Coronary microcirculation and peripheral endothelial function evaluation after acute ST elevation myocardial infarction treated with primary angioplasty

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Ph.D. Co-supervisor: Prof. Doutor José Fragata
Background
P-PCI for STEMI – Some patients do well...
... while others don’t...
A significant proportion of STEMI patients (from 20% to 60%) has a poor outcome because of microvascular coronary damage.

The negative prognostic implications (both on the risk of LV remodeling and on the risk of hard endpoints, including death) associated with coronary microvascular damage has been repeatedly confirmed, with several invasive and non-invasive indicators.

Several mechanisms proposed:

- Mechanical obstruction (due to distal embolization of atherothrombotic debris)
- Coronary endothelial dysfunction (mediated by the release of vasoactive factors, like endothelin-1 and tissue factor)
- Reperfusion injury (through several mechanisms)
Coronary microvascular damage in STEMI

Consequence, cause, or both?

STEMI

Coronary microvascular dysfunction

Endothelial dysfunction

Mechanical obstruction

Reperfusion injury
Coronary microvascular damage in STEMI

**Consequence, cause, or both?**

![Diagram showing the relationship between STEMI and coronary microvascular dysfunction]

- **Endothelial dysfunction**
- **Mechanical obstruction**
- **Reperfusion injury**

**Background**
Coronary microvascular damage in STEMI

Consequence, cause, or both?

- Endothelial dysfunction
- Mechanical obstruction
- Reperfusion injury
- Coronary microvascular dysfunction
- STEMI
Peripheral arterial tonometry (PAT)

- Noninvasive measurement of endothelial-dependent vasodilator function in the microcirculation of the finger.
- Pulse amplitude in the fingertip measured at rest and following the induction of reactive hyperemia.

EndoPAT 2000
(Itamar Medical, Caesarea, Israel)
Non-invasive evaluation of endothelial function

Peripheral arterial tonometry (PAT) and coronary endothelial function

- Endothelial-dependent dysfunction evaluated by PAT is correlated with coronary microvascular dysfunction in stable patients

- 94 patients with non-obstructive CAD
- Invasive evaluation of coronary endothelial function (acetylcholine)
- endoPAT evaluation

Sensitivity 80%
Specificity 85%

Endothelial dysfunction in CAD patients

Peripheral arterial tonometry (PAT) and extent of infarction in patients with STEMI
Peripheral arterial tonometry (PAT) and extent of infarction in patients with STEMI

- Endothelial dysfunction evaluated by RHI-PAT relates with the extension of myocardial infarction (P-PCI treated) measured by peak TnI

- 58 primary PCI patients
- Peak TnI
- EndoPAT evaluation

RHI-PAT <1.67 = only variable related with peak TnI on multivariate analysis
Peripheral arterial tonometry (PAT) and severity of CAD

- Endothelial-dependent dysfunction evaluated by RHI-PAT relates it to the severity of CAD disease

- 231 CAD patients
- Angiography performed
- endoPAT evaluation

RHI-PAT = only predictor of 3 vessel disease on multivariate analysis
Invasive evaluation of microvascular coronary circulation

Index of microvascular resistance (IMR)

Invasive and quantitative method for evaluating the microcirculation

- FFR: Specific for epicardial disease
- CFR: Affected by both epicardial and microcirculatory disease (cannot distinguish between the two)
- IMR: Specific for microcirculatory disease
Study Objectives
Study Hypothesis and Aims

Study hypothesis

- In patients with acute STEMI treated with primary PCI, endothelial dysfunction (evaluated by peripheral arterial tonometry) is related to the extent of microvascular damage and, consequently, to the extent of myocardial necrosis.

Study aims

- **Primary aim**: To evaluate the relation between endothelial dysfunction (evaluated with EndoPAT) and coronary microvascular dysfunction (evaluated by IMR) immediately after primary PCI.

- **Secondary aims**: Confirming IMR and evaluating endothelial dysfunction (as measured by peripheral arterial tonometry) as predictors of microvascular dysfunction and extension of the myocardial infarction.
Study outcome measures

**Primary outcome measures**

- IMR value in patients with endothelial dysfunction (RHI <1.67)
- IMR value according to the tertile of RHI

**Secondary outcome measures**

1. The relation between RHI values and:
   - The extent of myocardial necrosis
   - The extent of coronary microvascular obstruction

2. The relation between IMR values and:
   - The extent of myocardial necrosis
   - The extent of coronary microvascular obstruction
Population and Methods
Population

Type of Study

Observational, prospective, single centre, cohort study, performed in the Cardiology Department of Hospital Prof. Doutor Fernando da Fonseca (Amadora, Portugal).

