Microvasculature
Clinical Importance

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Collateral connections
1. Exist in the healthy heart
2. Microvascular density correlates with disease
3D stereo-arteriography resolves:
Collateral connections vs. 2D overlap

Adult, ‘normal’ coronary arteries

Fulton WF
Acute MI

Infarct scar

Remodelling

vascularity

Chronic MI

Remodelling

vascularity

Fulton WF
The Clinical Importance of the Microcirculation

- Major determinant of myocardial blood flow and therefore maximal hyperaemia
- Significant impact on prognosis - FFR/CFR discordance
- Critically important in shock states
\[ F = \frac{\bigcirc P}{R_{\text{epi}} + R_{\text{myo}}} \]

\( P_a \)

\( F \)

\( R_{\text{epi}} \)

\( R_{\text{myo}} \)

\( P_v \)

\( K. \) Lance Gould, 1974
\[ F = \frac{\mathbf{R}_{\text{epi}} \times P}{\mathbf{R}_{\text{myo}} + \mathbf{R}_{\text{epi}}} \]

K. Lance Gould, 1974
\[ F = \frac{R_{\text{epi}} + R_{\text{myo}}}{P} \]
\[ F = \frac{\bigotimes P}{R_{epi} + R_{myo}} \]

% Control Flow

% Area Stenosis

K. Lance Gould, 1974
\[ F = R_{\text{epi}} + R_{\text{myo}} \]
The Microcirculation and Maximal Hyperaemia?

- FFR requires that myocardial microvascular resistance be rendered constant and minimal. This allows the impact of any epicardial stenosis on myocardial blood flow to be interrogated.

- When we measure FFR we are testing the ability of the microcirculation subtended by the artery being studied to maximally dilate by administering a potent vasodilator combination of GTN/adenosine.

- A common question about and criticism of FFR is: “How Do I Know if Minimal Resistance (maximal hyperaemia) Has Been Attained?”
The Microcirculation and Maximal Hyperaemia?

- The degree of hyperaemia obtained with pharmacological vasodilatation is more feasible, predictable and repeatable than that achieved during exercise testing.

- Dose response studies have confirmed that in the majority of patients, maximal hyperaemia is achieved with:
  - intravenous adenosine: 140mcg/kg/min
  - intracoronary adenosine: 100mcg

- Variation in the absolute level of minimal resistance (maximal hyperaemia) obtained is a strength of FFR:
  - reflects myocardial perfusion
  - describes unique vessel-level coronary physiology
50% area stenosis

\[ F = \frac{\otimes P}{R_{\text{epi}} \uparrow + R_{\text{myo}} \downarrow} \]

\[ \text{FFR} = 0.85 \]
50% area stenosis

\[ F = \frac{\otimes P}{R_{\text{epi}} \uparrow + R_{\text{myo}} \downarrow} \]

\[ \text{FFR} = 0.70 \]
\[ F = \frac{\mathbf{P}}{R_{\text{epi}} + R_{\text{myo}}} \]

90% area stenosis

\[ \text{FFR} = 0.70 \]
90% area stenosis

\[ F = \frac{\prod P}{R_{epi} + R_{myo}} \]

FFR = 0.85
90% area stenosis with severe MVO

\[ F = \frac{\otimes P}{R_{epi} + R_{myo}} \]

\[ FFR = 1.00 \]

(No Reflow)
The Clinical Importance of the Microcirculation

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- Significant impact on prognosis - FFR/CFR discordance
- Critically important in shock states
Meuwissen et al. Circulation 2001
Protocol update

Treatment plan

CFR and FFR:
- FFR > 0.8 = defer PCI (but CFR will be measured simultaneously)
- FFR ≤ 0.8:
  - CFR ≥ 2.0 = defer PCI
  - CFR < 2.0 = perform PCI
The Clinical Importance of the Microcirculation

- Major determinant of myocardial blood flow and therefore maximal hyperaemia
- Significant impact on prognosis - FFR/CFR discordance
- Critically important in shock states
High versus Low Blood-Pressure Target in Patients with Septic Shock

Pierre Asfar, M.D., Ph.D., Ferhat Meziani, M.D., Ph.D., Jean-François Hamel, M.D., Fabien Grelon, M.D., Bruno Megarbane, M.D., Ph.D., Nadia Anguel, M.D., Jean-Paul Mira, M.D., Ph.D., Pierre-François Dequin, M.D., Ph.D., Soizic Gergaud, M.D., Nicolas Weiss, M.D., Ph.D., François Legay, M.D., Yves Le Tulzo, M.D., Ph.D., Marie Conrad, M.D., René Robert, M.D., Ph.D., Frédéric Gonzalez, M.D., Christophe Guittton, M.D., Ph.D., Fabienne Tamion, M.D., Ph.D., Jean-Marie Tonnelier, M.D., Pierre Guezennec, M.D., Thierry Van Der Linden, M.D., Antoine Vieillard-Baron, M.D., Ph.D., Eric Mariotte, M.D., Gaël Pradel, M.D., Olivier Lesieur, M.D., Jean-Damien Ricard, M.D., Ph.D., Fabien Hervé, M.D., Damien Du Cheyron, M.D., Ph.D., Claude Guerin, M.D., Ph.D., Alain Mercat, M.D., Ph.D., Jean-Louis Teboul, M.D., Ph.D., and Peter Radermacher, M.D., Ph.D. for the SEPSISPAM Investigators*
Figure 2. Mean Arterial Pressure during the 5-Day Study Period.
Mean arterial pressures were significantly lower in the low-target group than in the high-target group during the 5 protocol-specified days (P=0.02 by repeated-measures regression analysis), although the values exceeded the target values of 80 to 85 mm Hg in the high-target group and 65 to 70 mm Hg in the low-target group. The I bars represent 95% confidence intervals.

