Coronary microvascular dysfunction after elective percutaneous coronary intervention: correlation with exercise stress test results

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• Declaration of interest: none.
Exercise stress test (EST) has a primary role in the diagnosis and prognostic assessment of coronary artery disease (CAD).

EST performed after a percutaneous coronary intervention (PCI) has been found to be of limited utility in identifying patients with coronary restenosis.

Michaelides AP, Am Heart J 1998; 135:449-56
Schroeder E, Eur Heart J 1989; 10:18-21
Background (2)

The causes of ST-segment depression during EST after PCI, however, remain debatable

- Although it is usually considered a false positive result, it might instead reflect myocardial ischemia caused by vasoconstriction at the level of, or distally to, the treated lesion, or by coronary microvascular dysfunction
  
  Lanza GA, Circulation 2010; 121:2317-25
  Waters DD, Circulation 1982; 65:265-74
  el-Tamimi H, Circulation 1991; 84:2307-12

- Some previous studies have in fact suggested an impairment of coronary microvascular function after PCI
  
  Wilson RF, Circulation 1988; 77:873-85
  Uren NG, J Am Coll Cardiol 1993; 21:612-21
No previous study, however, investigated the relation between positive EST and coronary microvascular dysfunction (CMVD) after PCI.

Moreover, no study assessed the time course of EST results in relation to CMVD after successful PCI.
AIM OF THE STUDY

1) To assess whether EST results after successful PCI are influenced by the presence of CMVD in the territory of the treated coronary artery vessel

2) To assess the relation between changes in coronary microvascular function and EST results over a follow-up period of 6 months after successful PCI
INCLUSION CRITERIA

- Stable CAD for ≥6 months
- ST-segment depression ≥0.1 mV at ECG-EST prior to PCI
- Isolated disease of the left anterior descending (LAD) coronary artery (stenosis ≥75%)
- Absence of any stenosis (>30%) in other coronary arteries
- Successful PCI (residual stenosis <20% and TIMI flow=3)
- No PCI-related complications following the procedure

EXCLUSION CRITERIA

- Any history of previous coronary intervention or acute coronary syndromes
- Inflammatory or malignant disease or asthma
- ECG changes impairing ST-segment analysis
- Inability to perform maximal EST
Study design

29 stable CAD pts

CLINICAL EVALUATION

PCI

24 hours

EST & assessment of CMVD

3 months

EST & assessment of CMVD

6 months

EST & assessment of CMVD
Methods (1)

Endothelium-independent coronary microvascular dilator function:
Coronary blood flow response (CBF) to i.v. adenosine
Methods (2)

Endothelium-dependent coronary microvascular dilator function:
CBF response to cold pressor test
Methods (3)

Exercise stress test
General EST results

### Positive EST
- **24 hours**: 11 pts
- **3 months**: 12 pts
- **6 months**: 13 pts

### Negative EST
- **24 hours**: 18 pts
- **3 months**: 17 pts
- **6 months**: 16 pts

**Changes**
- Positive EST:
  - 1 pt from 11 pts to 12 pts
  - 1 pt from 12 pts to 13 pts
- Negative EST:
  - 2 pts from 18 pts to 17 pts
  - 1 pt from 17 pts to 16 pts
## Main clinical characteristics at 24 hours after PCI

<table>
<thead>
<tr>
<th></th>
<th>Positive EST (n=11)</th>
<th>Negative EST (n=18)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (yrs)</strong></td>
<td>62±7</td>
<td>64±6</td>
<td>0.40</td>
</tr>
<tr>
<td><strong>Sex (M)</strong></td>
<td>8 (73%)</td>
<td>15 (83%)</td>
<td>0.41</td>
</tr>
<tr>
<td><strong>CV risk factors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family history of CAD</td>
<td>3 (27%)</td>
<td>8 (44%)</td>
<td>0.45</td>
</tr>
<tr>
<td>Hypertension</td>
<td>8 (73%)</td>
<td>15 (83%)</td>
<td>0.65</td>
</tr>
<tr>
<td>Smoking</td>
<td>7 (64%)</td>
<td>14 (78%)</td>
<td>0.43</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>10 (91%)</td>
<td>15 (83%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>6 (55%)</td>
<td>7 (34%)</td>
<td>0.47</td>
</tr>
<tr>
<td><strong>Angiographic data</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean LAD stenosis (%)</td>
<td>88±8</td>
<td>87±11</td>
<td>0.78</td>
</tr>
<tr>
<td>Number of lesions</td>
<td>1.3±0.5</td>
<td>1.1±0.3</td>
<td>0.24</td>
</tr>
<tr>
<td>Length of lesion (mm)</td>
<td>20.1±6.6</td>
<td>20.3±11.8</td>
<td>0.95</td>
</tr>
<tr>
<td>Proximal LAD stenosis</td>
<td>7 (64%)</td>
<td>7 (39%)</td>
<td>0.26</td>
</tr>
<tr>
<td>LAD diameter (mm)</td>
<td>3.3±0.5</td>
<td>3.0±0.5</td>
<td>0.18</td>
</tr>
<tr>
<td><strong>Echocardiographic data</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV septal thickness (mm)</td>
<td>10±0.9</td>
<td>10±0.8</td>
<td>1.0</td>
</tr>
<tr>
<td>LV posterior wall thickness (mm)</td>
<td>9.6±1.1</td>
<td>9.8±0.9</td>
<td>0.71</td>
</tr>
<tr>
<td>LV ejection fraction (%)</td>
<td>61±3</td>
<td>62±3</td>
<td>0.74</td>
</tr>
<tr>
<td>Post-PCI TnT levels (ng/ml)</td>
<td>0.05±0.04</td>
<td>0.03±0.03</td>
<td>0.24</td>
</tr>
</tbody>
</table>
CBF response to adenosine

