Cardiac shockwave therapy in patients with end-stage coronary artery disease

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Rationale

- Despite advances in medical and invasive revascularization therapy, a substantial number of patients shows progression to end-stage ischemic coronary artery disease with chronic refractory angina.
Chronic refractory angina

- Occurrence of chest pain due to myocardial ischemia in patients with severe CAD who cannot be managed adequately by medical therapy and who are not candidates for revascularization (interventional or surgical).

Gibbons RJ et al. J.Am.Coll Cardiol 2003;41:159
Additional therapeutic options – medication

- Ranolazine - prevention of Ca overload
- Nicorandil - potassium channel activator
- Trimetazidine, perhexiline – inhibition of fatty acid oxidation
- Allopurinol – decrease myocardial oxygen demand
- Ivabradine – sinus node pacemaker current inhibitor

....
Other therapies

- Rehabilitation
- Enhanced external counterpulsation
- Spinal cord stimulation (T1-T2 level)
- Sympathectomy
- Transmyocardial laser revascularization?
- Gene therapy?
- Stem cells?
- Cardiac shockwave therapy?

2006
Shockwave effects

- Cavitation (rapid formation and collapse of vapor pockets in and outside cells with the formation of jet streams and free radicals)

Shockwave in cardiology

- Preclinical studies and limited clinical data suggest a positive effect of very low energy shockwaves (0.09mJ/mm²) on cardiac ischemia.

- Upregulation of vascular endothelial growth factor (VEGF) mRNA and protein expression result in increased capillary density in ischemic myocardium.

Shockwave treatment for advanced angina in Maastricht SWAAM study
Shockwave treatment for advanced angina in Maastricht SWAAM study

Chronic refractory angina

Ischemia (MIBI SPECT)

No revascularization option (hart team)

Informed consent, acoustic window

Shockwave treatment
Inclusion criteria

- Reversible ischemia
- Anginal complaints CCS Class III-IV
- No candidates for revascularization (PCI / CABG)
- Chronic stable angina pectoris > 3 months
- Maximal tolerable anti-ischemic medication (stable for at least 6 weeks)
Exclusion criteria

- Acute MI < 3 months prior to treatment
- Intraventricular thrombus
- Active endocarditis, myocarditis or pericarditis
- Pregnancy
- Malignancy
- No acoustic window
Treatment scheme

Week 1

Week II

Week III

Week IV

Week V

Week VI

Week VII

Week VIII

Week IX
## Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>N= 50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years; mean, SD)</td>
<td>68.7±9</td>
</tr>
<tr>
<td>Male</td>
<td>40 (80%)</td>
</tr>
<tr>
<td>Body mass index (mean, SD)</td>
<td>28.6 ±4.7</td>
</tr>
<tr>
<td>Smoking</td>
<td>10 (20%)</td>
</tr>
<tr>
<td>Positive family history</td>
<td>20 (40%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>22 (44%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>40 (80%)</td>
</tr>
<tr>
<td>Hypercholesterolaemia</td>
<td>47 (94%)</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>5 (12%)</td>
</tr>
<tr>
<td>History of PCI</td>
<td>29 (58%)</td>
</tr>
<tr>
<td>History of CABG</td>
<td>35 (70%)</td>
</tr>
</tbody>
</table>
## Results

<table>
<thead>
<tr>
<th></th>
<th>N= 50</th>
<th>baseline</th>
<th>1 month follow up</th>
<th>4 months follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AP CCS class</strong></td>
<td></td>
<td>3.2±0.2</td>
<td>2.1±0.6 p&lt;0.01</td>
<td>1.8±0.7 p&lt;0.01</td>
</tr>
<tr>
<td><strong>Nitrates use/week</strong></td>
<td></td>
<td>9.5±8.3</td>
<td>2.1±3.4 p&lt;0.01</td>
<td>1.5±2.5 p&lt;0.01</td>
</tr>
<tr>
<td><strong>Exercise test (min)</strong></td>
<td></td>
<td>8.2±3.2</td>
<td>9.2±3.8 p=0.028</td>
<td>9.6±3.8 p&lt;0.01</td>
</tr>
<tr>
<td><strong>Ejection fraction (%)</strong></td>
<td></td>
<td>53.4±11.7</td>
<td>53.7±11.3 p=NS</td>
<td></td>
</tr>
<tr>
<td><strong>Scar (MRI) % 8pts</strong></td>
<td></td>
<td>5.3±4.3</td>
<td>5.6±4.3 p=NS</td>
<td>5.8±5.0 p=NS</td>
</tr>
</tbody>
</table>
Less ischemic burden

baseline

4 months follow up
## Results - nuclear perfusion

<table>
<thead>
<tr>
<th>Nuclear perfusion (%)</th>
<th>baseline</th>
<th>1 month follow up</th>
<th>4 months follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stress treated</td>
<td>54.4±9.3</td>
<td>55.0±10.5 p=NS</td>
<td>56.1±10.6 p=0.023</td>
</tr>
<tr>
<td>Stress untreated</td>
<td>59.8±7.8</td>
<td>59.7±7.2 p=NS</td>
<td>60.0±7.2 p=NS</td>
</tr>
<tr>
<td>Rest treated</td>
<td>60.8±10.1</td>
<td>59.3±9.6 p=NS</td>
<td>60.3±10.7 p=NS</td>
</tr>
<tr>
<td>Rest untreated</td>
<td>61.4±7.5</td>
<td>60.8±6.7 p=NS</td>
<td>61.4±7.8 p=NS</td>
</tr>
</tbody>
</table>
Safety

- Transient dizziness and warm sensations (5 out of 50 patients)
- Headache (2 patients)
- No CK/troponin rise
- No ECG changes
- No increase in scar volume
- No clinical signs of dyspnea or coughing
- No arrhythmias
- No skin erythema or burns
Cardiac shockwave

- **Advantages**
  - Non invasive
  - No relevant side-effects

- **Disadvantages**
  - Time consuming
  - Dependent on echo window
Conclusion

- Relieve anginal complaints
- Decreased use of nitrates
- Reduced ischemic burden
- No relevant side effects