IMR in Stable Patients

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Indications for IMR in Stable Patients

- To evaluate the etiology of chest pain/abnormal stress test in a patient with angiographically appearing normal coronaries
- To assess for the likelihood of peri-PCI myocardial infarction
- Research purposes
Clinical Application of IMR

65 year old man with HTN, ↑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 x 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
IVUS of LAD
139 patients referred for coronary angiography because of symptoms and/or abnormal stress test and found to have “normal” appearing coronaries

FFR, IMR, CFR, IVUS and acetylcholine challenge were performed down the LAD

Lee, Tremmel, et al. Unpublished data
# Chest Pain and “Normal Coronaries”

<table>
<thead>
<tr>
<th>Patient Characteristic</th>
<th>n=139</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>54 ±11</td>
</tr>
<tr>
<td>Female</td>
<td>77%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>53%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>23%</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>63%</td>
</tr>
<tr>
<td>Tobacco Use</td>
<td>8%</td>
</tr>
<tr>
<td>Typical Angina</td>
<td>32%</td>
</tr>
<tr>
<td>Positive Stress Test</td>
<td>42%</td>
</tr>
</tbody>
</table>

Lee, Tremmel, et al. Unpublished data
Chest Pain and “Normal Coronaries”

- The mean IMR was 19.6 ±9.1
- Microvascular dysfunction was present in 21% (defined as IMR ≥ 25)
  - Typical angina was more frequent (52% vs 26%, p=0.01) in patients with microvascular dysfunction
  - Positive stress tests were more common (65% vs. 41%, p=0.04)
- Predictors of microvascular dysfunction were age, BMI, and typical angina

Lee, Tremmel, et al. Unpublished data
Chest Pain and “Normal Coronaries”

- 4% of patients had an FFR of the LAD ≤ 0.80
- 44% had epicardial endothelial dysfunction
- 44% had a myocardial bridge

- 42% had nonischemic FFR, normal IMR, no significant endothelial dysfunction
- 34% had nonischemic FFR, normal IMR, no endothelial dysfunction and no “bridge”

Lee, Tremmel, et al. Unpublished data
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IMR after PCI in Stable Patients

- 50 patients randomized to conventional stenting with predilatation versus direct stenting
- IMR measured after PCI and correlated with troponin release
- In the 10 patients with elevated Tn post PCI, IMR was 24.7 ±13.3 vs. 16.9 ±10.2, p=0.04.

Is IMR Independent of Epicardial Stenosis?

### Comparison of IMR and TMR Values Under Various Epicardial and Microcirculatory Conditions

<table>
<thead>
<tr>
<th></th>
<th>Normal Microcirculation</th>
<th>Abnormal Microcirculation</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IMR, U</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total group</td>
<td>16.9±6.5</td>
<td>25.9±14.4</td>
<td>0.002</td>
</tr>
<tr>
<td>Stenosis absent</td>
<td>14.7±4.8</td>
<td>23.9±3.8</td>
<td>0.01</td>
</tr>
<tr>
<td>Stenosis present</td>
<td>19.2±7.3</td>
<td>28.6±14.5</td>
<td>&lt;0.03</td>
</tr>
<tr>
<td><strong>TMR, mm Hg · mL⁻¹ · min⁻¹</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total group</td>
<td>0.51±0.14</td>
<td>0.79±0.32</td>
<td>0.0001</td>
</tr>
<tr>
<td>Stenosis absent</td>
<td>0.48±0.14</td>
<td>0.71±0.25</td>
<td>0.005</td>
</tr>
<tr>
<td>Stenosis present</td>
<td>0.58±0.16</td>
<td>0.90±0.39</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Importance of Collaterals when Measuring IMR

- Resistance = Pressure / $Q_{myo}$

- $Q_{myo} = Q_{cor} + Q_{coll}$

- Simplified IMR = $P_d \times T_{mn}$

- But $T_{mn}$ is inversely proportional to *coronary flow*

Importance of Collaterals when Measuring IMR

\[ Q_{\text{cor}} \quad Q_{\text{coll}} \quad P_d \quad R_{\text{myo}} \]

Importance of Collaterals when Measuring IMR

Flow ↓’s more than it should, $T_{mn}$ ↑’s and $IMR_{app} = P_d \times T_{mn}$ ↑’s

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

$$IMR = P_d \times T_{mn} \times \frac{FFR_{cor}}{FFR_{myo}}$$

IMR is not affected by epicardial stenosis severity:

Animal Validation

![Graph showing the relationship between fractional flow reserve and IMR units. The graph indicates that IMR is not affected by epicardial stenosis severity, with no significant difference between no stenosis, moderate stenosis, and significant stenosis.](image-url)
IMR is not affected by epicardial stenosis severity:

