Functional estimation of stenoses
Advantages and disadvantages of FFR

1st Case presentation

Ioannis Ntarladimas, MD
Catheterization Laboratory
General Hospital of Elefsina “Thriasio”
Speaker’s name: Ioannis Ntarladimas, MD

☒ I have the following potential conflicts of interest to report:

☐ Consulting
☐ Employment in industry
☐ Stockholder of a healthcare company
☑ Owner of a healthcare company
☐ Other(s)

☑ I do not have any potential conflict of interest
Clinical presentation

• 65 y/o male presenting with palpitations and angina like symptoms

• Physical examination: BP 145/78 mmHg, HR 73bpm, BMI 31.3 kg/m²

• Risk factors: Hypertension, smoker 30p/ys

• Past medical history: COPD, Left hip replacement surgery (2010)
<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>15.1 g/dl</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.88 mg/dl</td>
</tr>
<tr>
<td>CRP</td>
<td>1.95 mg/L</td>
</tr>
<tr>
<td>Cholesterol (total)</td>
<td>183 mg/L</td>
</tr>
<tr>
<td>HDL</td>
<td>43 mg/L</td>
</tr>
<tr>
<td>LDL</td>
<td>60 mg/L</td>
</tr>
<tr>
<td>HbA1c</td>
<td>5.9 %</td>
</tr>
</tbody>
</table>
Right Coronary angiography

5F diagnostic cath, radial approach
Left Coronary angiography

5F diagnostic cath, radial approach

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Left Coronary angiography

5F diagnostic cath, radial approach

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Moderate LM stenosis
How should we treat?
Decision making

1. Angiography
2. Exercise test
3. Stress echo/ SPECT
4. IVUS
5. FFR
Specific Characteristics of LM Stenoses (I)

1. Large myocardial mass depending on the LM
2. Rarely isolated/often associated with co-morbidities
3. Difficult to appreciate non-invasively
Specific Characteristics of LM Stenoses (II)

4. Difficult to appreciate angiographically
   • Overlap of the catheter and LAD/LCX
   • No reference segment
   • Diffuse disease in short segment
   • Contrast medium spill over
   • Insufficient mixing of contrast and blood
   • Calcification
   • Ostial or bifurcation lesion

...lead to LM stenosis severity underestimation!
QCA vs. FFR in LM stenosis

$r=-0.38$, $p<0.001$
Visual assessment vs. FFR

74% concordance
Limitations of Non-Invasive Testing in LM Stenosis

Ischemic Cascade

- Angina
- ΔECG
- Systolic Dysfunction
- Diastolic Dysfunction
- Perfusion Abnormalities

- Stress ECG
- Stress Echo/MRI
- Nuclear Imaging

- Poor spatial resolution
- Detects systolic dysfunction
- Homogeneous flow maldistribution

Duration and severity of ischemia
Value of MPI for LM stenosis detection

101 patients with angiographic left main CAD (>50% stenosis)

Assessment of perfusion data alone by visual or quantitative analysis underestimates the severity of LM

Berman et al, J Nucl Cardiology 2007
IVUS for LM assessment: LITRO study

6 mm² cut-off value for revascularization
IVUS for LM assessment: LITRO study

6 mm$^2$ cut-off value for revascularization

MACE free survival

Survival free of cardiac death

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De la Torre Hernandez et al JACC 2011
IVUS for LM assessment

- Useful for sizing, apposition, coverage and post-interventional lumen area in LM PCI

**BUT**

- Limited by calcifications of the LM
- Difficulty to maintain the catheter coaxial during pull-back
- No consensus for cut-off values
- Unable to assess the stenosis functional significance

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FFR-guided revascularization for patients with equivocal LM
FFR-guided revascularization for patients with equivocal LM
What we did: FFR LM
adenosine infusion IV
140μg/kg/min

Medical Treatment

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FFR in LM stenosis

- IV adenosine preferably
- Equalization in the aorta. Alternatively do not advance sensor of pressure wire beyond LM stenosis if feasible
- Disengage catheter from ostium during equalization and hyperemia
- Slow pullback of pressure wire
- Measure in both LAD and LCA
- Consider cut-off value at 0.80
### Indications for revascularisation in stable angina or silent ischaemia

#### Subset of CAD by anatomy

<table>
<thead>
<tr>
<th>For prognosis</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left main &gt; 50%*</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Any proximal LAD &gt; 50%*</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>2VD or 3VD with impaired LV function*</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Proven large area of ischaemia (&gt; 10% LV)</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Single remaining patent vessel &gt; 50% stenosis*</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>1VD without proximal LAD and without &gt; 10% ischaemia</td>
<td>III</td>
<td>A</td>
</tr>
</tbody>
</table>

#### Subset of CAD by anatomy

<table>
<thead>
<tr>
<th>For symptoms</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any stenosis &gt; 50% with limiting angina or angina equivalent, unresponsive to OMT</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Dyspnoea/CHF and &gt; 10% LV ischaemia/viability supplied by &gt; 50% stenotic artery</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>No limiting symptoms with OMT</td>
<td>III</td>
<td>C</td>
</tr>
</tbody>
</table>

* With documented ischaemia or Fractional Flow Reserve (FFR) < 0.80 for angiographic diameter stenosis 50-90%.
Conclusions

- In patients with equivocal LM stenosis, angiography alone does not allow appropriate decision making regarding revascularization and often underestimates the functional significance of the stenosis.