Population

Patients admitted to Hospital Prof. Doutor Fernando da Fonseca with a first acute ST elevation myocardial infarction, treated with primary angioplasty.
Population

Inclusion Criteria

• Age > 18 years

• ST elevation (first) myocardial infarction defined as:
  - Thoracic pain with ≥ 20 min and/or
  - ST elevation ≥1 mm in two or more contiguous ECG leads

• Time pain-to-balloon < 6 hours (or between 6 and 12 horas, if pain clearly persists)

• Successful PCI of the culprit artery (no significant residual lesion, independently of the final TIMI flow) in a native coronary artery

• Informed consent obtained
Exclusion Criteria

- LBBB or pacemaker
- Previous myocardial infarction (STEMI or nSTEMI)
- Killip class IV
- PCI in the previous 3 months or previous CABG (anytime)
- Long-QT syndrome, 2nd or 3rd degree AV block, sinus node disease
- Arrhythmias considered by the investigator to contra-indicate adenosine
- Severe asthma or COPD
- Previous severe side effects to adenosine or other contra-indication for adenosine use
- Life expectancy <12 month
- Inclusion in other trials
Non-invasive evaluation of endothelial function

**Methods**

**Peripheral arterial tonometry (PAT)**

- PAT probe positioned in one finger of each hand
- Blood pressure cuff is inflated on one arm to suprasystolic pressures for 5 minutes.

Invasive evaluation of microvascular coronary circulation

Methods

Index of microvascular resistance (IMR)

- Immediately after successful PCI of the culprit artery
- Certus Pressure-Wire® (St. Jude Medical)
- RadiAnalyzer Xpress (St. Jude Medical®)
- Maximal hyperemia obtained with adenosine (perfusion by central or large peripheral vein)
Index of microvascular resistance (IMR)

Myocardial resistance = \text{pressure} \text{ drop across the myocardium divided by flow}

\text{Myocardial resistance} = \frac{\Delta \text{ pressure}}{\text{flow}}

\Delta \text{Pressure} = P_d - P_v = P_d \quad \text{(assuming } P_v = 0) \\
\text{Flow} \approx 1 / T_{mn} \\
\text{IMR} = P_d / \left(1 / T_{mn}\right) \\
\text{IMR} = P_d \times T_{mn} \quad \text{(at maximal hyperemia)}
Infarct extension evaluation

**Methods**

- **Troponin I release**
  - Dimension Vista™ Intelligent Lab System, Siemens Healthcare Diagnostics™
  - Blood samples collected at admission, 6, 12, 18, 24, 36 and 48h
  - Peak TnI values and the area under the curve (AUC) of TnI release

- **Echocardiography**
  - Performed in the first hours after P-PCI and at 3 months
  - LV volumes, LVEF, WMSI and global longitudinal strain

- **Contrast enhanced cardiac magnetic resonance (ceCMR)**
  - Performed on the 7-8th day post-MI
  - 1.5-T MRI system (Avanto, Siemens Medical System, Erlangen, Germany)
  - Infarct size, percent of infarct size
Coronary microvascular obstruction evaluation

**Methods**

- **ECG ST-elevation resolution**
  - ECGs collected before, immediately after/90 min/180 min after P-PCI
  - % of total ST-elevation resolution was calculated vs. pre-PCI ECG

- **Angiographic indicators** (measured at the end of the procedure)
  - Corrected TIMI frame count (cTFC)
  - TIMI myocardial perfusion grade (MPG)

- **Contrast enhanced cardiac magnetic resonance (ceCMR)**
  - Presence of microvascular obstruction (no reflow)
  - Mass of microvascular obstruction
Results
Included population

Main Epidemiological characteristics

N: 60 patients
Mean age: $59.6 \pm 12.7$ years

Culprit Artery

- RCA: 19 (31.7%)
- LCx: 13 (21.7%)
- LAD: 28 (46.7%)

Time Delays

- Pain-to-balloon time: 209 (IQR 148) min
- Door-to-balloon time: 78 (IQR 45) min

