Stem Cell Therapy in AMI
The optimal delivery strategy for stem cells

전남의대
안영근
Cardiac Regeneration: Stem Cell Therapy

Potentially repairing myocardium

Delivery of MSCs

Mechanisms of action

- Engraftment and differentiation
- Reverse remodeling in chronic ischemic CMP
- Prevention of remodeling after AMI
- Scar size reduction
- Increase tissue perfusion
- Improved regional contractility
- Increased ejection fraction

Functional and Structural Effects

- Angiogenesis
- Paracrine signaling
- Anti-inflammatory effects
- Activate endogenous cardiac stem cells

Emerging Issues

- Engraftment
- Procedural safety
- Extracardiac retention of stem cells
- Improvement of heart function
Methods of delivery will affect the outcome of stem cell therapies, perhaps significantly.
TNF-alpha enhances engraftment of mesenchymal stem cells into infarcted myocardium.


Source
Cardiovascular Research Institute, Chonnam National University, Gwanju, South Korea.

Between days 3 and 7 after AMI

B) by TNF-alpha, up-regulates the expression of molecules which are involved in inflammation and cell adhesion. For these reasons, we assessed the extent that treatment of MSC with tumor necrosis factor (TNF)-alpha modifies the characteristics of MSC, important to their engraftment in experimental myocardial infarct. Here, we show that pre-treatment of MSC prior to transplantation with tumor necrosis factor (TNF)-alpha increases adhesiveness, and migration of MSC in vitro and leads to increased expression of bone morphogenetic protein (BMP)-2 by MSC. Moreover, this treatment increases the rate of engraftment of MSC and improves recovery of cardiac function after myocardial infarction. These insights might provide better strategies for the treatment of myocardial infarction.
Enhancement of Proliferation Activity

LAD
- Total occlusion
- 5 min Bal and 5 min Rep
- 4 times repeat

Enhancement of Proliferation Activity

- Total occlusion
- 5 min Bal and 5 min Rep
- 4 times repeat

**Occlusion site**

**After 20 hours**

1.00E+05
2.01E+07
4.01E+07
6.01E+07
8.01E+07
1.00E+08
1.20E+08

**BSA**

**Sham**

**EP**

**MI EP**

20~22D
Stem Cells can be Delivered to the Heart

<table>
<thead>
<tr>
<th>Intravenous</th>
<th>Intracoronary</th>
<th>Direct endocardial</th>
</tr>
</thead>
</table>

Direct epicardial | Coronary sinus

have been used in clinical trials
1. Intravenous Route

- **Advantage**: Easiest and most practical method
- **Disadvantage**: Pulmonary entrapment

### BM-MSC 10 to 14 days after MI (Rat)

- **IV infusion** vs. **LV cavity infusion**

---

1. Intravenous Route

A Randomized, Double-Blind, Placebo-Controlled, Dose-Escalation Study of Intravenous Adult Human Mesenchymal Stem Cells (Prochymal) After Acute Myocardial Infarction

2. Intracoronary Route

Over the wire balloon

Connect to infusion pump
“Stem cell infusion”

Connect to inflator

2. Intracoronary Route
**Clinical steps of the procedure Using MSC in AMI patients**

1. **Obtain adult stem cell from patients (Autologous)**
2. **Expand cells in vitro**
3. **Deliver cells to injured Myocardium via IC injection**

**A Randomized, Open labeled, multicenter trial for Safety and Efficacy of intracoronary adult human mesenchymal STEM cells after acute Myocardial Infarction (ROSE-STEMMI)**
## 2. Intracoronary Route

**Advantages**

1. Effectively deliver cells to ischemic tissue after full reperfusion therapy after AMI
2. Familiarity of angioplasty techniques to interventionist
3. Ability to deliver cells during PCI for Acute MI

**Disadvantages**

1. Concern about inducing ischemia during coronary artery occlusion
2. Lack of vessels in chronically
3. Occluded areas of scar tissue
Effect on Left Ventricular Function of IC transplantation of Autologous Bone Marrow MSC in Patients With AMI (PPCI <12 hr Sx onset)

Several imagining techniques demonstrated that bone marrow mesenchymal stem cells significantly improved left ventricular function.

