Index of Microcirculatory Resistance: Derivation, Validation and Practical Aspects

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Why is Microvascular Dysfunction Important?

- Up to 30% of patients continue to have angina despite successful coronary revascularization.

- ~20% of patients with chest pain are found to have no angiographic apparent apparent CAD.

- Microvascular dysfunction predicts adverse outcomes in a variety of clinical settings.
Importance of the Microcirculation

In 313 patients with FFR > 0.80, those with low CFR and high IMR (microvascular dysfunction) had significantly higher rate of death, MI, or revascularization.

<table>
<thead>
<tr>
<th>Group</th>
<th>CFR</th>
<th>IMR</th>
<th>Hazard Ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>High</td>
<td>Low</td>
<td>1.000 (Reference)</td>
<td>NA</td>
</tr>
<tr>
<td>B</td>
<td>High</td>
<td>High</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>C</td>
<td>Low</td>
<td>Low</td>
<td>2.116 (0.386-11.589)</td>
<td>0.388</td>
</tr>
<tr>
<td>D</td>
<td>Low</td>
<td>High</td>
<td>5.623 (1.234-25.620)</td>
<td>0.026</td>
</tr>
</tbody>
</table>

Breslow P for overall comparison = 0.002

Assessment of the Microvasculature

- Extremely challenging diagnosis
  - Heterogeneous patient population
  - Variety of pathogenetic mechanisms
  - Poor anatomic resolution
  - Potentially patchy nature of the disease

Therefore, assessment of the microvasculature is primarily *functional* and not *anatomic*
Evaluating the Microcirculation... 
...in the Cath Lab

TIMI Myocardial Perfusion Grade:
Evaluating the Microcirculation... 
...in the Cath Lab

TIMI Myocardial Perfusion Grade:
- Easy to obtain
- Specific for microvasculature
- Predictive of outcomes in large studies

Drawbacks:
- Qualitative
- Interobserver variability
- Not as useful in smaller studies
Coronary Wire-Based Assessment

Doppler Deceleration Time

Circulation 2002;106:3051-56.
Doppler Wire Coronary Flow Reserve

\[ \text{CFR} = \frac{\text{Hyperemic Flow}}{\text{Resting Flow}} \]
Coronary Wire-Based Assessment

Coronary Flow Reserve

- Not microvascular specific
- No clearly defined normal value
- Affected by resting hemodynamics
Index of Microcirculatory Resistance

Epicardial Vessel

Microvasculature

FFR

IMR
Index of Microcirculatory Resistance

*Potential Advantages:*

- Readily available in the cath lab
- Specific for the microvasculature
- Quantitative and reproducible
- Predictive of outcomes
Estimation of Coronary Flow


Calculation of mean transit time
Derivation of IMR:

- Resistance = \( \Delta \text{Pressure} / \text{Flow} \)
- \( \Delta \text{Pressure} = P_d - P_v \quad \text{Flow} \approx 1 / T_{mn} \)
- IMR = \( P_d - P_v / (1 / T_{mn}) \)
- IMR = \( P_d \times T_{mn} \quad \text{at maximal hyperemia...} \)

IMR Case Example

Cardiac transplant recipient enrolled in study evaluating ACE inhibition
IMR Case Example

Cardiac transplant recipient enrolled in study evaluating ACE inhibition
Accessing IMR
Flushing the System
Resting $T_{mn}$ Measurements
Hyperemic $T_{mn}$ Measurements
Practical Measurement of IMR

\[
IMR = P_d \times \text{Hyperemic } T_{mn} \\
= 89 \times 0.37 \\
= 33
\]
Animal Validation of IMR

Animal Validation of IMR

![Bar graph showing IMR comparison between normal and abnormal microcirculation with p = 0.002](image)

