Calculation of the Index of Microcirculatory Resistance without Coronary Wedge Pressure Measurement in the Presence of Epicardial Stenosis

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Conflict of Interest Disclosure

No conflict of interest to declare
Index of Microcirculatory Resistance (IMR) as a Measure of Microcirculatory Status

Measured using a pressure-temperature sensor wire

Fearon et al. *Circulation* 2003
Ng et al. *Circulation* 2006
Index of Microcirculatory Resistance (IMR) as a Measure of Microcirculatory Status

Measured using a pressure-temperature sensor wire

Specific quantitative assessment of the microcirculation

Fearon et al. Circulation 2003
Ng et al. Circulation 2006
IMR represents minimal microcirculatory resistance measured during conditions of peak flow.

Calculation of IMR

\[ \text{Microcirculatory resistance} = \frac{\text{pressure drop across microcirculation}}{\text{flow}} \]

(during maximal hyperemia)

Derivation of IMR

**Pressure gradient**

**Flow**

**Pd**  
**Pv**

**IMR = pressure** drop across microcirculation divided by **flow** (during maximal hyperemia)

Coronary flow $\simeq 1 / T_{mn}$

$\Delta$ Pressure $= P_d - P_v = P_d$ (assuming $P_v = 0$)

**Simplified IMR** $= P_d \times T_{mn}$ (at maximal hyperemia)

Microcirculatory Flow = Coronary Flow in the Absence of Epicardial Stenosis

Coronary flow $\approx \frac{1}{T_{mn}}$
In the Presence of Epicardial Stenosis

Microcirculatory Flow = Coronary Flow + Collateral Flow

Aarnoudse et al. Circulation 2004
Fearon et al. Circulation 2004
IMR Calculation Requires Pw Measurement in the Presence of Epicardial Stenosis

IMR corrected for collateral flow:

\[ \text{IMR corrected} = \frac{\text{Pa} \times \text{Tmn} \times (\text{Pd} - \text{Pw})}{\text{Pa} - \text{Pw}} \]

Aarnoudse et al. Circulation 2004
Fearon et al. Circulation 2004
Uncorrected IMR Overestimates Microcirculatory Resistance in the Presence of Epicardial Stenosis

Aarnoudse et al. *Circulation* 2004
Fearon et al. *Circulation* 2004
Elevated Baseline IMR Predicts Peri-procedural Myocardial Infarction

Existing microcirculatory impairment predisposes towards infarction due to embolic and ischemic insults from PCI

Calculation of IMR in the Presence of Epicardial Stenosis Requires Wedge Pressure Measurement

Corrected true IMR can only be calculated by performing balloon inflation in the presence of significant epicardial stenosis
Hypothesis
IMR may be calculated from existing coronary physiology measurements obtained prior to PCI without the need for wedge pressure measurement.

Aim
Develop a novel method/index to enable IMR calculation without the wedge pressure.
Methods & Results: Study Population

Derivation cohort:
45 patients scheduled for PCI of single target lesion from single tertiary referral center:
- 36 LAD, 5 RCA and 4 LCx
- 30 stable angina, 9 UAP, 6 NSTEMIs

Validation cohort:
27 patients scheduled for PCI of a single target lesion from a separate tertiary referral center:
- all LAD with stable angina
Derivation and Validation Cohorts:

<table>
<thead>
<tr>
<th>Variable</th>
<th>Derivation cohort (N = 45)</th>
<th>Validation cohort (N = 27)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean - years</td>
<td>61.2 ± 9.7</td>
<td>67.0 ± 9.5</td>
<td>0.017</td>
</tr>
<tr>
<td>Male sex – no. (%)</td>
<td>35 (77.8)</td>
<td>24 (88.9)</td>
<td>0.346</td>
</tr>
<tr>
<td>Body mass index</td>
<td>28.9 ± 5.5</td>
<td>29.2 ± 4.8</td>
<td>0.813</td>
</tr>
<tr>
<td>Co-morbidities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>9 (20.0)</td>
<td>9 (33.3)</td>
<td>0.121</td>
</tr>
<tr>
<td>Hypertension</td>
<td>27 (60.0)</td>
<td>21 (77.8)</td>
<td>0.195</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>29 (64.4)</td>
<td>23 (85.2)</td>
<td>0.100</td>
</tr>
<tr>
<td>Family history</td>
<td>14 (31.1)</td>
<td>4 (14.8)</td>
<td>0.161</td>
</tr>
<tr>
<td>History of smoking</td>
<td>23 (51.1)</td>
<td>6 (22.2)</td>
<td>0.068</td>
</tr>
<tr>
<td>Creatinine – mmol/L</td>
<td>84.7 ± 21.7</td>
<td>93.4 ± 21.3</td>
<td>0.100</td>
</tr>
<tr>
<td>Lesion characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lesion diameter stenosis - %</td>
<td>81.8 ± 9.5</td>
<td>77.7 ± 10.7</td>
<td>0.045</td>
</tr>
<tr>
<td>Fractional flow reserve</td>
<td>0.55 ± 0.15</td>
<td>0.64 ± 0.16</td>
<td>0.011</td>
</tr>
<tr>
<td>IMR</td>
<td>23.1 ± 14.1</td>
<td>20.6 ± 12.5</td>
<td>0.449</td>
</tr>
</tbody>
</table>
Formula Conception in Derivation Cohort

