Anatomy and Pathology of
Left main coronary artery

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Anatomy – Definition

✓ Left main coronary artery (LMCA): The proximal segment of the left coronary artery that arises from the left aortic sinus just below the sinotubular junction to its bifurcation into the LAD and LCX

✓ LMCA is responsible for supplying approximately 75% of the left ventricular cardiac mass
Anatomy

- LMCA is generally divided into 3 anatomic regions
  1. Ostium (Origin of LMCA from aorta)
  2. Middle portion
  3. Distal (Bifurcation) portion
- Approximately one-third of cases have triflication
- The Average length of LMCA: $10.8 \pm 5.2\text{mm}$ ($2\text{-}23\text{mm}$)
- The Average angle of terminal brunches: $87 \pm 29^\circ$ ($40\text{-}165^\circ$)
- Positive correlation: length and angle

*Reig J et al. Clin Anat 2004*
Anatomy Specific Features…

- Ostium portion of LMCA is rich in aortic smooth muscle cells and elastic fibers

  ⇒ Elastic recoil

- Bifurcation at the distal portion

  ⇒ Flow disturbance (Susceptible to develop the plaque)
  ⇒ Procedural Complexity
### Anatomic features and the development of atherosclerotic plaque in left main coronary artery: IVUS data

<table>
<thead>
<tr>
<th>Location</th>
<th>Short LMCA (&lt;10mm) (n=44)</th>
<th>Long LMCA (≥10mm) (n=43)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ostium</td>
<td>55%</td>
<td>18%</td>
</tr>
<tr>
<td>Middle</td>
<td>7%</td>
<td>5%</td>
</tr>
<tr>
<td>Distal bifurcation</td>
<td>38%</td>
<td>77%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stenosis Location</th>
<th>Ostial stenosis (n=32)</th>
<th>Non-ostial stenosis (n=55)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumen area (mm²)</td>
<td>6.2</td>
<td>4.6</td>
</tr>
<tr>
<td>Plaque burden (%)</td>
<td>62</td>
<td>80</td>
</tr>
<tr>
<td>Remodeling index</td>
<td>0.87</td>
<td>1.01</td>
</tr>
</tbody>
</table>

Plaque Formation – Luminal Narrowing

Mean cross sectional luminal narrowing, left main, by age, sudden coronary death

Data from CVPath sudden cardiac death registry

N=194
Plaque Formation in LMCA

Maximal cross sectional luminal narrowing, 194 cases of sudden coronary death

Location of stenosis (>75%)

N=194
Patients with >75% LM stenosis

Proximal LAD and/or LCX involvement

- LM+LCX (33%)
- LM+LAD (27%)
- LM+LAD+LCX (33%)
- LM only (7%)
Plaque Progression in LMCA

PIT  Early NC  Late NC  TCFA
Advanced plaque in LMCA

**Intraplaque hemorrhage**

**Erosion**

**Plaque rupture**
Types of plaque in LMCA in sudden coronary death cases

All sudden coronary death cases (n=374)

- Pathologic intimal thickening (157) - 42%
- Fibroatheroma (82) - 22%
- Fibrocalcific (63) - 17%
- Adaptive intimal thickening (19) - 5%
- Fibrous plaque (13) - 4%
- Healed rupture (12) - 3%
- Acute rupture / fissure (8) - 2%
- Fatty streak (8) - 2%
- Nodular calcification (6) - 2%
- Nodular calcification (6) - 1%
- Thin-cap fibroatheroma (5) - 1%
- Erosion (1) - 1%
Types of plaque in LMCA in sudden coronary death cases with stenosis $\geq 50\%$

Cases with stenosis $\geq 50\%$ in sudden coronary death (n=171)

- **Fibroatheroma (53)**
- **Fibrocalcific (45)**
- **Pathologic intimal thickening (38)**
- **Healed rupture (10)**
- **Nodular calcification (6)**
- **Acute rupture / fissure (5)**
- **Thin-cap fibroatheroma (5)**
- **Fibrous plaque (5)**
- **Fatty streak (3)**
- **Erosion (1)**
LM Length and Luminal Narrowing, Calcification

**Sudden coronary death victims with LM luminal narrowing ≥50% (n=71)**

- **Luminal area stenosis of LM**
  - Longer left main had severe luminal narrowing.
  - No significant relationship between LM length and calcification.

- **Calcification (% Area)**
  - Calcification was the greatest in prox LAD and the least in prox LCX.