Circulation 2003;107:3129-3132
Animal Validation of IMR

Circulation 2003;107:3129-3132
Animal Validation of IMR

% Change after Disruption of the Microcirculation

- **Total Group**
- **Stenosis Absent**
- **Stenosis Present**

**p = NS**

- **IMR**
- **TMR**
## 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>

Ng, et al. Circulation 2006;113:2054-61. † p<0.05
Reproducibility of IMR

Mean correlation coefficients of IMR, CFR and FFR values comparing baseline measurement with each hemodynamic intervention

P<0.05

Reproducibility of IMR

Coefficient of variation between pairs of baseline values of IMR and CFR

Repeated IMR measurements obtained by 4 different operators in 12 STEMI patients were highly correlated ($r=0.99$, $P<0.001$), with a mean difference between IMR measurements of 0.01 (mean standard error 1.59 [95% CI -3.52 to 3.54], $P=0.48$).


- Correlation between IMR and cardiac MR assessment of microvascular obstruction in 108 patients after STEMI
IMR: Normal Value

An IMR < 25 is considered normal

- The mean IMR measured in 15 subjects (22 arteries) without any evidence of atherosclerosis and no/minimal risk factors was 19±5.

- The mean IMR measured in 18 subjects with normal stress tests and normal coronary angiography was 18.9±5.6.

- The mean IMR in 20 subjects with no CAD or risk factors was 14.0 with all values <23.

**Importance of Collaterals when Measuring IMR**

*IMR = \(\frac{P_d}{\text{Myocardial Flow}}\) and Myocardial Flow = \(Q_{\text{cor}} + Q_{\text{coll}}\)*

<table>
<thead>
<tr>
<th>(Q_{\text{cor}})</th>
<th>(P_d)</th>
<th>IMR(_{\text{app}})</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑</td>
<td>↑</td>
<td>→</td>
</tr>
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<td>↑</td>
<td>↑</td>
<td>→</td>
</tr>
</tbody>
</table>

Flow ↓’s more than it should, \(T_{\text{mn}}\) ↑’s and IMR\(_{\text{app}}\) = \(P_d \times T_{\text{mn}}\) ↑’s

*To measure true IMR, must measure coronary wedge pressure to incorporate collateral flow*

\[ IMR = P_d \times T_{\text{mn}} \times \left( \frac{\text{FFR}_{\text{cor}}}{\text{FFR}_{\text{myo}}} \right) \]

IMR is not affected by epicardial stenosis severity:

**Animal Validation**

![Graph showing the relationship between fractional flow reserve and IMR](image-url)

Circulation 2004;109:2269-2272
IMR is not affected by epicardial stenosis severity:

*Human Validation*

When should we be thinking about microvascular dysfunction?
Clinical Application of IMR

65 year old man with HTN, \( \uparrow \) Chol, and chest pain with anterior ischemia on ETT-Echo
IMR = 77 \times 0.12 = 9
Clinical Application of IMR

59 year old man with HTN, dyslipidemia and chest pain with emotional stress and septal ischemia on Nuclear Scan
IMR = 76 \times 0.70 = 53
Clinical Application of IMR

68 year old man HTN and tobacco use with negative stress echo 4 months ago, but increasingly severe classic exertional angina
IMR = 26 \times 0.25 = 8
Slow Pullback in LAD

Distal LAD

Proximal LAD

(59)
Pd mean

(33)
Pd mean

0.57
FFR

0.01
CURSOR

RESET
IVUS of LAD
IMR after Heart Transplantation

74 transplant recipients had FFR and IMR measured at baseline and 1 year.

74 transplant recipients had FFR and IMR measured at baseline and 1 year.

74 transplant recipients had FFR and IMR measured at baseline and 1 year.

Limitations of IMR

- Invasive

- Interpatient and intervessel variability?
  - Sensor distance

- Independent of epicardial stenosis
  - Coronary wedge pressure
Conclusion

*IMR is:*

- Readily available in the cath lab
- Relatively easy to perform
- Specific for the microvasculature
- Defined normal value
- Quantitative
- Reproducible
- *Predictive of outcomes*