Is Plaque Erosion a Woman's Disease?

Renu Virmani, MD.
CVPath Institute Inc.
Gaithersburg, MD, USA
Causes of Coronary Thrombosis

Gross and Light Microscopic Features of Plaque Rupture

60% of Thrombi in Sudden Coronary Death occur form Plaque Rupture

Fig 3-1
Calcified Nodule

Frequency 2-7% of SCD, Older individuals, usually Men, equally common in tortuous right and left coronary arteries
Plaque Erosion:
30-35% of thrombi in SCD

Plaque erosion in a 33 year-old female complaining of chest pain for two weeks and discharged from the emergency room with a diagnosis of anxiety.
Serial Sections of Coronary Plaque Erosion

38F, Sudden Coronary Death Victim

Proximal LAD → Distal

Underlying plaque: PIT or fibroatheroma → rich in SMCs in a proteoglycan matrix, an absence of endothelial lining, and infrequently calcified.

Currently, no distinct morphological features of erosion-prone plaques have been identified.
Multiple Simultaneous Plaque Erosion in 3 Coronary Arteries

34-year-old man with history of smoking and untreated hyperlipidemia who had suffered from epigastric pain and was found dead at home.
Patients dying from Sudden coronary Death: Extent of Coronary calcification by decades

Severe Coronary Artery Disease, n=36, 64±14 yrs

Coronary calcium score

- Whites
- Blacks

Coronary calcium score

Mean calcification score

Radiograph

Movat Stain

Ground Section (40 µm)

Pathologic intimal thickening

# Erosion and rupture in plaques with acute thrombosis: distribution of patients, clinical data, and pathological findings

<table>
<thead>
<tr>
<th></th>
<th>Plaque erosion (n = 74)</th>
<th>Plaque rupture (n = 217)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/female</td>
<td>34/40</td>
<td>150/67</td>
<td>0.0004</td>
</tr>
<tr>
<td>Age (mean (SD)) (years)</td>
<td>70 (9)</td>
<td>68 (11)</td>
<td>NS</td>
</tr>
<tr>
<td>AMI site</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterolateral</td>
<td>49 (66.2)</td>
<td>119 (54.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Lateral</td>
<td>3 (4.1)</td>
<td>22 (10.1)</td>
<td>NS</td>
</tr>
<tr>
<td>Posterior</td>
<td>22 (29.7)</td>
<td>76 (35.1)</td>
<td>NS</td>
</tr>
<tr>
<td>Heart rupture</td>
<td>17 (22.9)</td>
<td>27 (12.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Non-Q wave AMI</td>
<td>1 (1.3)</td>
<td>10 (4.6)</td>
<td>NS</td>
</tr>
<tr>
<td>Scars</td>
<td>21 (28.4)</td>
<td>74 (34.1)</td>
<td>NS</td>
</tr>
<tr>
<td>Multiple thrombi</td>
<td>11 (14.9)</td>
<td>18 (8.3)</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Arbustini, E., et al. Heart 1999; 82(3): 269-272*
### Sudden Coronary Death in Men and Women

<table>
<thead>
<tr>
<th></th>
<th>Age</th>
<th>Rupture</th>
<th>Erosion</th>
<th>CTO</th>
<th>Stable (no CTO)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Male</strong></td>
<td>N=612</td>
<td>49±11</td>
<td>232 (38%)</td>
<td>54 (9%)</td>
<td>155 (25%) 246 (40%)</td>
</tr>
<tr>
<td><strong>Female</strong></td>
<td>N=238</td>
<td>51±14</td>
<td>45 (19%)</td>
<td>46 (19%)</td>
<td>33 (14%) 126 (53%)</td>
</tr>
<tr>
<td><strong>P value</strong></td>
<td></td>
<td>0.026</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>0.0002 0.0008</td>
</tr>
</tbody>
</table>
Frequency of Coronary Thrombi in Culprit Lesions by Decade in Men Dying Sudden Coronary Death

![Bar chart showing the frequency of different types of coronary lesions by age group.](chart.png)