Primary PCI

- Abciximab: 14 (23.3%)
- Mechanical thrombectomy: 26 (43.3%)
- Stent: 57 (95.0%)
- Direct stenting: 25 (41.7%)
- Post-dilatation: 28 (38.3%)

Results

- Hypertension: 43 (71.7%)
- Diabetes: 15 (25.0%)
- Dyslipidemia: 30 (50.0%)
- Smoking habits: 26 (43.3%)
Index of microvascular resistance (IMR)

**Results**

**Example 1**
- 28 years ♂
- Inferior STEMI
- Proximal RCA occlusion
- Successful P-PCI
- IMR = 17

**Example 2**
- 75 years ♀
- Inferior STEMI
- Proximal LCx occlusion
- Successful P-PCI
- IMR = 76

**Median value:** 23.9 (IQR 32.9)
Peripheral arterial tonometry (EndoPAT)

Examples of normal and abnormal results

**Example 1**
Patient with normal endothelial function

**Example 2**
Patient with endothelial dysfunction
## Peripheral arterial tonometry (EndoPAT)

### Results

#### Reactive hyperaemia index (RHI) values on the 1\textsuperscript{st} and 2\textsuperscript{nd} EndoPAT

<table>
<thead>
<tr>
<th></th>
<th>1\textsuperscript{st} EndoPAT</th>
<th>2\textsuperscript{nd} EndoPAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>60</td>
<td>38</td>
</tr>
<tr>
<td>RHI \textsuperscript{a}</td>
<td>2.15±0.58</td>
<td>2.16±0.52</td>
</tr>
<tr>
<td>Endothelial dysfunction (RHI&lt;1.67) \textsuperscript{b}</td>
<td>11 (18.3)</td>
<td>6 (15.8)</td>
</tr>
<tr>
<td>L_RHI \textsuperscript{a}</td>
<td>0.73±0.28</td>
<td>1.87±0.60</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Presented as mean±standard deviation; \textsuperscript{b} Presented as N(%). \textsuperscript{c} p-value for the comparison between first and second EndoPAT only in patients with 2 evaluations; paired samples T-Test for continuous variables and Chi-square test for categorical variables; RHI: reactive hyperaemia index; L_RHI: logarithmic RHI.
Outcome measures

**Primary outcome measures**
- IMR value in patients with endothelial dysfunction (RHI < 1.67)
- IMR value according to the tertile of RHI

**Secondary outcome measures**
1. The relation between RHI values and:
   - The extent of myocardial necrosis
   - The extent of coronary microvascular obstruction
2. The relation between IMR values and:
   - The extent of myocardial necrosis
   - The extent of coronary microvascular obstruction
Outcome measures

Primary outcome measures

• IMR value in patients with endothelial dysfunction (RHI < 1.67)
• IMR value according to the tertile of RHI

In the 1st EndoPAT (acute)

In the 2nd EndoPAT (24-h)
## Primary Outcome – IMR and RHI values

### IMR values according to the presence of ED (RHI<1.67)

<table>
<thead>
<tr>
<th>1st EndoPAT</th>
<th>2nd EndoPAT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IMR</strong></td>
<td><strong>IMR</strong></td>
</tr>
<tr>
<td><strong>RHI &lt;1.67</strong></td>
<td><strong>RHI &lt; 1.67</strong></td>
</tr>
<tr>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>24.0 [31.2]</td>
<td>40.5 [54.4]</td>
</tr>
<tr>
<td><strong>Endothelial dysfunction present in 11/60 patients (18.3%)</strong></td>
<td><strong>Endothelial dysfunction present in 16/38 patients (42.1%)</strong></td>
</tr>
</tbody>
</table>

Presented as Median [Interquartile Range]

Mann-Whitney test

*p* = 0.17

*p* = 0.09
Primary Outcome – IMR and RHI values

IMR values according to tertiles of RHI

1\textsuperscript{st} EndoPAT

\begin{itemize}
  \item 1 (RHI<1.92) IMR values: 19.4 [32.9]
  \item 2 (RHI 1.92 - 2.30) IMR values: 40.5 [31.2]
  \item 3 (RHI> 2.30) IMR values: 23.3 [30.3]
\end{itemize}

\textit{Kruskal-Wallis test: } \( p = 0.26 \)

2\textsuperscript{nd} EndoPAT

\begin{itemize}
  \item 1 (RHI<1.62) IMR values: 39.0 [43.4]
  \item 2 (RHI 1.62 - 1.96) IMR values: 23.8 [42.5]
  \item 3 (RHI> 1.96) IMR values: 19.5 [30.6]
\end{itemize}