True IMR = Pa x Tmn x \( \frac{Pd - Pw}{Pa - Pw} \)
True IMR = Pa x Tmn x \( \frac{P_d - P_w}{Pa - P_w} \) FFRcor
True IMR = Pa x Tmn x \( \frac{Pd - Pw}{Pa - Pw} \) \( FFR_{cor} \)

\( FFR_{cor} = \) coronary flow in stenosed artery
\( \frac{\text{coronary flow in normal coronary artery}}{\text{coronary flow in normal coronary artery}} \)
True IMR = \( Pa \times Tmn \times \frac{Pd - Pw}{Pa - Pw} \)  

\[ \text{FFRcor} \]

\( \text{FFRcor} = \frac{\text{coronary flow in stenosed artery}}{\text{coronary flow in normal coronary artery}} \)

\( \text{FFRmyo} = \frac{\text{myocardial flow perfused by stenosed coronary artery}}{\text{myocardial flow perfused by normal coronary artery}} = \frac{Pd}{Pa} \)

 Alla during hyperemia)
True IMR = Pa x Tmn x \( \frac{P_d - P_w}{Pa - P_w} \) FFRcor

**FFRcor** = coronary flow in stenosed artery 
\[ \frac{\text{coronary flow in normal coronary artery}}{\text{coronary flow in normal coronary artery}} \]

**FFRmyo** = myocardial flow perfused by stenosed coronary artery 
\[ \frac{\text{myocardial flow perfused by normal coronary artery}}{\text{myocardial flow perfused by normal coronary artery}} = \frac{P_d}{Pa} \]

It is likely that FFRcor correlates with FFRmyo in a mathematically predictable manner.
Derivation Cohort: FFRcor and FFRmyo

FFRcor = \frac{Pd - Pw}{Pa - Pw}

FFRmyo = \frac{Pd}{Pa}

Derivation Cohort: $\text{FFR}_{\text{cor}} = 1.35 \text{FFR}_{\text{myo}} - 0.32$

$r^2 = 0.85$
$p < 0.001$

$y = 1.35x - 0.32$
Validation Cohort Measurements

Calculated IMR:
$$\text{Pa} \times \text{Tmn} \times (1.35 \frac{\text{Pd}}{\text{Pa}} - 0.32)$$

True IMR corrected for collateral flow:
$$\text{Pa} \times \text{Tmn} \times \frac{\text{Pd} - \text{Pw}}{\text{Pa} - \text{Pw}}$$

Validation Cohort: Good Correlation and Agreement between Measured and Calculated FFRcor

Measured FFRcor = \frac{P_d - P_w}{P_a - P_w}

Calculated FFRcor = (1.35 \times \frac{P_d}{P_a}) - 0.32

r^2 = 0.89
p < 0.001
Validation Cohort: Good Correlation and Agreement between True and Calculated IMR

True IMR = \( Pa \times Tmn \times \frac{Pd - Pw}{Pa - Pw} \)

Calculated IMR = \( Pa \times Tmn \times (1.35 \frac{Pd}{Pa} - 0.32) \)
Agreement between True and Calculated IMR Deviates when FFR < 0.45
Limitations

Small sample size and limited number of patients with non-LAD and acute coronary syndromes

All patients had IMR measured in either LAD, LCx or RCA:
Results cannot be extrapolated to left main coronary artery or branch vessel

Differences between validation and derivation cohorts
Conclusions

Demonstrate a method to calculate IMR without the need for wedge pressure measurement in the presence of significant epicardial stenosis

Caveat: When FFR <0.45
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Elevated Baseline Calculated IMR without Wedge Predicts Peri-procedural Myocardial Infarction

AUC = 0.80, p < 0.005

Calculated IMR ≥25 U:
Sensitivity = 80.0%
Specificity = 74.0%
Pathogenesis of Peri-procedural MI

Microvascular vasospasm

Distal plugging

Epicardial artery

Microcirculation

Other Methods to Calculate IMR without Wedge

No relationship between $Pw$ and $FFR_{myo}$ or $Pd$
Other Methods to Calculate IMR without Wedge

A

\[ r^2 = 0.39 \]
\[ p < 0.001 \]
\[ y = 0.46x + 7 \]