Figure 3. Kaplan–Meier Curves for Cumulative Survival.
Data for the survival analysis, which was performed in the intention-to-treat population, were censored at 90 days. There was no significant difference in survival between the high-target group and the low-target group (P=0.57 at 28 days; P=0.74 at 90 days).
A Randomized Trial of Protocol-Based Care for Early Septic Shock

The ProCESS Investigators*
Cardiogenic Shock: In-hospital Mortality

Registry: 70 of 106 Hospitals in Switzerland
23696 ACS patients -> 1977 with cardiogenic shock (564 at admission; 1413 after admission)

# STEMI with cardiogenic shock:
## single or multivessel PCI?

**National Cardiovascular Data Registry**

<table>
<thead>
<tr>
<th></th>
<th>1 vessel PCI</th>
<th>Multi-vessel PCI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>2654</td>
<td>433</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>27.8%</td>
<td>36.5%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Death in lab</td>
<td>2.7%</td>
<td>5.8%</td>
<td>0.25</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.5%</td>
<td>2.6%</td>
<td>0.18</td>
</tr>
<tr>
<td>Bleeding</td>
<td>12.5%</td>
<td>13.8%</td>
<td>0.44</td>
</tr>
<tr>
<td>Renal failure</td>
<td>7.1%</td>
<td>9.7%</td>
<td>0.03</td>
</tr>
</tbody>
</table>

**Odds ratios mortality**

- **Excluding Patients with Cardiogenic Shock**
  - Unadjusted: 1.29 (1.03-1.62), p = 0.03
  - Adjusted: 1.23 (0.94-1.61), p = 1.23

- **Patients with Cardiogenic Shock**
  - Unadjusted: 1.58 (1.27-1.96), p <0.01
  - Adjusted: 1.54 (1.22-1.95), p <0.01

**Multi- vs. 1-vessel PCI**

[www.escardio.org/acuteccc](http://www.escardio.org/acuteccc)

*Saving lives is our mission*
Multivessel PCI or Culprit Lesion Only PCI


Graph showing the comparison between Preventive PCI and No preventive PCI. The hazard ratio is 0.35 (95% CI, 0.21–0.58); P<0.001. The number of patients at risk for each group is as follows:

- Preventive PCI: 234, 196, 166, 146, 118, 89, 67
- No preventive PCI: 231, 168, 144, 122, 96, 74, 50
CULPRIT-SHOCK Trial – Study Flow

Primary Endpoint: Mortality and/or severe renal failure 30 days
Systemic microcirculation

Sidestream Dark Field imaging

14 Megapixel sensor, pixelsize 1.4 μm

Light weight (150 grams)

Optics/sensor resolution optimized

Camera and illumination PC control

Stepping motor focus control

Quality control of image acquisition

Automatic image quantification

Adapted from C Ince
Recent technological advances allow intravascular and noninvasive assessment of microvascular function.

- **Myocardial**
  - Doppler
  - Thermodilution

- **Systemic**
  - Sidestream Darkfield
Coronary microvascular dysfunction due to essential thrombocythemia and polycythemia vera: the missing piece in the puzzle of their increased cardiovascular risk?

- LAD - CFR by TTDE at rest, and during adenosine infusion
- The mutation of JAK2 gene was associated with abnormal CFR.

<table>
<thead>
<tr>
<th></th>
<th>ET</th>
<th>PV</th>
<th>CONTROLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>CFR</td>
<td>2.9+/-0.94</td>
<td>2.2+/-0.7</td>
<td>3.8+/-0.7</td>
</tr>
<tr>
<td>CFR &lt; 2.5</td>
<td>38.5%</td>
<td>68.2%</td>
<td>4.1%</td>
</tr>
<tr>
<td>CFR &lt; 2.0</td>
<td>15.4%</td>
<td>40.9%</td>
<td>0</td>
</tr>
</tbody>
</table>
The Clinical Importance of the Microcirculation

- Major determinant of myocardial blood flow
- Explains why anatomy cannot predict FFR
- Explains why non-hyperaemic indices cannot predict FFR
- Significant impact on prognosis
- Critically important in shock states - ongoing trials
- Possible target for new therapeutic agents and strategies especially in STEMI
Figure 2 Examples of results of pixel-wise quantitative first-pass cardiovascular magnetic resonance perfusion imaging (ml/g/min) for (A) severe microvascular dysfunction and (B) non-severe patients. Stress images are shown on the top row and rest images on the bottom row for identical basal, mid-ventricular and apical slices together with their corresponding pixel maps.