\textit{Kruskal-Wallis test: } \( p = 0.64 \)
Outcome measures

Primary outcome measures

• IMR value in patients with endothelial dysfunction (RHI <1.67)
• IMR value according to the tertile of RHI

Secondary outcome measures

1. The relation between RHI values and:
   • The extent of myocardial necrosis

In the 1\textsuperscript{st} EndoPAT (acute)

In the 2\textsuperscript{nd} EndoPAT (24-h)
### Secondary Outcomes (1<sup>st</sup> EndoPAT)

#### Endothelial dysfunction and extent of myocardial infarction

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total Population</th>
<th>Endothelial Dysfunction (RHI&lt;1.67)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No (n=49)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Yes (n=11)</td>
<td></td>
</tr>
<tr>
<td><strong>Troponin Release</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TnI&lt;sub&gt;peak&lt;/sub&gt; &lt;sup&gt;a&lt;/sup&gt;</td>
<td>117±82</td>
<td>117±87</td>
<td>115±55</td>
</tr>
<tr>
<td>TnI&lt;sub&gt;AUC&lt;/sub&gt; &lt;sup&gt;a&lt;/sup&gt;</td>
<td>1938±1283</td>
<td>1951±1376</td>
<td>1883±787</td>
</tr>
<tr>
<td><strong>Echocardiography</strong> (n=40 for GLS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEF (%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>47.9±6.7</td>
<td>47.9±6.8</td>
<td>47.8±5.9</td>
</tr>
<tr>
<td>Wall motion score index&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.41 (0.35)</td>
<td>1.41 (0.35)</td>
<td>1.53 (0.18)</td>
</tr>
<tr>
<td>Global longitudinal strain&lt;sup&gt;a&lt;/sup&gt;</td>
<td>-13.54±2.28</td>
<td>-13.38±2.30</td>
<td>-14.7±1.96</td>
</tr>
<tr>
<td><strong>ceCMR (n=49)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEF (%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>53.6±8.7</td>
<td>53.9±8.7</td>
<td>52.4±9.3</td>
</tr>
<tr>
<td>Wall motion score index&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.42±0.29</td>
<td>1.41±0.030</td>
<td>1.46±0.23</td>
</tr>
<tr>
<td>Transmural necrosis&lt;sup&gt;c&lt;/sup&gt;</td>
<td>23 (46.9)</td>
<td>18 (46.2)</td>
<td>5 (50.0)</td>
</tr>
<tr>
<td>Infarct mass&lt;sup&gt;b&lt;/sup&gt;</td>
<td>14.7 (12.6)</td>
<td>11.7 (9.8)</td>
<td>19.9 (11.9)</td>
</tr>
<tr>
<td>Percent infarct mass&lt;sup&gt;b&lt;/sup&gt;</td>
<td>12.6 (14.4)</td>
<td>11.6 (12.9)</td>
<td>20.3 (14.5)</td>
</tr>
<tr>
<td>Indexed to BARI score&lt;sup&gt;b&lt;/sup&gt;</td>
<td>3.8 (4.3)</td>
<td>3.0 (3.6)</td>
<td>5.5 (5.1)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Presented as mean±standard deviation; <sup>b</sup> Presented as median (interquartile range); <sup>c</sup> Presented as number (%);
## Secondary Outcomes (2nd EndoPAT)

