FFR, CFR, iFR etc...

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CHUV, Lausanne
Fractional flow reserve

Measure the impact of a stenosis on the maximal flow in a given artery

\[
\text{FFR} = \frac{\text{Pressure distal}}{\text{Pressure proximal}} = 0.70
\]

70% of maximum flow
FFR threshold

FFR is the *only* functional index which has ever been validated versus a *true gold standard.*

*(Prospective multi-testing Bayesian methodology)*

*ALL* studies ever performed in a wide variety of clinical and angiographic conditions found threshold between 0.75 and 0.80

**diagnostic accuracy: 95%**
The power of angiography to detect ischemia
DEFER: Best treatment for stenosis with FFR > 0.75

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

Pijls, JACC, 2007
DEFER: it is true also 15 years after

Myocardial infarction

- Significant higher infarct rate in perform group
- Most infarctions related to target vessel

FU 92%

Fearon, EuroPCR, 2015
FAME II: Best treatment for stenosis with FFR<0.8

A Primary End Point

PCI vs. medical therapy:
Hazard ratio, 0.32 (95% CI, 0.19–0.53); P<0.001

PCI vs. registry:
Hazard ratio, 1.29 (95% CI, 0.49–3.39); P=0.61

Medical therapy vs. registry:
Hazard ratio, 4.32 (95% CI, 1.75–10.70); P<0.001

De Bruyne, nejm, 2012
Fame II, FU 2 years

44% relative risk reduction $p = 0.04$

De Bruyne, nejm, 2014
FAME I: Best treatment for Stenosis with FFR < 0.8

FAME Study: One Year Outcomes
1005 patients with 2-3 vessel CAD randomized to angio or FFR-guided PCI

<table>
<thead>
<tr>
<th>Event</th>
<th>Angio-Guided</th>
<th>FFR-Guided</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>3</td>
<td>1.8</td>
<td></td>
</tr>
<tr>
<td>MI</td>
<td>8.7</td>
<td>5.7</td>
<td></td>
</tr>
<tr>
<td>Repeat Revasc</td>
<td>9.5</td>
<td>6.5</td>
<td></td>
</tr>
<tr>
<td>Death/MI</td>
<td>11.1</td>
<td>7.3</td>
<td>0.04</td>
</tr>
<tr>
<td>MACE</td>
<td>18.3</td>
<td>13.2</td>
<td>0.02</td>
</tr>
</tbody>
</table>

FAME I: it is true also after 2 years

FAME Study: Two Year Outcomes

Death/MI was significantly reduced from 12.9% to 8.4% (p=0.02)

Survival Free of MACE

FFR-Guided

Angio-Guided

730 days 4.5%

Change of revascularization strategy based on FFR

Van Belle, Circulation 2014
Revascularization in clinical practice

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>FFR is recommended to identify hemodynamically relevant coronary lesion(s) when evidence of ischaemia is not available.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Revascularization of stenoses with FFR &lt;0.80 is recommended in patients with angina symptoms or a positive stress test.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>IVUS or OCT may be considered to characterize lesions.</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>IVUS or OCT may be considered to improve stent deployment.</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>Revascularization of an angiographically intermediate stenosis without related ischaemia or without FFR &lt;0.80 is not recommended.</td>
<td>III</td>
<td>B</td>
</tr>
</tbody>
</table>

Pijls, FAME I, 2 years FU, JACC 2010
Hamilos, Muller, Left main, Circulation, 2010
Pijls, DEFER, 5 years FU, JACC 2007

De Bruyne, FAME II, NEJM 2012

Pijls, FAME I, 2 years FU, JACC 2010
Pijls, DEFER, 5 years FU, JACC 2007

ESC, Guidelines of SCAD, EHJ, 2013
Special situation of left main stenosis and proximal LAD stenosis

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

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

\[
\text{FFR}_{\text{epicardial}} = \frac{40}{61} = 0.66
\]
Assessment of FFR of left main stenosis depend on the severity of the LAD stenosis
Be careful with left main and LAD stenosis
What’s next: FAME III

FAME 3:

Objective
- The primary objective of the FAME 3 Trial is to demonstrate that FFR-guided PCI with the 2nd generation Resolute DES is non-inferior to CABG in patients with multivessel CAD.

Tonino, NEJM 2009 and Pijls, EHJ 2012
iFR

Maximal flow (adenosine)?