Chen SL et al (Am J Cardiol 2004;94:92–95)
2. Intracoronary Route

Cardiovasc Res 2006 (70:530-542)

IF 6.051 (89회 인용)

Cells transduced with Akt in a porcine infarction model

Youngkeun Ahn\textsuperscript{a,*}, Myung Ho Jeong\textsuperscript{a}, Kwang Il Nam\textsuperscript{b}, Jeong Gwan Cho\textsuperscript{a}, Jong Chun Park\textsuperscript{a}

\textsuperscript{a}Chonnam National University Hospital, 8 Hak Dong, Dong Ku, 57, South Korea

\textsuperscript{b}Chonnam National University Medical School, Gwangju, South Korea

Massachusetts General Hospital and Harvard Medical School, Boston, USA
Cardiac stem cells in patients with ischaemic cardiomyopathy (SCIPIO): initial results of a randomised phase 1 trial (EF ≤ 40%, 113 days after CABG)


2. Intracoronary Route

Intracoronary cardiosphere-derived cells for heart regeneration after myocardial infarction (CADUCEUS): a prospective, randomised phase 1 trial (EF ≤ 25-45%, 2-4 wks after AMI)


면역적합성 줄기세포 융합
치료제 개발 및 작용기전 연구
모델: 자연계에서의 조직 재생

도렁뇽의 사지재생

1. 근육세포
2. 단핵화된 세포
3. 재분화 + 증식

사지재생

본 연구진의 간단하고, 효과적인 화학물 카테일

1. 포유류 근육조직
2. 단핵화된 세포
3. 재분화 + 증식

화학적으로 유도된 분화능능성 세포 (ci-PSCs)

Step 1:
20 μM myoseverin

합성식

CH3O

CH2O

HN

HN

H3N
3. Endocardial Route

- **Device and method**: stem cell injection directly into the myocardium with a catheter navigated in the LV by fluoroscopic guidance or electroanatomic mapping.

*BioCardia Helical Infusion Catheter*: 2 fluid ports, 1 for therapeutic agent and 1 for contrast.

*Myostar Cordis-Biosense Webster Needle Injection Catheter*

3. Endocardial Route

- NOGA mapping and 3D NOGA-guided intramyocardial injections

Arrows indicate site of injection

3. Endocardial Route

Viper cardiac injection catheter
3. Endocardial Route

- **Procedural safety**
  - Perforation of myocardium, with the potential for cardiac tamponade
  - Induction of arrhythmias
  - Scar formation of injection site


- **Efficacy**

  **Pre-clinical: allo BM-MSC 3 days after AMI (Pig)**

  - **TE route group vs. Control group**

  ![Image A](image1.png)

  - C-Kit-positive myocytes

  ![Image B](image2.png)

  - Ki67-positive myocytes

  *Amado LC, et al. PNAS 2005;102:11474 –11479*
3. Endocardial Route

Subendocardial rim thickness

Hyperenhanced area by MRI

Ejection fraction: from 25% to 42% at 8 weeks after injection
Pressure-volume loops: improved LV relaxation and systolic compliance

Allogeneic MSCs injected into regions of damaged myocardium 3 d after MI engraft, stimulate cardiac regeneration, and profoundly decrease myocardial infarct size

3. Endocardial Route

■ Efficacy

Clinical: BM-MNC 68±34 days after AMI

TE route group vs. Control group

NOGA-guided subanalysis of the MYSTAR prospective randomised study

▲ Inclusion criteria: Patients with recent AMI (STEMI) and post-infarction cardiac dysfunction (LVEF 30~45%)

## 3. Endocardial Route

<table>
<thead>
<tr>
<th></th>
<th>Before BM-MNC therapy</th>
<th>Three months after BM-MNC therapy</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical data</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NYHA</td>
<td>2.0 ± 0.9</td>
<td>1.4 ± 0.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CCS</td>
<td>1.8 ± 0.7</td>
<td>1.2 ± 0.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Transthoracic echocardiography</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LA [mm]</td>
<td>53.6 ± 9.0</td>
<td>48.3 ± 7.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>EDD [mm]</td>
<td>54.2 ± 7.0</td>
<td>51.9 ± 7.3</td>
<td>0.070</td>
</tr>
<tr>
<td>WMSI</td>
<td>1.8 ± 0.5</td>
<td>1.7 ± 0.4</td>
<td>0.200</td>
</tr>
<tr>
<td><strong>Ventriculography</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EDP [mmHg]</td>
<td>23.4 ± 7.7</td>
<td>20.5 ± 8.8</td>
<td>0.186</td>
</tr>
<tr>
<td>Infarct size [%]</td>
<td>27.2 ± 10.7</td>
<td>24.1 ± 11.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>EF [%]</td>
<td>38.0 ± 6.1</td>
<td>41.5 ± 8.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ESV [ml]</td>
<td>166.9 ± 78.2</td>
<td>137.6 ± 36.1</td>
<td>0.002</td>
</tr>
<tr>
<td>EDV [ml]</td>
<td>206.9 ± 69.2</td>
<td>207.4 ± 75.4</td>
<td>0.764</td>
</tr>
</tbody>
</table>

