FFR in Left Main Disease

William F. Fearon, MD
Associate Professor of Medicine
Director, Interventional Cardiology
Stanford University Medical Center
Why FFR instead of IVUS?

- Physiologic versus anatomic information
- Limitations of IVUS for assessing Left Main (LM)
- Data supporting FFR assessment of LM
- Limitations/Practical Aspects of FFR of LM
Why FFR instead of IVUS?

- Physiologic versus anatomic information
- Limitations of IVUS for assessing Left Main (LM)
- Data supporting FFR assessment of LM
- Limitations/Practical Aspects of FFR of LM
Factors impacting ischemic potential of a stenosis

\[ \Delta P = f_1\left(\frac{1}{A_s^2}, l, \dot{Q}\right) + f_2\left(\frac{1}{A_s^2}, \frac{1}{A_n^2}, \dot{Q}^2\right) \]

Viscous

Separation

Variability of IVUS Assessment of the LM

- 73 patients with distal left main disease underwent IVUS pullback from the LAD and from the L Cx.

- The average MLA of the LM from the LAD pullback was 6.7 ±3.1 mm² and from the L Cx pullback was 6.8 ±3.3 mm².

- However, in ½ the patients the L Cx measurement was smaller and in 11% the difference was > 1 mm².

- In the other ½ of the patients the LAD measurement was smaller and in 16% the difference was > 1 mm².

Variability of IVUS Cutoff Values

3 Yr Follow-up in 214 Intermediate Left Mains Assessed by IVUS

Fassa et al. J Am Coll Cardiol 2005;45:204-211
Variability of IVUS Cutoff Values

55 patients with ambiguous left main disease
Variability of IVUS Cutoff Values

55 patients with 30-80% LM and FFR and IVUS

A. MLA predicting FFR<0.80

Cut-off = 4.8 mm²

Cutoff = 4.8 mm²

Variability of IVUS Cutoff Values

6 MM$^2$ TOO SMALL?
- 6 mm$^2$
- 55% stenosis
- FFR = 0.60

6 MM$^2$ SUFICIENT?
- 6 mm$^2$
- 10% stenosis
- FFR = 0.90
Why FFR instead of IVUS?

- Physiologic versus anatomic information
- Limitations of IVUS for assessing Left Main (LM)
- Data supporting FFR assessment of LM
- Limitations/Practical Aspects of FFR of LM
Is it safe to defer LM Rx based on FFR?

**FFR measured in 54 patients with equivocal left main**


![Graph showing freedom from death with FFR values](image)

- **FFR ≥ 0.75**
- **FFR < 0.75**

$p = NS$
Is it safe to defer LM Rx based on FFR?

**FFR measured in 54 patients with equivocal left main**

Is it safe to defer LM Rx based on FFR?

55 patients with ambiguous left main disease

# Summary of Published Studies

<table>
<thead>
<tr>
<th>Patient #</th>
<th>Total population</th>
<th>Defer group*</th>
<th>Surgical group</th>
<th>FFR Cut-off value</th>
<th>FU Mean (months)</th>
<th>EFS Defer group* (%)</th>
<th>EFS Surgical group (%)</th>
<th>Survival Defer group* (%)</th>
<th>Survival Surgical group (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>54</td>
<td>24</td>
<td>30</td>
<td></td>
<td>0.75</td>
<td>29±15</td>
<td>76</td>
<td>83</td>
<td>100</td>
<td>97</td>
</tr>
<tr>
<td>51</td>
<td>37</td>
<td>14</td>
<td></td>
<td>0.75</td>
<td>25±11</td>
<td>90</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>27</td>
<td>20</td>
<td>7</td>
<td></td>
<td>0.75</td>
<td>26±12</td>
<td>90</td>
<td>86</td>
<td>100</td>
<td>86</td>
</tr>
<tr>
<td>38</td>
<td>20</td>
<td>18</td>
<td></td>
<td>0.75</td>
<td>24±12</td>
<td>90</td>
<td>89</td>
<td>100</td>
<td>89</td>
</tr>
<tr>
<td>15</td>
<td>8</td>
<td>7</td>
<td></td>
<td>0.75</td>
<td>33±10</td>
<td>100</td>
<td>71</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>51</td>
<td>24</td>
<td>27</td>
<td></td>
<td>0.75</td>
<td>29±16</td>
<td>69</td>
<td>66</td>
<td>100</td>
<td>81</td>
</tr>
<tr>
<td>(236)</td>
<td>(133)</td>
<td>(103)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Lindstaedt. Int J Cardiol 2008;130:326
FFR and Intermediate Left Main

274 patients with LMCA

213 patients enrolled

- 138 Nonsurgical group
  - 2 patients lost in FU
  - 136 patients included in the analysis

- 75 Surgical group
  - 2 patients lost in FU
  - 73 patients included in the analysis

26 patients with protected LMCA

- 10 patients with valvular disease
- 4 patients requiring surgery but treated medically
- 21 patients requiring surgery for other vessel disease

Poor correlation between “eyeball” and FFR

FFR for Assessing LM Significance

Survival Rate

FFR for Assessing LM Significance

**MACE Rate**

![Graph with MACE rate over time for FFR ≥ 0.80 and FFR < 0.80 with p=0.5]

<table>
<thead>
<tr>
<th>Months</th>
<th>FFR ≥ 0.80</th>
<th>FFR &lt; 0.80</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>136</td>
<td>73</td>
</tr>
<tr>
<td>12</td>
<td>106</td>
<td>56</td>
</tr>
<tr>
<td>24</td>
<td>77</td>
<td>40</td>
</tr>
<tr>
<td>36</td>
<td>57</td>
<td>29</td>
</tr>
<tr>
<td>48</td>
<td>42</td>
<td>15</td>
</tr>
<tr>
<td>60</td>
<td>30</td>
<td>10</td>
</tr>
</tbody>
</table>

Why FFR instead of IVUS?

