FFR, IMR, CFR Discordance: Should We Abandon CFR?

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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

**Affiliation/Financial Relationship**
- Grant/Research Support
- Consulting Fees/Honoraria
- Major Stock Shareholder/Equity
- Royalty Income
- Ownership/Founder
- Intellectual Property Rights
- Other Financial Benefit

**Company**
- St. Jude Medical, Medtronic, NHLBI
- Medtronic
- Minor stock options: HeartFlow
What is Coronary Flow Reserve?

Resting Flow

CFR

Hyperemic Flow

FFR

Hyperemic Flow with Stenosis

Hyperemic Flow without Stenosis
Noninvasive Assessment of CFR

**PET**

**MRI**

**Echo**

Coronary Flow Reserve

Because flow is proportional to velocity, CFR can be estimated by measuring velocity at rest and at maximal hyperemia.
Coronary Flow Reserve

**Thermodilution-Derived CFR**

- **Proximal “Thermistor”**
- **Distal Thermistor**
First Description of CFR:

Measurement of myocardial blood flow at rest contains only limited diagnostic information

DEBATE Study:

**CFR measured in 297 patients after PTCA and found to predict outcomes**

Importance of the Microcirculation

Infarct-Free Survival based on Echo-Derived CFR in 394 Patients with Chest Pain and Normal Coronaries

Importance of the Microcirculation

2,423 patients undergoing PET-derived CFR

Importance of the Microcirculation

328 patients undergoing PET-derived CFR and Invasive Angiography

Freedom from cardiac death or CHF admission

CADPI indicates CAD Prognostic Index

Predicting Outcomes: *IMR vs. CFR*

*IMR was an independent predictor of survival in 253 STEMI patients while CFR was not.*

![Graph showing survival rates for IMR ≤40 and IMR >40 over 3 years.](image)

- **No. at risk:**
  - IMR ≤40: 173, 154, 149, 84
  - IMR >40: 80, 69, 63, 33

*Circulation 2013;127:2436-41.*
Predicting Outcomes: *IMR vs. CFR*

*Pre PCI FFR, IMR and CFR measured to predict peri-procedural MI*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients With Periprocedural Infarction (n=10)</th>
<th>Patients Without Periprocedural Infarction (n=40)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary physiology pre-PCI, U</td>
<td>15.7±10.9</td>
<td>16.5±9.2</td>
<td>0.808</td>
</tr>
<tr>
<td>Coronary wedge pressure</td>
<td>0.18±0.12</td>
<td>0.20±0.12</td>
<td>0.583</td>
</tr>
<tr>
<td>Collateral flow index</td>
<td>0.61±0.16</td>
<td>0.58±0.18</td>
<td>0.614</td>
</tr>
<tr>
<td>Fractional flow reserve</td>
<td>2.1±1.5</td>
<td>2.1±1.1</td>
<td>0.995</td>
</tr>
<tr>
<td>IMR</td>
<td>31.6±11.8</td>
<td>17.6±9.7</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Predicting Outcomes: IMR vs. CFR

IMR and CFR measured 1 year after heart transplantation in 74 patients with long-term follow-up (mean=4.5 years)

Is there a discordance?

*CFR and FFR measured in 438 patients from the literature.*
Is there a discordance?

**FFR, IMR and CFR measured across 91 lesions in 78 patients.**

Is there a discordance?

CFVR and FFR measured in 157 intermediate stenoses in 157 patients.

Is the discordance relevant?

CFVR and FFR measured in 157 intermediate stenoses in 157 patients.

MACE is a composite of cardiac death, MI and revascularization.

Is the discordance relevant?

CFVR and FFR measured in 157 intermediate stenoses in 157 patients.

5 Year Death/MI Rate

- 14% (3/22)
- 20% (5/26)
- 6% (6/100)

No. at risk:

<table>
<thead>
<tr>
<th>Category</th>
<th>No.</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>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>FFR ≥ 0.75 / CFVR ≥ 2.0</td>
<td>100</td>
<td>95</td>
<td>90</td>
<td>83</td>
<td>74</td>
<td>61</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FFR ≥ 0.75 / CFVR &lt; 2.0</td>
<td>22</td>
<td>12</td>
<td>12</td>
<td>11</td>
<td>10</td>
<td>8</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FFR &lt; 0.75 / CFVR ≥ 2.0</td>
<td>26</td>
<td>24</td>
<td>21</td>
<td>18</td>
<td>14</td>
<td>11</td>
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</tbody>
</table>

Why is there a discordance?