### Endothelial dysfunction and extent of myocardial infarction

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<th>Variable</th>
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<tbody>
<tr>
<td>Troponin Release</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\text{TnI}_{\text{peak}}$&lt;sup&gt;b&lt;/sup&gt;</td>
<td>95 (96)</td>
<td>67 (81)</td>
<td>118 (186)</td>
</tr>
<tr>
<td>$\text{TnI}_{\text{AUC}}$&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1293 (1580)</td>
<td>1076 (1042)</td>
<td>2305 (2486)</td>
</tr>
<tr>
<td>Echocardiography&lt;sup&gt;(n=21 for GLS)&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEF (%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>48.6±7.1</td>
<td>51.4±4.7</td>
<td>45.3±8.3</td>
</tr>
<tr>
<td>Wall motion score index&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.44 (0.41)</td>
<td>1.35 (0.47)</td>
<td>1.77 (0.47)</td>
</tr>
<tr>
<td>Global longitudinal strain&lt;sup&gt;a&lt;/sup&gt;</td>
<td>-13.16±2.35</td>
<td>-14.32±1.72</td>
<td>-11.89±2.35</td>
</tr>
<tr>
<td>ceCMR&lt;sup&gt;(n=29)&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEF (%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>53.9±8.4</td>
<td>56.6±8.1</td>
<td>49.5±7.2</td>
</tr>
<tr>
<td>Wall motion score index&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.37±0.33</td>
<td>1.28±0.31</td>
<td>1.53±0.32</td>
</tr>
<tr>
<td>Transmural necrosis&lt;sup&gt;c&lt;/sup&gt;</td>
<td>12 (38.7%)</td>
<td>4 (22.2%)</td>
<td>7 (63.6%)</td>
</tr>
<tr>
<td>Infarct mass&lt;sup&gt;b&lt;/sup&gt;</td>
<td>11.6 (9.3)</td>
<td>10.1 (10.3)</td>
<td>17.5 (15.4)</td>
</tr>
<tr>
<td>Percent infarct mass&lt;sup&gt;b&lt;/sup&gt;</td>
<td>11.5 (13.7)</td>
<td>10.2 (7.6)</td>
<td>17.5 (21.8)</td>
</tr>
<tr>
<td>Indexed to BARI score&lt;sup&gt;b&lt;/sup&gt;</td>
<td>3.4 (5.8)</td>
<td>2.3 (2.7)</td>
<td>5.1 (11.5)</td>
</tr>
</tbody>
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<sup>a</sup> Presented as mean±standard deviation; <sup>b</sup> Presented as median (interquartile range); <sup>c</sup> Presented as number (%);
Primary outcome measures

- IMR value in patients with endothelial dysfunction (RHI <1.67)
- IMR value according to the tertile of RHI

Secondary outcome measures

1. The relation between RHI values and:
   - The extent of myocardial necrosis
   - The extent of coronary microvascular obstruction

In the 1<sup>st</sup> EndoPAT (acute)

In the 2<sup>nd</sup> EndoPAT (24-h)
### Secondary Outcomes (1\textsuperscript{st} EndoPAT)

#### Endothelial dysfunction and microvascular obstruction

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<tr>
<th>Variable</th>
<th>Total Population</th>
<th>Endothelial Dysfunction (RHI&lt;1.67)</th>
<th>p value</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td>No (n=49)</td>
<td>Yes (n=11)</td>
</tr>
<tr>
<td><strong>ECG</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% ST resolution</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immediately after P-PCI (^b)</td>
<td>74.5 (39.0)</td>
<td>74.0 (42.0)</td>
<td>77.0 (37.0)</td>
</tr>
<tr>
<td>90 min after P-PCI (^b)</td>
<td>79.5 (32.0)</td>
<td>78.0 (34.0)</td>
<td>86.0 (25.0)</td>
</tr>
<tr>
<td><strong>Residual total ST elevation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immediately after P-PCI (^b)</td>
<td>3.3 (6.0)</td>
<td>3.5 (6.0)</td>
<td>2.5 (6.0)</td>
</tr>
<tr>
<td>90 min after P-PCI (^b)</td>
<td>1.5 (4.0)</td>
<td>1.5 (5.0)</td>
<td>1.5 (4.0)</td>
</tr>
<tr>
<td><strong>ceCMR</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MVO present (^c)</td>
<td>13 (26.5)</td>
<td>10 (25.6)</td>
<td>3 (30.0)</td>
</tr>
<tr>
<td><strong>Angiography</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corrected TIMI frame count(^b)</td>
<td>17.0 (7.0)</td>
<td>18.0 (8.0)</td>
<td>14.0 (8.0)</td>
</tr>
<tr>
<td>TIMI myocardial perfusion grade 2-3(^c)</td>
<td>49 (81.7)</td>
<td>38 (77.6)</td>
<td>11 (100.0)</td>
</tr>
<tr>
<td>Index of microvascular resistance (^b)</td>
<td>23.9 (32.9)</td>
<td>24.0 (31.2)</td>
<td>16.0 (37.3)</td>
</tr>
</tbody>
</table>

\(^a\) Presented as mean±standard deviation; \(^b\) Presentec as median (interquartile range); \(^c\) Presented as number (%);
### Secondary Outcomes (2nd EndoPAT)

