FFR, NHPR (IFR) and CFR: How do they help in the Cath Lab

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Disclosure:

Morton J. Kern, MD

Within the past 12 months, the presenter or their spouse/partner have had a financial interest/arrangement or affiliation with the organization listed below.

<table>
<thead>
<tr>
<th>Company Name</th>
<th>Relationship</th>
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<tbody>
<tr>
<td>Abbott Medical Inc.</td>
<td>Speakers’ Bureau</td>
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<td>Boston Sci Inc</td>
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<td>Philips Volcano</td>
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<td>Acist Medical Inc.</td>
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<td>Opsens</td>
<td>Speakers’ Bureau</td>
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</table>
Coronary Physiology in the Cath Lab

1. What is being measured and why?
2. What are the problems making the measurements?
3. What decisions should we make with the measurements?
Coronary Artery Disease Assessment

Anatomic Evaluation

Functional Testing
What do you want to measure?

- Stenosis – use FFR
- Coronary Reserve - use CFR
- Myocardial Resistance - use IMR
CFR = max flow/ basal flow = sum of flow thorough epicardial and bed bed
CFR cannot tell us if the problem is a stenosis or an impaired microcirculation.
Invasive physiological assessment of coronary disease: non-hyperaemic indices (iFR).

Nieves Gonzalo, Hernán Mejía-Rentería, Angela McInerney, Javier Escaned

\[ \Delta P = fQ + sQ^2 \]

Ischemic

Non-Ischemic
Invasive Translesional Pressure Measurements

Non-hyperemic Pressure ratios, NHPR

\[
\text{FFR} = \frac{P_{\text{distal (hyper)}}}{P_{\text{aortic (hyper)}}}
\]

\[
\text{iFR} = \frac{P_{\text{distal (rest, wfp)}}}{P_{\text{aortic (rest, wfp)}}}
\]

\[
\frac{P_{\text{d}}}{P_{\text{a}}} = \frac{P_{\text{distal (rest)}}}{P_{\text{aortic (rest)}}}
\]
Myocardial flow ($Q_s$) across stenosis/myocardial flow ($Q_n$) without stenosis = FFR

1. First Principle:
Aortic pressure, $P_a$, is the same along the length of the normal vessel.

2. Resistance = $P/Q$

3. Flow, $Q = P/R$

4. $Q_s/Q_n = (P_d/R_s)/(P_a/R_n)$

5. If $R_s = R_n$, then
$Q_s/Q_n = P_d/P_a$, hence

6. FFR = $P_d/P_a$, at max hyperemia

*NHJ Pijls et al. Circulation 1993*
Comparison of FFR, CFR and iFR (NPHR)

Hyperemia determines FFR and CFR.

Basal flow determines iFR, Pd/Pa.

Flow, $Q$

Pressure

$\text{FFR} = \frac{Q_s^{\text{max}}}{Q_N^{\text{max}}} = \frac{P_d}{R_s}$

$\text{CFR} = \frac{Q_s^{\text{max}}}{Q_{\text{base}}}$

During WFP

$\text{NHPR} = \frac{P_d}{P_a}$
2020 Technology: New Pressure Sensor Wires & Microcatheter

Piezoelectric Pressure Wires (Abbott & Philips)

Electrical sensor

ACIST Optical Fiber Microcatheter

2nd Gen Fiber Optic (3rd Gen Opsens)

1st Gen Fiber-Optic Sensor (BSC, Acist)

2nd Generation Fiber-Optic (Opsens)
# How to measure FFR accurately

<table>
<thead>
<tr>
<th>Action</th>
<th>Specifics</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticoagulate</td>
<td>Heparin 50-70u/kg</td>
<td></td>
</tr>
<tr>
<td>Administer NTG</td>
<td>100-200mcg</td>
<td>Flow effect &lt;2’ Vessel effect &gt;10’</td>
</tr>
<tr>
<td>Equalize pressures</td>
<td>Match wire to guide</td>
<td>In central Ao, in or out of guide. Not beyond ostium</td>
</tr>
<tr>
<td>Pass Wire</td>
<td>May disconnect wire</td>
<td>Remove wire introducer</td>
</tr>
<tr>
<td>Disengage guide</td>
<td>Caution w IC admin</td>
<td></td>
</tr>
<tr>
<td>Give adenosine</td>
<td>LCA 100-200mcg</td>
<td>IV 140mcg/kg/min</td>
</tr>
<tr>
<td></td>
<td>RCA 50-100mcg</td>
<td></td>
</tr>
<tr>
<td>Take Smart Minimum FFR</td>
<td>Use automatic read out</td>
<td>Check wave forms</td>
</tr>
<tr>
<td>Pullback and drift check</td>
<td>Co-register, if available</td>
<td>Check wave forms</td>
</tr>
</tbody>
</table>
Errors in the use of FFR and NHPR

1. **Equipment factors (FFR/NHPR):**
   - Erroneous zero, (tubing/connector leaks)
   - Faulty electric wire connection
   - Pressure signal drift, miscalibration, ECG

2. **Procedural factors**
   - Guide catheter damping
   - Incorrect sensor position
   - Inadequate hyperemia
   - Changing basal flow
Watch the Pressure Waveform -
Do not use Guide Catheter Side Holes. Damping?

From Nico Pijls
A Basic Question

• A patient undergoes FFR assessment of an intermediate lesion using intravenous adenosine.

Which point is the best place to measure FFR?

A) 0.68  B) 0.76  C) 0.85
Variation of IV adenosine pressures

- Even two paired tracings can differ 31% of the time in the pattern.
- However, the lowest FFR had the highest reproducibility (98%) and correlation with core lab analysis. Therefore...