<table>
<thead>
<tr>
<th>LM length (mm)</th>
<th>&lt;10 (n=20)</th>
<th>≥10, &lt;15 (n=35)</th>
<th>≥15 (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left Main</td>
<td>p=0.48</td>
<td>p=0.19</td>
<td>p=0.85</td>
</tr>
<tr>
<td>Prox LAD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prox LCX</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Plaque distribution in bifurcation lesion

LM  PLAD  PLCx  RI
Plaque Formation in Bifurcation

Plaque thickness

Plaque Formation

LM + LAD severe stenosis
IVUS classification for LMCA bifurcation plaque distribution

Why so susceptive to get diseased?

Steady Laminar Blood Flow

Shear Stress

NO
PGI₂
tPA
Thrombomodulin

Antithrombogenic
Antimigration

Pro-survival
Endothelium
Smooth Muscle

Antigrowth
TGF-β

Flow Reversal

Low Mean Shear

Prothrombotic
Promigration

Pro-apoptosis
Endothelium
Smooth Muscle

Progrowth
Ang II
PDGF
Endothelin-1

Atherosclerotic Lesion
Pathology of Left Main Coronary Artery Stenting

Data from CVPath Autopsy Registry
## BMS vs DES in LMCA @ Autopsy

Vorwahl M et al. ACC2010

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>BMS (n=15)</th>
<th>DES (n=12)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>56.0 ± 12.8</td>
<td>73.2 ± 8.8</td>
<td>0.001</td>
</tr>
<tr>
<td>Gender (f/m)</td>
<td>4/11</td>
<td>3/9</td>
<td>0.53</td>
</tr>
<tr>
<td>Duration of Survival (days)</td>
<td>189 ± 206</td>
<td>212 ± 324</td>
<td>0.98</td>
</tr>
<tr>
<td>CABG</td>
<td>5</td>
<td>6</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lesion Characteristics</th>
<th>BMS (n=15)</th>
<th>DES (n=12)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stent lesion length (mm)</td>
<td>16.2 ± 5.5</td>
<td>29.6 ± 18.0</td>
<td>0.02</td>
</tr>
<tr>
<td>Isolated Left Main</td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Bifurcation (single vessel)</td>
<td>11</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Bifurcation (&gt;2 vessels)</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Indication</th>
<th>BMS (n=15)</th>
<th>DES (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACS/AMI</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Stable Angina</td>
<td>13</td>
<td>9</td>
</tr>
</tbody>
</table>
**BMS vs DES in LMCA @ Autopsy**

<table>
<thead>
<tr>
<th>Pathology</th>
<th>BMS &gt; 30 days (n=11)</th>
<th>DES &gt; 30 days (n=10)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration</td>
<td>288 ± 189</td>
<td>340 ± 374</td>
<td>0.7019</td>
</tr>
<tr>
<td>Stent diameter</td>
<td>3.73±0.67</td>
<td>3.95±0.57</td>
<td>0.4437</td>
</tr>
<tr>
<td>Vessel Diameter</td>
<td>5.73±1.00</td>
<td>5.93±0.93</td>
<td>0.6532</td>
</tr>
<tr>
<td>Vessel Area</td>
<td>19.47±4.67</td>
<td>20.25±4.61</td>
<td>0.7037</td>
</tr>
<tr>
<td>Stent Area</td>
<td>7.6±1.93</td>
<td>8.51±2.52</td>
<td>0.3725</td>
</tr>
<tr>
<td>Plaque Area</td>
<td>11.84±3.85</td>
<td>11.73±3.46</td>
<td>0.9476</td>
</tr>
</tbody>
</table>

**Lumen Area**

- BMS: 12, P=0.0804
- DES: 8, P=0.0804

**Neointimal Area**

- BMS: 6, P=0.1525
- DES: 4, P=0.1525

**% Area Stenosis**

- BMS: 80, P=0.1825
- DES: 60, P=0.1825

**Neointimal Thickness**

- BMS: 0.2, P=0.0187
- DES: 0.4, P=0.0187

Vorpahl M et al. ACC2010
### Cause of Death at Autopsy with LMCA stenting

<table>
<thead>
<tr>
<th>Cause of Death</th>
<th>BMS (n=15)</th>
<th>DES (n=12)</th>
<th>p=0.26</th>
</tr>
</thead>
<tbody>
<tr>
<td>SRD</td>
<td>6 (40)</td>
<td>7 (58)</td>
<td></td>
</tr>
<tr>
<td>NSRD</td>
<td>4 (26)</td>
<td>4 (33)</td>
<td></td>
</tr>
<tr>
<td>NCD</td>
<td>5 (33)</td>
<td>1 (8)</td>
<td></td>
</tr>
</tbody>
</table>

**SRD:** Stent Thrombosis/ Restenosis  
**NSRCD:** SCD and patent stent  
**NCD:** other

*Vorpahl M et al. ACC2010*
Early Stent thrombosis
73F, Cypher stent implantation in LMCA
Sudden death 2 days after implantation
Very Late Stent Thrombosis in LM stent (PES2.5 years)

SCD seven days after discontinuation of Clopidogrel and ASS for lung biopsy.

