Fractional Flow Reserve: FAME and Practice Guidelines

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I, William Fearon, DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.
Treatment Options for Multivessel CAD

- **Medical Treatment**
- **FFR-Guided PCI**
- **CABG**

- COURAGE
- FAME
- SYNTAX
Fractional Flow Reserve (FFR)

Maximum flow down a vessel in the presence of a stenosis...

...compared to the maximum flow in the hypothetical absence of the stenosis

Pijls and De Bruyne, Coronary Pressure
Fractional Flow Reserve

$$FFR = \frac{P_d}{P_a}$$
during maximal flow

$$P_d / P_a = 60 / 100$$
$$FFR = 0.60$$
FFR in Intermediate Lesions

FFR $< 0.75$:
- Sensitivity $= 88\%$
- Specificity $= 100\%$

Importance of Revascularization when Ischemia is Present

*Nuclear perfusion scans performed in > 5000 patients*

**Graph:**
- **Nuclear Scan Result:**
  - NI
  - Mild Abnl
  - Mod Abnl
  - Sev Abnl
- **Cardiac Death (%/yr):**
  - NI: 0.3, 0
  - Mild Abnl: 0.8, 0.9
  - Mod Abnl: 2.3, 1.1
  - Sev Abnl: 4.6, 1.3

*Medical Therapy* vs *Revascularization*

COURAGE Nuclear Substudy

Comparison of death/MI in patients with mod-severe pre-treatment ischemia

Shaw et al. Circulation 2008;117:1283
Frequency of Stress Testing to Document Ischemia Prior to Elective Percutaneous Coronary Intervention

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R. Adams Dudley, MD, MBA
F. L. Lucas, PhD
David J. Malenka, MD
Eric Vittinghoff, PhD
Rita F. Redberg, MD, MSc

**Context** Guidelines call for documenting ischemia in patients with stable coronary artery disease prior to elective percutaneous coronary intervention (PCI).

**Objective** To determine the frequency and predictors of stress testing prior to elective PCI in a Medicare population.

**Design, Setting, and Patients** Retrospective, observational cohort study using claims data from a 20% random sample of 2004 Medicare fee-for-service beneficiaries aged 65 years or older who had an elective PCI (N=23 887).

**Main Outcome Measures** Percentage of patients who underwent stress testing within 90 days prior to elective PCI; variation in stress testing prior to PCI across 306 hospital referral regions; patient, physician, and hospital characteristics that predicted the appropriate use of stress testing prior to elective PCI.

**Results** In the United States, 44.5% (n=10 629) of patients underwent stress testing within the 90 days prior to elective PCI. There was wide regional variation among the hospital referral regions with stress test rates ranging from 22.1% to 70.6% (national mean, 44.5%; interquartile range, 39.0%-50.9%). Female sex (adjusted odds ratio [AOR], 0.91; 95% confidence interval [CI], 0.86-0.97), age of 85 years or older (AOR, 0.83; 95% CI, 0.72-0.95), a history of congestive heart failure (AOR, 0.85; 95% CI, 0.79-0.92), and prior cardiac catheterization (AOR, 0.45; 95% CI, 0.38-0.54) were associated with a decreased likelihood of prior stress testing. A history of chest pain (AOR, 1.28; 95% CI, 1.09-1.54) and black race (AOR, 1.26; 95% CI, 1.09-1.46) increased the likelihood of stress testing prior to PCI. Patients treated by physicians performing 150 or more PCIs per year were less likely to have stress testing prior to PCI (AOR, 0.84; 95% CI, 0.77-0.93). No hospital characteristics were associated with receipt of stress testing.

**Conclusion** The majority of Medicare patients with stable coronary artery disease do not have documentation of ischemia by noninvasive testing prior to elective PCI.