- **30-39**: Acute Thrombus: *; p=0.05
- **40-49**: Acute Thrombus: *; p=0.05
- **50-59**: Acute Thrombus: *; Plaque Rupture: #; p=0.05
- **60-69**: Acute Thrombus: *; Plaque Erosion: #; p=0.05

Legend:
- Acute Thrombus
- Plaque Rupture
- Plaque Erosion
- Stable Plaque

Note: * indicates significance at p=0.05.
Influence of Age on Coronary Thrombosis in Men and Women

Plaque Erosions in Men and Women Stratified by Age

Men

Women

*P=0.01, †P=0.02, ¥P=0.01, ‡P=0.03

All P > 0.05

Risk factors and type of coronary thrombosis in 59 sudden death cases (Men)

Plaque rupture n=41, Plaque erosion n=18

Burke AP, N Engl J Med 1997;336:1276-82
Burke AP et al., Circulation, 1998
## The Role of Risk Factor
Multivariate logistic regression analysis

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Rupture</th>
<th></th>
<th></th>
<th>Erosion</th>
<th></th>
<th></th>
<th>Calcified Nodule</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95%CI</td>
<td>P value</td>
<td>OR</td>
<td>95%CI</td>
<td>P value</td>
<td>OR</td>
<td>95%CI</td>
<td>P value</td>
</tr>
<tr>
<td>Age (10 year increase)</td>
<td>1.09</td>
<td>0.86-1.38</td>
<td>0.48</td>
<td>0.75</td>
<td>0.53-1.05</td>
<td>0.10</td>
<td><strong>2.14</strong></td>
<td><strong>1.24-3.69</strong></td>
<td><strong>0.01</strong></td>
</tr>
<tr>
<td>Male sex</td>
<td><strong>1.84</strong></td>
<td><strong>0.92-3.70</strong></td>
<td><strong>0.08</strong></td>
<td><strong>0.43</strong></td>
<td><strong>0.21-0.89</strong></td>
<td><strong>0.02</strong></td>
<td>0.72</td>
<td>0.13-3.91</td>
<td>0.70</td>
</tr>
<tr>
<td>African American</td>
<td>0.66</td>
<td>0.37-1.16</td>
<td>0.15</td>
<td>0.73</td>
<td>0.36-1.48</td>
<td>0.39</td>
<td>0.23</td>
<td>0.03-1.99</td>
<td>0.18</td>
</tr>
<tr>
<td>BMI</td>
<td>1.02</td>
<td>0.98-1.06</td>
<td>0.30</td>
<td>0.96</td>
<td>0.91-1.02</td>
<td>0.17</td>
<td>1.07</td>
<td>0.97-1.18</td>
<td>0.18</td>
</tr>
<tr>
<td>Hb A1c</td>
<td>1.09</td>
<td>0.97-1.21</td>
<td>0.13</td>
<td>0.96</td>
<td>0.81-1.13</td>
<td>0.64</td>
<td>0.94</td>
<td>0.65-1.38</td>
<td>0.76</td>
</tr>
<tr>
<td>HTN</td>
<td>0.92</td>
<td>0.52-1.64</td>
<td>0.77</td>
<td>0.57</td>
<td>0.25-1.33</td>
<td>0.20</td>
<td>1.17</td>
<td>0.27-4.97</td>
<td>0.83</td>
</tr>
<tr>
<td>Smoker</td>
<td><strong>1.89</strong></td>
<td><strong>1.12-3.17</strong></td>
<td><strong>0.02</strong></td>
<td><strong>3.42</strong></td>
<td><strong>1.61-7.28</strong></td>
<td><strong>0.001</strong></td>
<td>2.71</td>
<td>0.61-11.99</td>
<td>0.19</td>
</tr>
<tr>
<td>T.Cho (10mg/dl increase)</td>
<td><strong>1.12</strong></td>
<td><strong>1.07-1.16</strong></td>
<td><strong>&lt;0.0001</strong></td>
<td>0.98</td>
<td>0.94-1.03</td>
<td>0.53</td>
<td>0.95</td>
<td>0.85-1.08</td>
<td>0.44</td>
</tr>
</tbody>
</table>
The Endothelium in Fatal Plaque Erosion
Prevalence of Older Thrombus is an Independent Predictor of Long-Term Mortality In Patients with STEMI

