal reference segment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EEM CSA, mm(^2)</td>
<td>16.5 ± 5.8</td>
<td>15.2 ± 5.1</td>
<td>0.33</td>
</tr>
<tr>
<td>Lumen CSA, mm(^2)</td>
<td>8.8 ± 4.8</td>
<td>8.1 ± 2.4</td>
<td>0.46</td>
</tr>
<tr>
<td>P&amp;M CSA, mm(^2)</td>
<td>7.7 ± 2.9</td>
<td>7.1 ± 3.7</td>
<td>0.50</td>
</tr>
<tr>
<td>Plaque burden, %</td>
<td>47.9 ± 13.8</td>
<td>45.2 ± 11.8</td>
<td>0.39</td>
</tr>
<tr>
<td><strong>Distal Reference Segment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EEM CSA, mm(^2)</td>
<td>16.3 ± 5.7</td>
<td>14.4 ± 4.5</td>
<td>0.12</td>
</tr>
<tr>
<td>Lumen CSA, mm(^2)</td>
<td>8.1 ± 3.7</td>
<td>7.5 ± 2.1</td>
<td>0.39</td>
</tr>
<tr>
<td>P&amp;M CSA, mm(^2)</td>
<td>8.2 ± 2.7</td>
<td>6.9 ± 3.6</td>
<td>0.13</td>
</tr>
<tr>
<td>Plaque burden, %</td>
<td>50.1 ± 12.1</td>
<td>46.2 ± 13.4</td>
<td>0.21</td>
</tr>
</tbody>
</table>
VH-IVUS imaging characteristics

Attenuated plaque
P&M : 9.44 mm²
PB: 67.3%
NC area: 1.96 mm²
NC%: 20.8%

Non attenuated plaque
P&M : 8.8 mm²
PB: 61.7%
NC area: 0.54 mm²
NC%: 6.1%
VH-IVUS imaging characteristics

Attenuated plaque
- NC: 8%
- DC: 25%
- FI: 52%
- FF: 15%

Non-attenuated plaque
- NC: 5%
- DC: 17%
- FI: 63%
- FF: 15%

P<0.001
Attenuated plaque & NC

P<0.001

Attenuated plaque & Non-attenuated plaque

Incidence (%)

Necrotic core area

1st quartile (≤ 0.45mm²)
- 25 (39%)
- 3 (6%)

2nd quartile (0.45-0.95mm²)
- 17 (26%)
- 10 (21%)

3rd quartile (0.95-1.5mm²)
- 12 (18%)
- 18 (38%)

4th quartile (>1.5mm²)
- 11 (17%)
- 16 (34%)

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VH-IVUS phenotype

- Attenuated plaque
- Non-attenuated plaque

P < 0.001

<table>
<thead>
<tr>
<th>Region</th>
<th>Attenuated Plaque</th>
<th>Non-attenuated Plaque</th>
</tr>
</thead>
<tbody>
<tr>
<td>VH-TCFA</td>
<td>20 (43%)</td>
<td>19 (29%)</td>
</tr>
<tr>
<td>ThCFA</td>
<td>25 (53%)</td>
<td>15 (23%)</td>
</tr>
<tr>
<td>PIT</td>
<td>2 (4%)</td>
<td>31 (48%)</td>
</tr>
</tbody>
</table>

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Conclusions

Grayscale IVUS attenuated plaques are associated with a large amount of VH-IVUS necrotic core and are marker of the presence of a fibroatheroma (VH-TCFA or ThCFA). This may explain the reported biologic instability of these lesions.