Pressure 1

Pressure 2

Coronary artery

Myocardium

iFR

Pressure 2

Pressure 1

= 0.70

70% of maximum flow
Instantaneous wave-free ratio (iFR)

Sen, JACC, 2011
Instantaneous wave-free ratio (iFR)

\[\text{iFR} = \frac{P_{d_{\text{wave-free period}}}}{P_{a_{\text{wave-free period}}}}\]
Relationship between iFR and FFR
The Resolve study

![Graph A: Scatter plot of iFR vs. Method mean (iFR + FFR)/2]

![Graph B: Scatter plot of Pd/Pa vs. Method mean (Pd/Pa + FFR)/2]

Jeremias, JACC 2014
iFR accuracy to predict FFR

<table>
<thead>
<tr>
<th>Study/Participating Site</th>
<th>No. of Lesions</th>
<th>Cutoff Point</th>
<th>AUC From ROC (C statistic)</th>
<th>Overall Accuracy (%)</th>
<th>Correlation ($R^2$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>1,593</td>
<td>0.90</td>
<td>0.81</td>
<td>80.4</td>
<td>0.66</td>
</tr>
<tr>
<td>ADVISE*</td>
<td>432</td>
<td>0.91</td>
<td>0.82</td>
<td>81.9</td>
<td>0.71</td>
</tr>
<tr>
<td>VERIFY†</td>
<td>654</td>
<td>0.89</td>
<td>0.80</td>
<td>79.4</td>
<td>0.60</td>
</tr>
<tr>
<td>Seoul National University</td>
<td>179</td>
<td>0.92</td>
<td>0.83</td>
<td>82.7</td>
<td>0.68</td>
</tr>
<tr>
<td>Stony Brook University</td>
<td>149</td>
<td>0.93</td>
<td>0.81</td>
<td>79.2</td>
<td>0.54</td>
</tr>
<tr>
<td>Columbia University</td>
<td>95</td>
<td>0.91</td>
<td>0.84</td>
<td>82.1</td>
<td>0.62</td>
</tr>
<tr>
<td>AMC/VUMC/KCL</td>
<td>84</td>
<td>0.90</td>
<td>0.78</td>
<td>78.6</td>
<td>0.72</td>
</tr>
</tbody>
</table>

*Includes data from the ADVISE study and ADVISE registry. †Includes data from the prospective and retrospective VERIFY cohorts.

AMC = Academic Medical Center, University of Amsterdam; AUC = area under the curve; iFR = instantaneous wave-free ratio; KCL = King’s College London; P专项行动/University Medical Center, Amsterdam.
Fractional flow reserve & Ct-scan
Performance of CT-scan to detect FFR ≤ 0.8

- Retrospective, July 2004 and March 2007
- 64-slice CT scanner or dual-source CT scan
- Single discrete lesion
- 89 segments in 79 patients

Meijboom, JACC, 2008
FFRct

Patient-Specific cCTA Data

Geometry

Myocardial Mass

CCTA

Simulated physiologic conditions
- Aortic pressure
- Coronary flow at rest
- Effect of hyperemia on microcirculation

Equations of Blood Flow

\[
p\vec{v}_f + \rho \vec{v} \cdot \nabla \vec{v} = -\nabla p + \nabla \cdot \sigma
\]

\[
\nabla \cdot \vec{v} = 0
\]

Simulated Hyperemic Blood Flow & Pressure

Min, Journal of Cardiovascular Computed Tomography, 2011
The NXT trial: Study Endpoints

Primary Endpoint:
- Per-patient diagnostic performance as assessed by the area under the receiver operating characteristic curve (AUC) of $\text{FFR}_{\text{CT}}$ vs. coronary CTA for the diagnosis of ischemia.

(Reference standard: $\text{FFR} \leq 0.80$)

Secondary Endpoints:
- Diagnostic performance (accuracy, sensitivity, specificity, PPV and NPV) of $\text{FFR}_{\text{CT}}$, coronary CTA, and invasive coronary angiography
**Discrimination of Ischemia**

- FFR<sub>CT</sub> AUC: 0.90, 95% CI: 0.87, 0.94
- CT AUC: 0.81, 95% CI: 0.76, 0.87
- ΔAUC: 0.09, 95% CI: 0.04, 0.14
- P=0.0008

- FFR<sub>CT</sub> AUC: 0.93, 95% CI: 0.91, 0.95
- CT AUC: 0.79, 95% CI: 0.74, 0.84
- ΔAUC: 0.14, 95% CI: 0.09, 0.19
- P<0.0001

Greater discriminatory power for FFR<sub>CT</sub> versus CT stenosis

**Patient** (Δ 0.09, p<0.0008)

**Vessel** (Δ 0.14, p<0.0001)

*Area under the receiver operating characteristics curve*
Conclusions

• FFR is a validated index to be used in routine daily practice, easily reproducible, quick to measure, correlates very well with non invasive tests and has been extensively tested in different clinical trials.

• For these reasons, FFR received a class IA recommendation of ESC and ACC/AHA guidelines to identify hemodynamically relevant coronary lesions.

• i-FR is a new index which has been studied for the past 2 years, is questionable conceptually, and lacks clinical and experimental validation and cannot be recommended to be used in routine clinical practice yet.
Thank you

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