JAMA. 2008;300(15):1765-1773

www.jama.com
FFR vs. Nuclear Perfusion Scan in MVD

67 patients with angiographic 2 or 3 vessel CAD

<table>
<thead>
<tr>
<th>FFR</th>
<th>MPI</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.80</td>
<td>positive</td>
<td>38</td>
</tr>
<tr>
<td>&gt; 0.80</td>
<td>negative</td>
<td>24</td>
</tr>
<tr>
<td>42</td>
<td>97</td>
<td></td>
</tr>
</tbody>
</table>

FFR vs. Nuclear Perfusion Scan in MVD

67 patients with angiographic 2 or 3 vessel CAD

Limitation of Angiography

Comparison of QCA to FFR in over 3,000 lesions

Courtesy of Bernard De Bruyne, MD, PhD
Why FFR instead of IVUS?
MLA = 4.98 mm²
FFR = 0.75

Resting
Hyperemia
 Disconnect between Anatomy and Physiology

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**During Maximal Hyperemia**

- 50% Stenosis
  - FFR=0.85
  - Collaterals

- 50% Stenosis
  - FFR=0.75
  - Vessel-Supplied Myocardium
  - Collateral-Supplied Myocardium
IVUS cutoff is affected by size of vessel

**4 MM² TOO SMALL?**
- CSA 4 mm²
- 55% stenosis
- FFR = 0.60

**4 MM² SUFFICIENT?**
- CSA 4 mm²
- 10% stenosis
- FFR = 0.90
FFR is preferred to identify whether an intermediate lesion is functionally significant, and IVUS is preferred when assessing the anatomy of a lesion for sizing, position of plaque and adequacy of stent deployment.
Fractional Flow Reserve versus Angiography for Multivessel Evaluation

Lesions warranting PCI identified

PCI performed on indicated lesions only if FFR \(\leq 0.80\)

Randomized

Composite of death, MI and repeat revasc. (MACE) at 1 year

Primary Endpoint

Key Secondary Endpoints

Individual rates of death, MI, and repeat revasc., MACE, and functional status at 2 years

FFR-Guided

Angio-Guided
## Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Angio-Guided n = 496</th>
<th>FFR-Guided n = 509</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ±SD</td>
<td>64±10</td>
<td>65±10</td>
<td>0.47</td>
</tr>
<tr>
<td>Male, %</td>
<td>73</td>
<td>75</td>
<td>0.30</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>25</td>
<td>24</td>
<td>0.65</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>66</td>
<td>61</td>
<td>0.10</td>
</tr>
<tr>
<td>Current smoker, %</td>
<td>32</td>
<td>27</td>
<td>0.12</td>
</tr>
<tr>
<td>Hyperlipidemia, %</td>
<td>73</td>
<td>72</td>
<td>0.62</td>
</tr>
<tr>
<td>Previous MI, %</td>
<td>36</td>
<td>37</td>
<td>0.84</td>
</tr>
<tr>
<td>NSTE ACS, %</td>
<td>36</td>
<td>29</td>
<td>0.11</td>
</tr>
<tr>
<td>Previous PCI, %</td>
<td>26</td>
<td>29</td>
<td>0.34</td>
</tr>
<tr>
<td>LVEF, mean ±SD</td>
<td>57±12</td>
<td>57±11</td>
<td>0.92</td>
</tr>
<tr>
<td>LVEF &lt; 50%, %</td>
<td>27</td>
<td>29</td>
<td>0.47</td>
</tr>
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</table>
# Procedural Characteristics

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<tr>
<td>Indicated lesions / patient</td>
<td>2.7 ± 0.9</td>
<td>2.8 ± 1.0</td>
<td>0.34</td>
</tr>
<tr>
<td>Stents / patient</td>
<td>2.7 ± 1.2</td>
<td>1.9 ± 1.3</td>
<td>&lt;0.001</td>
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### Procedural Characteristics

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<td>Stents / patient</td>
<td>2.7 ± 1.2</td>
<td>1.9 ± 1.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Procedure time (min)</td>
<td>70 ± 44</td>
<td>71 ± 43</td>
<td>0.51</td>
</tr>
<tr>
<td>Contrast agent used (ml)</td>
<td>302 ± 127</td>
<td>272 ± 133</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Equipment cost (US $)</td>
<td>6007</td>
<td>5332</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Length of hospital stay (days)</td>
<td>3.7 ± 3.5</td>
<td>3.4 ± 3.3</td>
<td>0.05</td>
</tr>
</tbody>
</table>
## Adverse Events at 1 Year