"within reason, always take the minimum FFR value"

Johnson N et al, JACC CV Int 2017
Take the Smart Minimum FFR
Automated software records the lowest Pd/Pa as the FFR.

FFR 0.77
Pd/Pa 0.95
Pa:iPa 113:155
Pd:iPd 107:152
Q: Why can we not use IVUS/OCT for functional assessment?
A: A single cross-sectional area does not mean the same thing everywhere.
Validation – FFR

FFR < 0.75
Sensitivity 88%
Specificity 100%
Dx Accuracy 93%

Non-Hyperemic pressure

Pijls et al, NEJM 1996
Translesional Physiologic Options for LM assessment

- Hyperemic
  - Sub-Max Hyperemic
  - FFR: ≤0.80
  - cFFR: ≤0.83

- Non-Hyperemic Pressure Ratios (NHPR)
  - Whole-Cycle
    - Pd/Pa: ≤0.91
  - Diastolic/Sub-Cycle
    - DFR™: ≤0.89
    - iFR®: ≤0.89
    - RFR™: ≤0.89
    - dPR: ≤0.89
• 74 y/o man with HBP, HDL, DM, ESRD on HD, LBBB, and CAD mid LAD stent 6mo. ago (NSTEMI) now with ACS, CP w exertion.

• Same symptoms in 12/2018 which resolved after rotablator atherectomy followed by 3.0x38 mm Synergy DES post-dilated to 3.5mm.
Diagonal branch narrowing assessed

FFR = 0.86
• Successful PCI mid LAD 3.0x23mm Xience Sierra DES overlapping the prior LAD stent.

• Provisional bifurcation LAD stenting pinched D1 branch.

• D1 iFR = 0.90; Pd/Pa 0.91; FFR = 0.86,

• Further D1 intervention deferred.
3 Major FFR Outcome Studies

DEFER 15yr
It’s safe to rx medically and not stent.

FAME I – 5yr
Ischemia (FFR) directed stenting is better than angio-stent all approach.

FAME II – 5 yr
Blood is better than drugs if you have ischemia (+FFR)

Zimmerman EHJ 2015; 36, 3182–3188
Define Flair

Swede Heart

FAME

Bottom Line: iFR almost FFR but limited spectrum of studied patients
Outcomes of Deferral based on NHPR

(A) FFR

(B) Resting Pd/Pa

(C) iFR

(D) dPR

(E) RFR

(F) DFR

Jung-Min Ahn et al. IRIS-FFR Registry: Prognostic Performance of 5 Resting Pressure-Derived Indexes of Coronary Physiology. TCT 2018
When Can We Use FFR in ACS?

<table>
<thead>
<tr>
<th>Vessel</th>
<th>SIHD</th>
<th>NSTE-ACS</th>
<th>STEMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clear culprit</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Nonculprit</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Fearon WF, JACC. 2016 Sep 13;68(11):1192-4. (Table 1).
Baseline Pd/Pa = 0.94  
FFR = 0.80

How to Understand Discordance between NHPR and FFR
Discordance between NHPR and FFR:
2 ways to get FFR

Predictors of Discordance Between iFR/FFR: Stenosis Location, Severity, HR, Age, and BB’s

(FFR+/iFR-)=69/587

(FFR-/iFR+)=52/587

Physiological Pattern of Disease has an Influence on FFR/iFR Discordance

\[ \Delta P = f \cdot Q + s \cdot Q^2 \]

Algorithm for FFR/iFR Discordance

Intermediate lesion with Pd/Pa assessment

Pd/Pa < 0.87
INTERVENE

Pd/Pa = 0.87-0.93

Pd/Pa > 0.93
DEFER

CONTRAST FFR (cFFR) ASSESSMENT

cFFR < 0.75
INTERVENE

cFFR = 0.76-0.82

FFR > 0.83
DEFER

cFFR > 0.83
INTERVENE

FFR ASSESSMENT

FFR < 0.80
INTERVENE

FFR > 0.80
DEFER
## Clinical Challenges

– Patient Outcome Studies in Specific Subgroups

<table>
<thead>
<tr>
<th>Patient Subgroup</th>
<th>FFR</th>
<th>NHPR</th>
<th>Key Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stable IHD, Low Risk</td>
<td>✓</td>
<td>✓</td>
<td><em>Defer, Define-Flair, SwedeHeart</em></td>
</tr>
<tr>
<td>STEMI / NSTEMI</td>
<td>✓</td>
<td>✗</td>
<td>FFR valid in non-culprit ACS vessel if &lt;0.8</td>
</tr>
<tr>
<td>SVG Assessment</td>
<td>✓</td>
<td>✗</td>
<td>Physiology accurate, but biology of vein graft deterioration is critical role beyond “ischemia”</td>
</tr>
<tr>
<td>Ostial lesion, Left Main</td>
<td>✓</td>
<td>✗</td>
<td>IV hyperemia and caution for left main assessment and proximal LCX or LAD disease</td>
</tr>
<tr>
<td>Bypass Graft Failure</td>
<td>✓</td>
<td>✗</td>
<td>Early rate of bypass graft closure in non-physiologically significant vessels</td>
</tr>
<tr>
<td>Serial Lesions</td>
<td>?</td>
<td>?</td>
<td>iFR pullback looks promising</td>
</tr>
<tr>
<td>Aortic Stenosis &amp; TAVR</td>
<td>?</td>
<td>?</td>
<td>With increasing coronary blood flow after successful AVR, decrease in FFR</td>
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