- Physiologic versus anatomic information
- Limitations of IVUS for assessing Left Main (LM)
- Data supporting FFR assessment of LM
- Limitations/Practical Aspects of FFR of LM
FFR of Left Main

Pullback of Pressure Wire During Maximal Hyperemia

Across Mid LAD

Across LM

(96) Pa mean
(62) Pd mean
0.64 FFR
FFR of Left Main

Pullback of Pressure Wire During Maximal Hyperemia

Across Mid LAD

Across LM

(98) Pa mean
(82) Pd mean
0.84 FFR
After rotational atherectomy and 2.5x28 mm DES, post-dilated to 3.0 mm
FFR of Left Main

$\text{FFR of Left Main} = 0.72$

(In absence of LAD lesion)

Proximal to LAD stent

Across LM
Effect of Tandem Lesions

Myocardium

0.84  0.64

Myocardium

0.72
Left Main Stem 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 will be decreased by this distal lesion

- Severity
- Myocardial mass

Courtesy Bernard De Bruyne, MD, PhD
Left Main Stem 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 will be decreased by this distal lesion

- Severity
- Myocardial mass

Courtesy Bernard De Bruyne, MD, PhD
The influence of a distal stenosis on the FFR of the LM depends on the extent to which hyperemic flow across the LM stenosis will be decreased by this distal lesion.

- Severity
- Myocardial mass

Left Main Stem Stenoses are Rarely Isolated

 Courtesy Bernard De Bruyne, MD, PhD
The influence of a distal stenosis on the FFR of the LM depends on the extent to which hyperemic flow across the LM stenosis will be decreased by this distal lesion

- Severity
- Myocardial mass

Left Main Stem Stenoses are Rarely Isolated

Courtesy Bernard De Bruyne, MD, PhD
Effect of Epicardial Lesions on FFR Assessment of Intermediate LM Disease

In Vitro Model

Effect of Epicardial Lesions on FFR Assessment of Intermediate LM Disease

*In Vitro Model*

Effect of Epicardial Lesions on FFR Assessment of Intermediate LM Disease

In Vitro Model

Effect of Epicardial Lesions on FFR
Assessment of Intermediate LM Disease

In Vitro Model

Effect of Epicardial Lesions on FFR Assessment of Intermediate LM Disease

*In Vitro Model*

**LAD Only**

0.77±0.09 vs. 0.69±0.09

*p < 0.001*

**LCX Only**

0.78±0.07 vs. 0.73±0.06

*p < 0.001*

Effect of Epicardial Lesions on FFR Assessment of Intermediate LM Disease

**Animal Model**

**A**

\[ P_a = 61 \]

\[ \text{LCX} \]

\[ P_d = 45 \]

\[ \text{FFR}_{\text{true}} = \frac{45}{61} = 0.74 \]

**B**

\[ P_a = 61 \]

\[ \text{LCX} \]

\[ P_d = 47 \]

\[ \text{LAD} \]

\[ P_d = 40 \]

\[ \text{FFR}_{\text{app}} = \frac{47}{61} = 0.77 \]

\[ \text{FFR}_{\text{epicardial}} = \frac{40}{61} = 0.66 \]

Effect of Epicardial Lesions on FFR Assessment of Intermediate LM Disease

Animal Model

Effect of Epicardial Lesions on FFR Assessment of Intermediate LM Disease

Animal Model

Mild Epicardial Disease
(FFR\textsubscript{epicardial} 0.70-0.80)

Moderate Epicardial Disease
(FFR\textsubscript{epicardial} 0.60-0.69)

Effect of Epicardial Lesions on FFR Assessment of Intermediate LM Disease

**Animal Model**

Severe Epicardial Disease
(\(\text{FFR}_{\text{epicardial}} 0.40-0.59\))

Complete Epicardial Occlusion
(\(\text{FFR}_{\text{epicardial}} < 0.40\))

Effect of Epicardial Lesions on FFR Assessment of Intermediate LM Disease

**Animal Model**

**Proximal LAD Stenosis**

0.77±0.04 vs 0.81±0.05, \( P<0.001 \)

**Mid LAD Stenosis**

0.74±0.04 vs 0.76±0.05, \( P<0.001 \)

Effect of Epicardial Lesions on FFR Assessment of Intermediate LM Disease

Animal Model

FFR of “Jailed” Left Circumflex

29 patients with LM/LAD crossover stenting with FFR of “jailed” Cx

# FFR of “jailed” Circumflex

<table>
<thead>
<tr>
<th>Mean 20 month follow-up</th>
<th>Defer group n = 24</th>
<th>PCI group n = 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death, n</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Myocardial Infarction, n</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>TLR, n</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Stent Thrombosis, n</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total Events, n</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>

An Approach to the Equivocal LM

- First measure FFR in the least diseased vessel, preferably the LAD, with a pullback
  - If FFR < 0.80, then revascularize
  - If FFR >0.85, then treat medically
  - If FFR between 0.80 and 0.85 and there is significant downstream epicardial disease in the other epicardial vessel, then consider IVUS

- Never forget the patient and the clinical scenario
Practical Aspects

Intravenous adenosine is the ideal hyperemic agent because it allows time to pull the guide catheter out of the ostium.

If possible, confirm pressure gradient across left main by checking FFR in both the LAD and Circumflex and by performing a pullback of the pressure wire.

A physiologic evaluation of left main disease, compared to an anatomic evaluation alone, is safe and appropriate, just as it is in non-left main CAD.