Kramer MCA, et al
Circulation 2008: 118;1810-1816
# Patient Data, by Culprit Plaque

<table>
<thead>
<tr>
<th>Culprit Lesion</th>
<th>Patient age (years)</th>
<th>Male Gender</th>
<th>Diabetes</th>
<th>Hypertension</th>
<th>Smoking</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rupture (n=65)</td>
<td>52 ± 10</td>
<td>58 (89%)</td>
<td>7 (11)</td>
<td>15 (23)</td>
<td>11 (17)</td>
</tr>
<tr>
<td>Erosion (n=50)</td>
<td>43 ± 9</td>
<td>37 (74%)</td>
<td>6 (12)</td>
<td>6 (12)</td>
<td>10 (20)</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;0.0001</td>
<td>0.03</td>
<td>0.67</td>
<td>0.84</td>
<td>0.13</td>
</tr>
</tbody>
</table>

Continuous variables are expressed as mean± SD

*Kramer MC, et al. JACC 2010*
Plaque Rupture

Early (< 1 day)  
Lytic (1-3 days)  
Infiltrating (4-7 days)  
Healing (> 7 days)

A  
D  
G  
J  

B  
E  
H  
K  

C  
F  
I  
L  

Kramer MC, et al. JACC 2010
Plaque Erosion

Early (< 1 day)

Lytic (1-3 days)

Infiltrating (4-7 days)

Healing (> 7 days)

A

D

G

J

B

E

H

K

C

F

L

Kramer MC, JACC 2010
Thrombus Age

Kramer MC, ET AL. JACC 2010
Plaque Characteristics

IEL Area mm²
Plaque Area mm²
Percent Stenosis
% Necrotic core
Macrophage %

Kramer MC, et al JACC 2010
Plaque Erosion

Different Accumulation of Proteoglycan and Hyaluronan in Different Culprit lesions

A)
Rupture Erosion Stable

Versican

B)
Rupture Erosion Stable

Hyaluronan

C)
Rupture Erosion Stable

Biglycan

D)
Rupture Erosion Stable

Decorin

Kolodgie FD, ATVB 2002
Intramyocardial Emboli more Common in Plaque Erosion vs. Plaque Rupture

%Hearts with Intramyocardial Emboli

Schwartz et al. JACC 2010
Conclusions

- Erosion lesions are rich in smooth muscle cells with paucity of macrophages near the lumen, and 50 to 80% have an underlying necrotic core. Usually seen in younger individuals and in females who often present with atypical chest pain.
- Total cholesterol and HDL are not associated with erosion.
- It is conceivable that plaque erosion has a different etiology possibly secondary to vasospasm of the arterial wall rather than atherosclerosis.
- Hyaluronan may interfere with the integrity of normal vascular endothelium - endothelial cells from large vessels have lower potential for adherence to hyaluronan. Endothelial cells in culture demonstrate decreased cell growth and increased propensity to apoptosis.
Conclusions

- Plaque erosions are associated with late stage maturation of thrombus as compared to ruptures.
- Healing thrombi are seen in 85% of erosions versus 55% of ruptures and clinical studies have suggested that healing thrombi clinically have worse prognosis in patients presenting with STEMI.
- Plaque erosions have been associated with greater distal embolization as compared to rupture (74% vs. 38%).
- Therefore understanding erosions which are more common in women <50 years may need a different modality of artery interrogation as well as treatment strategies than men.
Acknowledgments

Funding
CVPath Institute Inc.

CVPath Institute
Kazuyuki Yahagi, MD
Fumiyuki Otsuka, MD, PhD
Kenichi Sakakura, MD
Elena Ladich, MD
Robert Kutz, MS
Russ Jones
Ed Acampado, DVM
Youhui Liang, MD
Abebe Atiso, HT
Jinky Beyer
Giselle Magsalin
Hedwig Avallone, HT
Lila Adams, HT
Hengying Ouyang, MD
Frank D Kolodgie, PhD
Aloke V. Finn, MD