#### Endothelial dysfunction and microvascular obstruction

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<tr>
<td>% ST resolution</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immediately after P-PCI b</td>
<td>74.5 (39.0)</td>
<td>76.5 (41.0)</td>
<td>0.23</td>
</tr>
<tr>
<td>90 min after P-PCI b</td>
<td>77.0 (29.0)</td>
<td>78.5 (28.0)</td>
<td>0.07</td>
</tr>
<tr>
<td><strong>Residual total ST elevation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immediately after P-PCI b</td>
<td>3.0 (6.0)</td>
<td>2.5 (5.0)</td>
<td>0.048</td>
</tr>
<tr>
<td>90 min after P-PCI b</td>
<td>1.8 (4.0)</td>
<td>1.3 (4.0)</td>
<td>0.036</td>
</tr>
<tr>
<td><strong>ceCMR (n=29)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MVO present c</td>
<td>8 (27.6%)</td>
<td>2 (11.1%)</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>Angiography</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corrected TIMI frame count b</td>
<td>17.0 (7.0)</td>
<td>16.4 (7.0)</td>
<td>0.07</td>
</tr>
<tr>
<td>TIMI myocardial perfusion grade 2-3c</td>
<td>28 (73.7%)</td>
<td>19 (86.4%)</td>
<td>0.09</td>
</tr>
<tr>
<td>Index of microvascular resistance b</td>
<td>23.4 (35.2)</td>
<td>22.0 (26.0)</td>
<td>0.09</td>
</tr>
</tbody>
</table>

*Presented as mean±standard deviation; b Presented as median (interquartile range); c Presented as number (%);*
Secondary Outcomes (2nd EndoPAT)

- Endothelial dysfunction, microvascular obstruction and infarct extension

Baptista SB et al. Revista Portuguesa de Cardiologia; 2017; xxx:xxx
Outcome measures

Primary outcome measures

- IMR value in patients with endothelial dysfunction (RHI < 1.67)
- IMR value according to the tertile of RHI

Secondary outcome measures

1. The relation between RHI values and:
   - The extent of myocardial necrosis
   - The extent of coronary microvascular obstruction

2. The relation between IMR values and:
   - The extent of myocardial necrosis
   - The extent of coronary microvascular obstruction
## Secondary Outcomes (IMR)

### IMR and infarct extension

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total Population</th>
<th>IMR &gt; 24</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No (n=30)</td>
</tr>
<tr>
<td><strong>Troponin Release</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TnI&lt;sub&gt;peak&lt;/sub&gt;</td>
<td>117±82</td>
<td>91±59</td>
</tr>
<tr>
<td>TnI&lt;sub&gt;AUC&lt;/sub&gt;</td>
<td>1938±1283</td>
<td>1459±898</td>
</tr>
<tr>
<td><strong>Echocardiography 3 months</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEF (%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>52.6±7.1</td>
<td>54.6±6.5</td>
</tr>
<tr>
<td>Wall motion score index&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.24 (0.35)</td>
<td>1.21±0.18</td>
</tr>
<tr>
<td>Global longitudinal strain&lt;sup&gt;a&lt;/sup&gt;</td>
<td>-15.77±3.11</td>
<td>-16.81±1.86</td>
</tr>
<tr>
<td><strong>ceCMR (n=49)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEF (%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>53.6±8.7</td>
<td>54.2±9.0</td>
</tr>
<tr>
<td>Wall motion score index&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.42±0.29</td>
<td>1.34±0.31</td>
</tr>
<tr>
<td>Transmural necrosis&lt;sup&gt;c&lt;/sup&gt;</td>
<td>23 (46.9)</td>
<td>8 (27.6)</td>
</tr>
<tr>
<td>Infarct mass&lt;sup&gt;b&lt;/sup&gt;</td>
<td>14.7 (12.6)</td>
<td>11.4 (10.9)</td>
</tr>
<tr>
<td>Percent infarct mass&lt;sup&gt;b&lt;/sup&gt;</td>
<td>12.6 (14.4)</td>
<td>11.6 (12.1)</td>
</tr>
</tbody>
</table>

<sup>a</sup> mean±standard deviation; <sup>b</sup> median (interquartile range); <sup>c</sup> number (%);
### Secondary Outcomes (IMR)

#### IMR and left ventricular remodelling

Difference between initial (acute) and follow up (3 months) Echo parameters according to median IMR