B

Poor agreement when using IMRuncorr to predict true IMR
Other Methods to Calculate IMR without Wedge

Poor agreement when using

\[ \text{True IMR} = 0.61 \times \text{IMRuncorr} + 37.6 \times \text{FFRmyo} \]
IMR without Pw: Formula Derivation

Derivation of corrected IMR:

\[
Q_{\text{myo}} = Q_{\text{cor}} + Q_{\text{collat}}
\]

\[
\text{FFR}_{\text{myo}} = \frac{Q_{\text{myo}}}{Q_{\text{cor}}}\sqrt{N_{\text{myo}}}
\]

\[
\text{FFR}_{\text{cor}} = \frac{Q_{\text{cor}}}{Q_{\text{myo}}}\sqrt{N_{\text{cor}}}
\]

\[
\text{FFR}_{\text{myo}} = \frac{(P_d - P_v)}{(P_a - P_v)}
\]

\[
\text{FFR}_{\text{cor}} = \frac{(P_d - P_w)}{(P_a - P_w)}
\]

\[
Q_{\text{cor}} \equiv \frac{1}{T_{\text{mn}}}, \text{where } T_{\text{mn}} = \text{hyperemic mean coronary thermodilution transit time}.
\]

(1)

\[
\text{IMR}_{\text{app}} = \frac{(P_d - P_v)}{Q_{\text{cor}}} = \frac{(P_d - P_v)}{Q_{\text{cor}} \times T_{\text{mn}}}
\]

\[
\frac{R_{\text{micro}}}{\text{IMR}} = \frac{(P_d - P_v)}{Q_{\text{cor}}}
\]

Restated, \( \text{IMR} = \left[ \frac{(P_d - P_v)}{Q_{\text{cor}}} \right] \times \left( \frac{Q_{\text{cor}}}{Q_{\text{myo}}} \right) \times \left( \frac{Q_{\text{myo}}}{Q_{\text{cor}}} \right) = \text{IMR}_{\text{app}} \times \frac{Q_{\text{myo}}}{Q_{\text{cor}}} = \text{IMR}_{\text{app}} \times \text{FFR}_{\text{myo}} \times \left( \frac{Q_{\text{myo}}}{Q_{\text{cor}}} \right)
\]

\[
\text{Because } Q_{\text{myo}}^{N} = Q_{\text{cor}}^{N}, \text{ IMR}_{\text{app}} \times \frac{\text{FFR}_{\text{cor}}}{\text{FFR}_{\text{myo}}}
\]

(2)

Assuming \( P_v \equiv 0 \), \( \text{IMR} = P_d \times T_{\text{mn}} \times \left( \frac{\text{FFR}_{\text{cor}}}{\text{FFR}_{\text{myo}}} \right) \)

If \( R_{\text{micro}} \) is substituted for \( \text{IMR} \), \( R_{\text{micro}} = \text{IMR}_{\text{app}} \times \left( \frac{\text{FFR}_{\text{cor}}}{\text{FFR}_{\text{myo}}} \right) \).

If there are no collaterals, as in the case of a normal epicardial artery, \( \text{FFR}_{\text{cor}} = \text{FFR}_{\text{myo}} \), and Equation 2 equals Equation 1. Equation 2 can be rewritten in terms of measured pressures, as follows:

\[
\text{IMR} = \left[ \frac{(P_d - P_v)}{Q_{\text{cor}}} \times T_{\text{mn}} \right] \times \left[ \frac{(P_d - P_w)}{(P_a - P_v)} \right] \times \left[ \frac{(P_d - P_v)}{(P_a - P_v)} \right] = \left[ \frac{(P_d - P_v)}{Q_{\text{cor}}} \times T_{\text{mn}} \right] \times \left[ \frac{(P_d - P_w)}{(P_a - P_v)} \right]
\]

\[
= \left( \frac{(P_a - P_v)}{T_{\text{mn}}} \right) \times \left[ \frac{(P_d - P_w)}{(P_a - P_v)} \right]
\]

Physiology measurements available pre-PCI:

\( Pa, Pd, TmnH, TmnR \)
Results: IMR Association with Statin Use

P = 0.002
True IMR, accounting for collateral flow, is the same before and after PCI
Difference between Pre- and Post-PCI IMR: No Relationship with Pd

\[ r^2 < 0.001 \]
\[ P = 0.949 \]
IMR, but not CFR, is Independent of Functional Epicardial Stenosis (FFR)

Pre-PCI FFR vs. Pre-PCI IMR

- $r^2 = 0.06$
- $P = 0.103$

Pre-PCI FFR vs. Pre-PCI CFR

- $r^2 = 0.53$
- $P < 0.001$
- $y = 4.7x - 0.6$