**Human Validation**

<table>
<thead>
<tr>
<th>Stenosis Level</th>
<th>FFR</th>
<th>IMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>10% AS</td>
<td>0.53 ± 0.19</td>
<td>22 ± 15</td>
</tr>
<tr>
<td>50% AS</td>
<td>0.90 ± 0.12</td>
<td>23 ± 14</td>
</tr>
<tr>
<td>75% AS</td>
<td>0.84 ± 0.08</td>
<td>23 ± 14</td>
</tr>
</tbody>
</table>

IMR is not affected by epicardial stenosis severity:

Human Validation

IMR is not affected by epicardial stenosis severity:

**IMR measured pre and post PCI in 43 patients with significant LAD disease**

IMR is not affected by epicardial stenosis severity:

IMR measured pre and post PCI in 43 patients with significant LAD disease

IMR is not affected by epicardial stenosis severity:

**IMR measured pre and post PCI in 43 patients with significant LAD disease**

IMR Before PCI in Stable Patients

*IMR measured before PCI in 50 stable patients undergoing LAD PCI*

**IMR Before PCI in Stable Patients**

*IMR measured before LAD PCI in 50 stable patients*

### Multivariable Regression Analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>$P$</th>
<th>Odds ratio</th>
<th>95% Confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMR</td>
<td>0.002</td>
<td>1.25</td>
<td>1.08 – 1.43</td>
</tr>
<tr>
<td>Beta-blocker</td>
<td>0.064</td>
<td>13.97</td>
<td>0.97 – 200.56</td>
</tr>
<tr>
<td>Post-dilation</td>
<td>0.072</td>
<td>0.09</td>
<td>0.01 – 1.24</td>
</tr>
<tr>
<td>Total inflation time</td>
<td>0.115</td>
<td>1.01</td>
<td>0.99 – 1.03</td>
</tr>
<tr>
<td>Stent length</td>
<td>0.35</td>
<td>1.08</td>
<td>0.92 – 1.27</td>
</tr>
</tbody>
</table>

**IMR Before PCI in Stable Patients**

*IMR measured before PCI in 54 stable patients*

**Multivariable Regression Analysis**

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMR culprit</td>
<td>10.9 (1.3 to 90.5)</td>
<td>0.02</td>
</tr>
<tr>
<td>IMR post</td>
<td>18.3 (0.9 to 354)</td>
<td>0.054</td>
</tr>
<tr>
<td>rPIMR</td>
<td>1.09 (1.0 to 1.19)</td>
<td>0.02</td>
</tr>
<tr>
<td>Inflation (n)</td>
<td>1.4 (1.0 to 1.9)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Estimating True IMR without Wedge

- IMR = $P_d \times T_{mn} \times \left( \frac{FFR_{cor}}{FFR_{myo}} \right)$
- IMR = $P_d \times T_{mn} \times \left( \frac{(P_d - P_w)}{(P_a - P_w)} \right) \times \left( \frac{P_d}{P_a} \right)$

If there is a relationship between $FFR_{cor}$ and $FFR_{myo}$, perhaps we can estimate $FFR_{cor}$ without having to measure the coronary wedge pressure.

Estimating True IMR without Wedge

In a derivation cohort of 50 patients, a strong linear relationship was found between $\text{FFR}_{\text{cor}}$ and $\text{FFR}_{\text{myo}}$.

$\text{FFR}_{\text{cor}}$

$\text{FFR}_{\text{myo}}$

$r^2 = 0.87$

*p* < 0.001

$y = 1.34x - 0.32$

Estimating True IMR without Wedge

In a validation cohort of 72 patients, there was no significant difference in IMR with estimate $\text{FFR}_{\text{cor}}$ or measured $\text{FFR}_{\text{cor}}$.

Estimating True IMR without Wedge

In a validation cohort of 72 patients, there was no significant difference in IMR with estimate $FFR_{cor}$ or measured $FFR_{cor}$.

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- To evaluate the etiology of chest pain/abnormal stress test in a patient with angiographically appearing normal coronaries
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- Research purposes
IMR post Statin Therapy

IMR measured after PCI in 80 patients randomized to either 1 month pretreatment with pravastatin or placebo

IMR post ACE Inhibitor Therapy

40 patients randomized to IC enalaprilat or placebo prior to PCI

40 patients randomized to IC enalaprilat or placebo prior to PCI

IMR post Stem Cell Therapy

**IMR measured in 15 patients with ischemic cardiomyopathy before and 6 months after intracoronary stem cell delivery**

Conclusions:

- Measurement of FFR and IMR can help to diagnose the etiology of chest pain/abnormal stress test in patient with angiographically normal appearing coronaries.
- IMR measured at the time of PCI can predict peri-procedural myocardial infarction.
- IMR is a useful research tool for evaluating the efficacy of various therapies.