- IVUS should be considered if LM PCI is planned.

- FFR should be assessed in equivocal LM stenoses. Revascularization should be decided on the basis of FFR <0.80 whereas patients with FFR >0.80 can be treated medically.
Thank you!
Coronary Hyperemic Stimuli

Intravenous Infusion (Preferably Central Line)

- Adenosine (or ATP) 140 µg/kg/min
- Dobutamine 20-40 µg/kg/min
- Binodenoson 1.5 µg/kg IV bolus

Intracoronary Bolus

- Adenosine (or ATP) 40-60 µg
- Papaverine 12 - 16 mg
- Nitroprusside 0.3-0.9 µg/kg
- Regadenoson 500 µg
Preparation of adenosine solution for IV infusion

• From a 100 ml N/S flacon we deduct 40 ml
• In the 60 remaining ml we add 15 ampules of Adenocor (1 amp=2ml=6mg Adenosine)
• Thus we obtain 15*6=90 mg Adenosine in a 60+30=90 ml solution: concentration=1mg/1ml
• We adjust dosage according to weight (dosage is 140 μg/kg/min)
Preparation of adenosine solution for intracoronary infusion

• Add 1.7 ml=5mg Adenocor to a 500 ml N/S flacon

• Thus we obtain 5mg/500ml=10μg/ml of Adenosine solution

• Inject 5 ml=5 μg bolus
DEFER Study Results at 5 years

In patients with proven CAD WITHOUT ischemia, annual death/MI rate is 1% and NOT improved by PCI

Pijls et al, JACC 2007
Guiding in Ostium
Guiding in Ostium
Guiding in Ostium
Guiding Disengaged
Guiding in Ostium

Guiding Disengaged
Left Main Stenoses are Rarely Isolated

The influence of a distal stenosis on the FFR of the LM depends on the extent to which hyperemic flow across the LM stenosis is decreased by the distal lesion

- Severity
- Myocardial mass

Courtesy of Bernard De Bruyne
The influence of a distal stenosis on the FFR of the LM depends on the extent to which hyperemic flow across the LM stenosis is decreased by the distal lesion.

- Severity
- Myocardial mass

Left Main Stenoses are Rarely Isolated

Courtesy of Bernard De Bruyne
FAQ: When there is a stenosis in the LAD, can we put the sensor in the LCx to assess the true severity of the left main stenosis?

NO!
Left Main Stem Stenoses are Rarely Isolated

Left Main Stem or Ostial LAD?
Left Main Stem Stenoses are Rarely Isolated

Left Main Stem or Ostial LAD?
Left Main Stem Stenoses are Rarely Isolated

Left Main Stem or Ostial LAD?
An IVUS guided treatment strategy based on deferral of revascularization in patients with MLA 7.5 mm$^2$ is safe.

Table 5. Long-Term Follow-Up

<table>
<thead>
<tr>
<th></th>
<th>MLA &lt;7.5 mm$^2$</th>
<th>MLA ≥7.5 mm$^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(Revascularization)</td>
<td>(Deferral)</td>
</tr>
<tr>
<td>n</td>
<td>71</td>
<td>12</td>
</tr>
<tr>
<td>n with follow-up</td>
<td>61 (85.9)</td>
<td>11 (91.7)</td>
</tr>
<tr>
<td>Follow-up period (yes)</td>
<td>3.2 ± 2.2</td>
<td>3.0 ± 2.2</td>
</tr>
<tr>
<td>Range (yes)</td>
<td>(0–7.7)</td>
<td>(0.1–7.1)</td>
</tr>
<tr>
<td>Target-vessel revascularization</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>All-cause death</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>Three-year freedom from MACE (%)</td>
<td>79.2</td>
<td>49.9</td>
</tr>
</tbody>
</table>

$^*p < 0.05$ across groups A, B, C, D; $^t p = 0.48$ across groups A, C; $^p = 0.28$ across groups A, D; $^t p = 0.86$ across groups C, D.

MACE = major adverse cardiac events; MLA = minimum lumen area.
How to ... measure FFR in the LMCA

Equalization of 2 pressures (guiding catheter \( P_a \) and PW \( P_d \)): to be performed with the GC disengaged!
How to ... measure FFR in the LMCA
How to ... measure FFR in the LMCA

Hyperemia with IV Adenosine infusion is strictly recommended!
How to ... measure FFR in the LMCA

With distal stenosis, FFR should be measured in both LAD ...
How to ... measure FFR in the LMCA

... and LCX!
Functional Assessment of CAD
Spatial Resolution

Exercise ECG: per patient analysis

Stress echocardiography: per territory analysis

Myocardial perfusion imaging: per territory analysis

FFR: per cm analysis

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Equalization
Decision making

- Obesity
- COPD
- History of orthopaedic surgery
- PVC’s

Difficult to assess LM non-invasively
Proportion of Patients with Adequate Exercise ECG (n=1814)

Unable to exercise (374) 21%
Uninterpretable (433) 24%
Submaximal (372) 21%
Adequate (635) 35%