<table>
<thead>
<tr>
<th>Echo parameters</th>
<th>IMR &lt; 24</th>
<th>IMR &gt; 24</th>
<th>P value&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2D measurements</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEdV (ml)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>102.5±23.9</td>
<td>101.2±20.3</td>
<td>0.78</td>
</tr>
<tr>
<td>LVEsV (ml)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>51.5±12.0</td>
<td>45.3±11.5</td>
<td>0.01</td>
</tr>
<tr>
<td>LVEF (%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>49.4±6.6</td>
<td>55.4±5.1</td>
<td>0.001</td>
</tr>
<tr>
<td>WMSI&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.41 (0.32)</td>
<td>1.12 (0.12)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Left atria (ml/m²)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>34.7±13.6</td>
<td>37.9±16.8</td>
<td>0.08</td>
</tr>
<tr>
<td><strong>Doppler measurements</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E/A' ratio&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.01±0.34</td>
<td>1.14±0.33</td>
<td>0.08</td>
</tr>
<tr>
<td>E/e' ratio&lt;sup&gt;a&lt;/sup&gt;</td>
<td>9.0±3.3</td>
<td>7.3±2.7</td>
<td>0.005</td>
</tr>
<tr>
<td><strong>2D speckle tracking imaging</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Global longitudinal strain&lt;sup&gt;a&lt;/sup&gt;</td>
<td>-14.6±1.4</td>
<td>-17.2±1.3</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

<sup>a</sup> mean±standard deviation; <sup>b</sup> median (interquartile range); <sup>c</sup> p-value for the comparison between the 2 echos
Results

Secondary Outcomes (IMR)

IMR and left ventricular remodelling

Difference between initial (acute) and follow up (3 months) Echo parameters according to median IMR

Journal of Interventional Cardiology, 2016

ORIGINAL INVESTIGATION

The Index of Microcirculatory Resistance as a Predictor of Echocardiographic Left Ventricular Performance Recovery in Patients With ST-Elevation Acute Myocardial Infarction Undergoing Successful Primary Angioplasty

MARIANA FAUSTINO, M.D., SÉRGIO BRAVO BAPTISTA, M.D., F.E.S.C., ANTÓNIO FREITAS, M.D., CÉLIA MONTEIRO, B.Sc., PAULO LEAL, B.Sc., MAURA NÉDIO, B.Sc., CLAUDIA ANTUNES, B.Sc., PEDRO FARITO E ABREU, M.D., VICTOR GIL, M.D., Ph.D., F.E.S.C., and CARLOS MORAIS, M.D.

From the Department of Cardiology, Hospital Professor Doutor Fernando da Fonseca, Amadora, Portugal

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DOI: 10.1111/jpc.12278
## Secondary Outcomes (IMR)

### IMR and microvascular obstruction

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total Population</th>
<th>IMR &gt; 24</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No (n=30)</td>
<td>Yes (n=30)</td>
</tr>
<tr>
<td>ECG – ST resolution (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immediately after P-PCI (^b)</td>
<td>74.5 (39.0)</td>
<td>79.0 (33.0)</td>
<td>52.5 (79.0)</td>
</tr>
<tr>
<td>90 min (^b)</td>
<td>79.5 (32.0)</td>
<td>86.5 (29.0)</td>
<td>75.5 (36.0)</td>
</tr>
<tr>
<td>180 min (^b)</td>
<td>84.5 (23.0)</td>
<td>90.0 (23.0)</td>
<td>81.5 (40.0)</td>
</tr>
<tr>
<td>Angiographic indicators</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cTFC (^a)</td>
<td>17.0 (7.0)</td>
<td>14.0 (7.0)</td>
<td>20.0 (10.0)</td>
</tr>
<tr>
<td>TMPG 2-3 (^b)</td>
<td>49 (81.7)</td>
<td>28 (93.3)</td>
<td>21 (70.0)</td>
</tr>
<tr>
<td>ceCMR (n=49)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MVO present (^b)</td>
<td>13 (26.5)</td>
<td>4 (13.8)</td>
<td>9 (45.0)</td>
</tr>
<tr>
<td>Mass of MVO (^a)</td>
<td>5.7 (4.0)</td>
<td>2.9 (2.9)</td>
<td>6.4 (11.5)</td>
</tr>
</tbody>
</table>

\(^a\) median (interquartile range); \(^b\) number (%);
Conclusions
Main findings of the study

- RHI measurement with EndoPAT immediately after primary PCI in ST elevation myocardial infarction patients probably cannot be performed, due to the serious unavoidable technical pitfalls in the acute phase.