Limitations of CFR

- No clearly defined normal value
- Does not distinguish epicardial from microvascular disease
- Affected by resting hemodynamics
“Resting” Hemodynamics and CFR

Effect of changing heart rate on CFVR and FFR

“Resting” Hemodynamics and CFR

Effect of changing blood pressure on CFVR and FFR

“Resting” Hemodynamics and CFR

Effect of changing contractility on CFVR and FFR

### Reproducibility of IMR

#### Effect of Pacing on FFR/CFR/IMR

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>RV Pacing at 110 bpm</th>
</tr>
</thead>
<tbody>
<tr>
<td>CFR</td>
<td>3.1±1.1</td>
<td>2.3±1.2†</td>
</tr>
<tr>
<td>IMR, U</td>
<td>21.8±6.5</td>
<td>22.9±6.9</td>
</tr>
<tr>
<td>FFR</td>
<td>0.88±0.07</td>
<td>0.87±0.07</td>
</tr>
</tbody>
</table>

#### Effect of Blood Pressure on FFR/CFR/IMR

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Nitroprusside</th>
</tr>
</thead>
<tbody>
<tr>
<td>CFR</td>
<td>2.9±0.9</td>
<td>2.5±1.2</td>
</tr>
<tr>
<td>IMR, U</td>
<td>23.85±6.1</td>
<td>24.00±7.9</td>
</tr>
<tr>
<td>FFR</td>
<td>0.88±0.04</td>
<td>0.87±0.05</td>
</tr>
</tbody>
</table>

#### Change in LV Contractility and FFR/CFR/IMR

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Dobutamine</th>
</tr>
</thead>
<tbody>
<tr>
<td>CFR</td>
<td>3.0±1.0</td>
<td>1.7±0.6†</td>
</tr>
<tr>
<td>IMR, U</td>
<td>22.2±6.0</td>
<td>23.6±8.2</td>
</tr>
<tr>
<td>FFR</td>
<td>0.88±0.06</td>
<td>0.87±0.06</td>
</tr>
</tbody>
</table>


† p<0.05
Sex Differences and CFR

FFR, IMR and CFR measured in 157 patients (40 men) with “normal” coronaries

- IMR was similar between the sexes (20.7±9.8 vs. 19.1±8.0, p=0.45), but CFR was lower in women (3.8±1.6 vs. 4.8±1.9, p=0.004).
- This was primarily due to a shorter resting $T_{mn}$ in women (p=0.005), suggesting increased resting coronary flow.
- Hyperemic $T_{mn}$ was identical (p=0.79).
- On multivariate analysis, female sex was an independent predictor of lower CFR and shorter resting $T_{mn}$, but not a predictor of IMR or hyperemic $T_{mn}$.

Sex Differences and CFR

FFR, IMR and CFR measured in 157 patients (40 men) with “normal” coronaries

Sex Differences and CFR

**FFR, IMR and CFR measured in 157 patients (40 men) with “normal” coronaries**

ANOVA  \( p=0.002 \) (A vs. D, \( p=0.002 \))

ANOVA  \( p=0.41 \)

“Resting Flow” and CFR

Doppler wire-derived CFR measured in 30 patients

Baseline flow

<table>
<thead>
<tr>
<th>CFR low</th>
<th>CFR high</th>
</tr>
</thead>
<tbody>
<tr>
<td>28.80±10.93</td>
<td>16.13±6.61</td>
</tr>
</tbody>
</table>

Hyperemic flow

<table>
<thead>
<tr>
<th>CFR low</th>
<th>CFR high</th>
</tr>
</thead>
<tbody>
<tr>
<td>61.33±26.20</td>
<td>54.53±16.83</td>
</tr>
</tbody>
</table>

Is there a discordance?

No!

- Epicardial Vessel
- Microvasculature
- FFR
- IMR
- CFR
Should we abandon CFR?

- Despite the aforementioned limitations, noninvasively derived CFR is clearly prognostic and therefore useful.

- In the cath lab, when dealing with an individual patient, FFR remains the gold standard for identifying epicardial disease capable of inducing ischemia and for guiding PCI.

- In the cath lab, IMR is more reproducible and specific for assessing the microvasculature and may be more predictive of outcomes.