LM: PES
LAD: PES
Diag: PES
LCX: PES
Lom: BMS

Occlusive Thrombus
Persisting Inflammation
Uncovered Struts
Fibrin Deposition

4.5 mm
Analysis of Bifurcation Stenting

From CVPath Autopsy Cases
# DES implantation in Bifurcation Lesion

<table>
<thead>
<tr>
<th></th>
<th>DES (n=19)</th>
<th>BMS (n=21)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (yrs)</strong></td>
<td>61 ± 16</td>
<td>58 ± 17</td>
<td>0.61</td>
</tr>
<tr>
<td><strong>Male Gender (%)</strong></td>
<td>15 (79)</td>
<td>13 (62)</td>
<td>0.41</td>
</tr>
<tr>
<td><strong>Mean duration (day)</strong></td>
<td>330 [188, 680]</td>
<td>150 [54, 540]</td>
<td>0.14</td>
</tr>
<tr>
<td><strong>&gt;30 days (%)</strong></td>
<td>12 (63)</td>
<td>14 (67)</td>
<td>0.81</td>
</tr>
<tr>
<td><strong>Technique</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 stent</td>
<td>10</td>
<td>9</td>
<td>0.38</td>
</tr>
<tr>
<td>2 stent, T/ V/ Crush</td>
<td>5/ 2/ 2</td>
<td>9/ 3/ 0</td>
<td></td>
</tr>
<tr>
<td><strong>Number of stents</strong></td>
<td>1.9 ± 0.8</td>
<td>1.8 ± 0.8</td>
<td>0.58</td>
</tr>
<tr>
<td><strong>Restenosis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MV (%)</td>
<td>1 (6)</td>
<td>7 (33)</td>
<td>0.03</td>
</tr>
<tr>
<td>SB (%)</td>
<td>3 (16)</td>
<td>6 (29)</td>
<td>0.7</td>
</tr>
<tr>
<td><strong>Thrombosis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 30 days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MV (%)</td>
<td>3 (43)</td>
<td>3 (43)</td>
<td>0.33</td>
</tr>
<tr>
<td>SB (%)</td>
<td>3 (43)</td>
<td>4 (57)</td>
<td>0.73</td>
</tr>
<tr>
<td>&gt; 30 days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MV (%)</td>
<td>9 (75)</td>
<td>5 (36)</td>
<td>0.04</td>
</tr>
<tr>
<td>SB (%)</td>
<td>5 (42)</td>
<td>2 (14)</td>
<td>0.35</td>
</tr>
<tr>
<td><strong>Timing of thrombus</strong></td>
<td>270 [195, 585]</td>
<td>60 [35, 105]</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Morphometric Analysis

- Neointimal thickness
- Fibrin deposition
- Uncovered struts

Lateral wall
Flow divider

1 or 2 sections

# Morphometric Analysis

## BMS

<table>
<thead>
<tr>
<th>BMS</th>
<th>Flow divider</th>
<th>Lateral wall</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neointimal thickness (mm)</td>
<td>0.42 ± 0.35</td>
<td>0.50 ± 0.34</td>
<td>0.15</td>
</tr>
<tr>
<td>Struts with fibrin (%)</td>
<td>24 ± 30</td>
<td>20 ± 30</td>
<td>0.31</td>
</tr>
<tr>
<td>Uncovered Strut (%)</td>
<td>17 ± 31</td>
<td>5 ± 10</td>
<td>0.08</td>
</tr>
</tbody>
</table>
**Morphometric Analysis**

**DES**

<table>
<thead>
<tr>
<th></th>
<th>Flow divider</th>
<th>Lateral wall</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neointimal thickness (mm)</td>
<td>0.08 ± 0.07</td>
<td>0.16 ± 0.09</td>
<td>0.003</td>
</tr>
<tr>
<td>Struts with fibrin (%)</td>
<td>52 ± 27</td>
<td>36 ± 33</td>
<td>0.03</td>
</tr>
<tr>
<td>Uncovered Strut (%)</td>
<td>48 ± 33</td>
<td>13 ± 24</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Flow disturbance induced by stenting

Conclusions

- LMCA show complex plaque especially when significantly narrowed
- LAD and/or LCX involvement was common in patients with LMCA stenosis
- Atherosclerotic plaque was predominantly seen in lateral wall rather than flow divider
- Because of the plaque complexity, the deployment is important in LMCA stenting
- Flow disturbance is the primary cause of delayed arterial healing in bifurcation lesion following DES implantation