ASSESSMENT OF CORONARY PHYSIOLOGY:
Impact on Patient Management

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CORONARY ANATOMY

- Angiography may result in both underestimation or overestimation of lesion severity.
- Angiographic disease correlates with prognosis, albeit weakly in many cases.
- Inconsistent literature regarding the impact of angiographically-guided on “hard” outcomes.
- Is coronary angiography alone the best procedure to decide therapy?
THE OCULO-DILATORY REFLEX?

ANATOMY IS NOT THE ANSWER!
PROGNOSTIC VALUE OF RADIONUCLIDE MYOCARDIAL PERFUSION IMAGING

Shaw L et al, 2012
JNC 1:1026

SPECT
n = 69,655

PET
n = 4,392

Normal/Mild Abn
Mod-Severe Abnormal
RISK OF CARDIAC DEATH AND INDUCIBLE ISCHEMIA

Role of Post-SPECT Therapy

Hachamovitch, Circulation 2003

10,627 pts

*p<0.001
SURVIVAL FREE OF DEATH FROM ANY CAUSE AND MYOCARDIAL INFARCTION

Number at Risk

<table>
<thead>
<tr>
<th>Medical Therapy</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1138</td>
<td>1017</td>
<td>959</td>
<td>834</td>
<td>638</td>
<td>408</td>
<td>192</td>
<td>30</td>
</tr>
<tr>
<td>PCI</td>
<td>1149</td>
<td>1013</td>
<td>952</td>
<td>833</td>
<td>637</td>
<td>417</td>
<td>200</td>
<td>35</td>
</tr>
</tbody>
</table>

Hazard ratio: 1.05
95% CI (0.87-1.27)
P = 0.62
COURAGE (SPECT MPI SUBSTUDY)
Cardiac Event-free Survival In Patients With Moderate-Severe Pre-Rx Ischemia Following PCI + OMT Or OMT (n=105)

Cumulative Event-Free Survival

Unadjusted p=0.001
Risk-Adjusted p=0.082

≥5% Reduction in Ischemic Myocardium (n=68)
No Significant Reduction in Ischemia (n=37)

Time to Follow-up (in Years)

Shaw Circulation 2008;117:1283-1291.
ANGIOGRAPHIC LESION SEVERITY VERSUS PHYSIOLOGY

Torino PA et al, 2010
JACC 55: 2816
ANATOMY ≠ PHYSIOLOGY
ATHEROSCLEROSIS ≠ ISCHEMIA

“Apples and Oranges”
Paul Cezanne
c. 1899
FLOW RESERVE

• FRACTIONAL FLOW RESERVE (FFR)
  – Similar to relative coronary flow reserve
  – Indirect index; uses several assumptions
  – Assessment of only epicardial stenosis

• ABSOLUTE FLOW RESERVE (CFR)
  – Impacted by factors impacting on maximal flow: stenosis severity, microcirculation, BP&HR
  – Reduced with hyperlipidemia, LVH
  – Related to stenosis dimensions, diffuse atherosclerosis and microvascular dysfunction

• RELATIVE FLOW RESERVE
  – Regional differences; value reduced with diffuse CAD
  – Insensitive to hemodynamics
  – Cornerstone of noninvasive testing
SIMPLIFIED RATIONALE OF FRACTIONAL FLOW RESERVE

\[
FFR = \frac{P_d - P_v}{P_a - P_v} = \frac{70}{100} = 0.7
\]

KEY: PHF, when resistance is minimal

Pijls, N. H. J. et al. 1995
Circulation; 92: 3183-3193
LESION-SPECIFIC ISCHEMIA: FRACTIONAL FLOW RESERVE (FFR)

**Fractional Flow Reserve Vs. Angiography for Multivessel Evaluation (FAME) Trial**

- FFR = Pressure Differences Across Stenosis
- Lesion-Specific Ischemia: \( \leq 0.80 \)

1,005 pts w/ multivessel CAD
1° Endpoint: Death, MI, repeat TVR

FFR vs. ANGIOGRAPHIC STRATEGY
The FAME, DEFER, and FAME2 Trials

Discordance between % stenosis and FFR results
→ >60% of moderate lesions (50-70%): insignificant

- Low event rates if no revascularization performed in absence of abnormal FFR
- PCI did not improve outcome if FFR normal
- Lower event rate when FFR strategy employed, in comparison with angiographic approach

Tonino et al, 2010 JACC 55: 2816
Pijls et al, 2007 JACC 49: 2105
Pijls et al, 2010 JACC 56: 177
De Bruyne et al, NEJM 2012; 367: 991
RELATIONSHIP BETWEEN FRACTIONAL FLOW RESERVE AND OUTCOME

Conceptual plot for FFR as continuous marker of risk

- **Highest**: Medically treated
- **Medium**: PCI decreases event rate most at low FFR
- **Low**: Revascularized
- **Optimal threshold**: PCI probably increases events at high FFR