<table>
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<tbody>
<tr>
<td><strong>Total no. of MACE</strong></td>
<td>113</td>
<td>76</td>
<td></td>
</tr>
<tr>
<td><strong>Death</strong></td>
<td>15 (3.0)</td>
<td>9 (1.8)</td>
<td>0.19</td>
</tr>
<tr>
<td><strong>Myocardial Infarction</strong></td>
<td>43 (8.7)</td>
<td>29 (5.7)</td>
<td>0.07</td>
</tr>
<tr>
<td>Small / peri-PCI (CK-MB 3-5xNI)</td>
<td>16</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Other infarctions (“late or large”)</td>
<td>27</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td><strong>CABG or repeat PCI</strong></td>
<td>47 (9.5)</td>
<td>33 (6.5)</td>
<td>0.08</td>
</tr>
<tr>
<td><strong>Death or Myocardial Infarction</strong></td>
<td>55 (11.1)</td>
<td>37 (7.3)</td>
<td>0.04</td>
</tr>
<tr>
<td><strong>Death, MI, CABG, or re-PCI</strong></td>
<td>91 (18.3)</td>
<td>67 (13.2)</td>
<td>0.02</td>
</tr>
</tbody>
</table>
Event-free Survival

Absolute Difference in MACE-Free Survival

- FFR-guided
- Angio-guided

30 days: 2.9%
90 days: 3.8%
180 days: 4.9%
365 days: 5.1%
1 Year Economic Evaluation

Bootstrap Simulation

- **Angio Better**
- **FFR Better**

**1 Year Costs**
- Angio ~ $14,000 / patient
- FFR ~ $12,000 / patient

AHA 2009
2 Year Survival Free of MACE

Late Breaking Trial, TCT 2009
# Adverse Events at 2 Years

<table>
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<th>FFR-Guided n = 509</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total no. of MACE</strong></td>
<td>139</td>
<td>105</td>
<td></td>
</tr>
<tr>
<td><strong>Individual Endpoints</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>19 (3.8)</td>
<td>13 (2.6)</td>
<td>0.25</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>48 (9.7)</td>
<td>31 (6.1)</td>
<td>0.03</td>
</tr>
<tr>
<td>CABG or repeat PCI</td>
<td>61 (12.3)</td>
<td>53 (10.4)</td>
<td>0.35</td>
</tr>
<tr>
<td><strong>Composite Endpoints</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death or Myocardial Infarction</td>
<td>63 (12.7)</td>
<td>43 (8.4)</td>
<td>0.03</td>
</tr>
<tr>
<td>Death, MI, CABG, or re-PCI</td>
<td>110 (22.2)</td>
<td>90 (17.7)</td>
<td>0.07</td>
</tr>
</tbody>
</table>

Late Breaking Trial, TCT 2009
2 Year Outcome of Deferred Lesions

513 Deferred Lesions in 509 FFR-Guided Patients

2 Years

31 Myocardial Infarctions

9 Late Myocardial Infarctions

1 Myocardial Infarction due to an Originally Deferred Lesion

22 Peri-procedural

8 Due to a New Lesion or Stent-Related

Only 1/513 or 0.2% of deferred lesions resulted in a late myocardial infarction

Late Breaking Trial, TCT 2009

Stanford
Implications of FAME

Death and MI in the COURAGE study

Survival Free of Death from Any Cause and Myocardial Infarction

Hazard ratio, 1.05; 95% CI (0.87–1.27); P=0.62

Implications of FAME

1 year MACE Rates

- PCI: 19.1%
- CABG: 11.2%
- PCI - angio: 18.4%
- PCI - FFR: 13.2%
1. FFR can be useful to determine if PCI is warranted, particularly if the noninvasive test is absent or equivocal. It is reasonable to use FFR for assessing the need for PCI of intermediate lesions (IIa)

2. FFR is not warranted to assess an angiographically significant stenosis if there is angina present and an unequivocally positive stress test in a concordant vascular distribution (III)
Final Thoughts:

• FFR-guided PCI improves outcomes and saves money compared to angio-guided

• FFR-guided PCI may help identify stable CAD which would benefit from PCI as compared to medical therapy alone

• FFR-guided PCI may result in equivalent outcomes compared to CABG