- RHI measurement with EndoPAT 24 hours after primary PCI in STEMI patients is feasible and related both to the extension of the infarct and to microvascular obstruction (including a tendency for lower IMR values in patients with higher RHI values).

- IMR measured immediately after primary PCI in STEMI patients predicts MVO and infarct extension - remodelling
Acknowledgments

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Dr. José Loureiro
Dr. Luis Brízida
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Radiology Technicians
Cath Lab Nurses

Dra. Mariana Faustino
Dr. António Freitas
Dr. Paulo Alves
Dr. Frederico Costa
Dr. João Augusto
Dra. Ana Oliveira Soares
Nursing staff

Dr. António Ferreira
Dr. João Abecassis

Prof. Pim Tonino
Prof. Marcel Vant’t Veer

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Michele de La Rosa

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Coronary microcirculation and peripheral endothelial function evaluation after acute ST elevation myocardial infarction treated with primary angioplasty

Sérgio Bravo Baptista, MD, FESC

Ph.D. Supervisor: Prof. Doutor Victor Gil
Ph.D. Co-supervisor: Prof. Doutor José Fragata
Backup Slides
Flow chart of patient inclusion

543 STEMI patients screened

- 275 patients not meeting all inclusion/exclusion criteria
  - 68 with pain onset unknown/\(>12\)h
  - 47 with previous myocardial infarction
  - 43 in shock / hemodynamic instability
  - 39 with left bundle block/pacemaker/without ECG criteria
  - 24 with bradycardia or 2\(^{nd}\)/3\(^{rd}\) degree AV block
  - 23 with mild hypotension (contra-indicating adenosine)
  - 14 with previous CABG/recent PCI
  - 11 with serious ventricular arrhythmia/cardiac arrest
  - 6 with collaterals Rentrop 2-3

- 57 patients not included for other reasons (small index vessel, severe valvular disease, referred for urgent CABG, unsuccessful PCI, distal occlusion, etc.)

- 11 patients died in the index PCI procedure

- 38 patients unable/unwilling to consent

- 99 patients not included due to operator’s decision/unclear reason

63 patients included in the Cath Lab

- 3 patients excluded due to technical problems with the pressure wire (IMR evaluation)

60 patients with IMR measurement and with first (acute) EndoPAT
Flow chart of patient inclusion

- 60 patients with IMR measurement and with first (acute) EndoPAT
  - 6 patients did not perform the Echo due to unplanned logistic restrictions
  - 3 patients did the Echo, but images are not available for analysis (DICOM error)
  - 4 patients did the Echo, but the quality of images was considered inappropriate for analysis

- 47 patients with first (<12h) Echo
  - 7 patients did the Echo, but the quality of images was considered inappropriate for analysis
  - 40 patients included in the speckle tracking imaging

- 38 patients with second (24h) EndoPAT
  - 4 patients refused to perform the ceCMR, mainly because of claustrophobia complaints
  - 3 patients did not perform the exam due to logistic limitations
  - 2 patient did perform the exam, but images were lost
  - 2 patients did perform the exam, but the quality of the images was considered inadequate for analysis

- 49 patients with contrast enhanced CMR
  - 4 patients lost for follow-up/refused to perform the exam
  - 2 patients did the Echo, but images are not available for analysis (DICOM error)

- 54 patients with second (3 month) Echo
  - 3 patients did the Echo, but the quality of images was considered inappropriate for analysis
  - 51 patients included in the speckle tracking imaging
Peripheral arterial tonometry (EndoPAT)

Results

- Reactive hyperaemia index (RHI) values on the 1st EndoPAT (complete cohort)
Limitations and Strengths
Limitations

Inclusion rate was very low and the cohort included represents only 11% of the population of patients with STEMI.

EndoPAT exams were not performed according to the recommendations for endothelial function evaluation.

The number of patients with the second EndoPAT evaluation is small.

Imaging exams (both ceCMR and echocardiograms) are not available for all patients.
Strengths

One of the world’s largest single-centre databases in IMR evaluation in STEMI patient.

Systematically evaluating all indirect indicators of microvascular reperfusion.

Evaluation of myocardial infarction by troponin release was also much more comprehensive.

Echo evaluation both acutely and at follow-up and using all available modes, including speckle-tracking analysis.