Johnson NP et al
JACC 2014; 64: 1641
GUIDELINES FOR THE USE OF FFR

<table>
<thead>
<tr>
<th>Publication</th>
<th>Recommendations</th>
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<tbody>
<tr>
<td>2011 ACCF/AHA/SCAI Guideline</td>
<td>Class IIa: angiographic intermediate coronary lesions (50-70%); For recommendations about revascularization</td>
</tr>
<tr>
<td>Expert consensus statement on FFR</td>
<td>In SIHD when <strong>noninvasive imaging is unavailable, nondiagnostic, or discordant</strong>, FFR should be used to assess functional significance of intermediate-severe coronary stenosis (50-90%)</td>
</tr>
<tr>
<td>2014 ESC/EACTS</td>
<td>Class I; FFR is indicated for moderate stenosis. Defer revascularization if FFR &gt;0.80</td>
</tr>
<tr>
<td>2013 ACC Appropriate use criteria for SIHD</td>
<td>Advocate for expanded use of intracoronary physiological testing</td>
</tr>
<tr>
<td>2017 ACC Appropriate use criteria for PCI</td>
<td><strong>If no stress test or results are indeterminant</strong>, FFR can be used to determine appropriateness of revascularization</td>
</tr>
</tbody>
</table>
U.S. TRENDS IN UTILIZATION OF FFR, FFR-GUIDED PCI, AND PCI FROM 2008 TO 2012

Naga V. et al., 2016
JACC;67:732-733
GLOBAL ADOPTION OF CORONARY PHYSIOLOGY TO GUIDE REVASCULARIZATION DECISION MAKING IN 2016

Reasons for low adoption
- Unavailable
- Time consuming
- Expensive
- Contraindications
- Adverse reactions

Gotberg M et al, 2017
JACC 70: 1379
WAVE-FREE PERIOD OF DIASTOLE AND ASSOCIATED HEMODYNAMICS

Gotberg M et al, 2017
JACC 70: 1379
## INVASIVE TOOLS TO ASSESS PHYSIOLOGY
### A Guide for Coronary Revascularization

<table>
<thead>
<tr>
<th></th>
<th>FFR</th>
<th>iFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lengthy procedure</td>
<td>Hyperemia independent</td>
<td>Excellent signal-to-noise ratio</td>
</tr>
<tr>
<td>Adenosine cost</td>
<td>Excellent signal-to-noise ratio</td>
<td>More rapid procedure</td>
</tr>
<tr>
<td>Availability of adenosine</td>
<td>More rapid procedure</td>
<td>Assess serial lesions</td>
</tr>
<tr>
<td>Inability to assess serial lesions</td>
<td>Assess serial lesions</td>
<td>Infrequent side effects</td>
</tr>
<tr>
<td>Frequent patient discomfort</td>
<td>Infrequent side effects</td>
<td></td>
</tr>
</tbody>
</table>
DEFERRAL OF REVASCULARIZATION ACCORDING TO iFR AND FFR

DEFINE FLAIR and iFR SWEDEHEART

- Single cutoff for iFR (0.98)
- Individual studies both revealed non-inferiority
- iFR avoid adenosine
  - Procedural time
  - Costs
  - Patient side effects
- Deferral of revascularization more common with iFR than with FFR
- iFR: The new standard?

Gotberg M et al, 2017
JACC 70: 1379
ASSESSMENT OF FFR FROM CT ANGIOGRAPHY
The DeFACTO Study (n=288)

Min JK et al, 2012
JAMA  308: 1237
INVASIVE CATHETERIZATION AND PRESENCE OF OBSTRUCTIVE DISEASE BASED ON STRATEGY
The PLATFORM Trial

Douglas PS et al
E Heart J 2015; 36: 3559

No MACE if ICA deferred based on FFR_{CT}
## NON-INVASIVE TESTING COMPARED WITH FFR
### A Meta-Analysis

<table>
<thead>
<tr>
<th>Test</th>
<th>Sens</th>
<th>Spec</th>
<th>NLR</th>
<th>AUC</th>
<th>Q-stat</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPECT</td>
<td>74%</td>
<td>79%</td>
<td>0.39</td>
<td>0.82</td>
<td>0.75</td>
</tr>
<tr>
<td>Echo</td>
<td>69%</td>
<td>84%</td>
<td>0.42</td>
<td>0.83</td>
<td>0.75</td>
</tr>
<tr>
<td>CMR</td>
<td>89%</td>
<td>87%</td>
<td>0.14</td>
<td>0.94</td>
<td>0.88</td>
</tr>
<tr>
<td>PET</td>
<td>84%</td>
<td>87%</td>
<td>0.14</td>
<td>0.93</td>
<td>0.87</td>
</tr>
<tr>
<td>CT</td>
<td>88%</td>
<td>80%</td>
<td>0.12</td>
<td>0.93</td>
<td>0.87</td>
</tr>
</tbody>
</table>

- CMR, CT and PET-r/o significant CAD and may serve as gatekeeper to cath lab
- CMR is test of choice
- BUT….Does FFR = functional testing?

Takx RAP et al, 2015
Circulation CV Img; 8: e002666
RELATIONSHIP BETWEEN CFR AND FFR

- CFR and FFR, even when discordance, reflect coronary physiology, not methodologic differences.

- Discordance explained by relative contribution of focal, diffuse, and small-vessel disease.
CONCLUSIONS

- Echocardiography, SPECT, PET, CCTA, CMR, and ICA have substantial prognostic value.
- COURAGE nuclear substudy and other image-guided trials support use on non-invasive testing to guide revascularization.
- FFR-directed PCI leads to improved outcomes based on FAME, DEFER and FAME 2 trials.
- iFR assessment may be preferable.
- Non-invasive evaluation of FFR appears.
- Determination of CFR provides assessment of more than just stenosis physiology, but ischemia at tissue level.
- Increasing evidence for PET-CFR to predict outcomes and plan strategy.
- FFR≠CFR, as different physiologic entities; use CFR to detect ischemia and FFR to determine candidacy for intervention?
- Guidelines support physiology-guided revascularization.