- 24 hours: p=0.003
- 3 months: p<0.001
- 6 months: p<0.001

- Positive EST
- Negative EST
**CBF response to CPT**

$p = 0.11$  \hspace{1cm}  $p = 0.67$  \hspace{1cm}  $p = 0.01$

- **Baseline**
  - 24 hours
  - 3 months
  - 6 months

**CBF response to CPT**

- Positive EST
- Negative EST
RPP at peak EST and exercise duration

RPP at peak EST:
- 24 hours: p=0.74
- 3 months: p=0.50
- 6 months: p=0.87

Exercise duration:
- 24 hours: p=0.69
- 3 months: p=0.75
- 6 months: p=0.57

Positive EST
Negative EST
RPP and exercise time at 1 mm ST depression in patients with positive EST

- **RPP (bpm * mmHg)**
  - Positive EST
  - 24 hours: Blue
  - 3 months: Red
  - 6 months: Green
  - \( p = 0.68 \)

- **Time to 1 mm ST (s)**
  - Positive EST
  - 24 hours: Blue
  - 3 months: Red
  - 6 months: Green
  - \( p = 0.67 \)
## Results (5)

<table>
<thead>
<tr>
<th></th>
<th>24-hr post-PCI</th>
<th>3-month FU</th>
<th>6-month FU</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All patients (n=29)</strong></td>
<td></td>
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<tr>
<td>CBF response to ADO</td>
<td>1.93±0.4</td>
<td>1.99±0.4</td>
<td>2.02±0.4</td>
<td>0.40</td>
</tr>
<tr>
<td>CBF response to CPT</td>
<td>1.56±0.3</td>
<td>1.58±0.3</td>
<td>1.66±0.4</td>
<td>0.41</td>
</tr>
<tr>
<td><strong>All positive ESTs (n=10)</strong></td>
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</tr>
<tr>
<td>CBF response to ADO</td>
<td>1.69±0.3</td>
<td>1.67±0.3</td>
<td>1.62±0.3</td>
<td>0.82</td>
</tr>
<tr>
<td>CBF response to CPT</td>
<td>1.45±0.4</td>
<td>1.41±0.3</td>
<td>1.36±0.2</td>
<td>0.74</td>
</tr>
<tr>
<td><strong>All negative ESTs (n=15)</strong></td>
<td></td>
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</tr>
<tr>
<td>CBF response to ADO</td>
<td>2.17±0.4</td>
<td>2.19±0.3</td>
<td>2.33±0.3</td>
<td>0.14</td>
</tr>
<tr>
<td>CBF response to CPT</td>
<td>1.58±0.3</td>
<td>1.64±0.3</td>
<td>1.88±0.4</td>
<td>0.02</td>
</tr>
</tbody>
</table>
Conclusions (1)

- Among patients with stable CAD of the LAD coronary artery successfully treated by PCI, coronary microvascular dilation in the LAD artery was significantly reduced 24 hours after PCI in those who showed positive EST, compared to those with negative EST, suggesting that CMVD was responsible for the ischemic ST-segment changes.

- CMVD and its relation with positive EST persisted substantially unchanged over a period of 6 months after PCI.
Conclusions (2)

- Our finding that CMVD persisted unchanged over a period of 6 months after PCI suggests that CMVD pre-existed to PCI and might have contributed to ischemic EST-induced ST-segment changes also before revascularization.

- The possible clinical implications of our findings deserve investigations in prospective studies.
Thank you!