*Silvia C, et al. Thromb Haemost 103:564-571*
4. Epicardial Route

- Most reliable method
- Highly accessible, due to exposure by surgical incision
- Most invasive delivery technique
- Requires either a thoracotomy or sternotomy
- Injections can be made into a beating or arrested heart
- Computer-driven injection devices
- Epicardial application of cell-seeded biocompatible patches or even scaffold-free cell sheets
4. Epicardial Route

- **Efficacy**

Pre-clinical: BM-MSC 12wks after AMI (Pig)

Injections were administered to the beating heart via left anterior thoracotomy.

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Number</th>
<th>Infarct Size % LV</th>
<th>Infarct Volume (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>PBS group</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 2</td>
<td>2X10^6 MSCs/kg</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 3</td>
<td>20X10^6 MSCs/kg</td>
<td>6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Direct epicardial route

- Group 1 (n=6): PBS group
- Group 2 (n=3): 2X10^6 MSCs/kg
- Group 3 (n=6): 20X10^6 MSCs/kg

Autologous MSCs can be safely delivered in an adult heart failure model, producing substantial structural and functional reverse remodelling.

5. Coronary Sinus Route

- Percutaneous retrograde coronary sinus delivery
  - Very safe
  - Potential advantages for more homogenous delivery across the myocardium than IC, IM delivery
  - Placement of a catheter into the coronary sinus via either the internal jugular or femoral vein, with the infusion catheter placed over a wire
  - A single or double balloon is inflated, followed by infusion
Preclinical Trials
: Comparative studies of different methods
1. IC vs. EC vs. IV

A quantitative, randomized study evaluating three methods of mesenchymal stem cell delivery following myocardial infarction

Pre-clinical: Allogeneic BM-MSC following AMI (Pig)

<table>
<thead>
<tr>
<th>Group 1 (n=6): Intracoronary route</th>
<th>Sacrificed 14±3 days after transplantation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 2 (n=6): Endocardial route</td>
<td>Confirmation of cellular engraftment</td>
</tr>
<tr>
<td>Group 3 (n=6): Intravenous route</td>
<td>: DiI and FISH labelling techniques.</td>
</tr>
</tbody>
</table>

Procedural safety: no adverse events
: following IC infusion, half of the pigs exhibited decreased blood flow distal to the infusion site

1. IC vs. EC vs. IV

Infarct zone engraftment rate of MSCs: IC >> EC >> IV
Extracardiac entrapment rate: EC << IC & IV


<table>
<thead>
<tr>
<th>Table 2</th>
<th>Engraftment of MSCs in tissues varies by delivery technique</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mesenchymal stem cell engraftment 14 days after delivery</td>
</tr>
<tr>
<td>Infarct zone (cells)</td>
<td>Infarct zone (cells/g)</td>
</tr>
<tr>
<td>IC</td>
<td>2,864,000 ± 983,000</td>
</tr>
<tr>
<td>EC</td>
<td>1,393,000 ± 618,000</td>
</tr>
<tr>
<td>IV</td>
<td>None detected</td>
</tr>
</tbody>
</table>

*IC vs. EC (P = 0.01), IC vs. IV (P = 0.0008).
**EC vs. IV (P = 0.003).
***EC vs. IC (P = 0.06), EC vs. IV (P = 0.02).

- IC was more efficient than EC and IV
- IC delivery was associated with decreased coronary blood flow.
- EC delivery was safe and well tolerated and decreased remote organ engraftment with compared with IC and IV deliveries.
2. IC vs. IM (epicardial) vs. EC

Analysis of Different Routes of Administration of Heterologous 5-Azacytidine–Treated Mesenchymal Stem Cells in a Porcine Model of Myocardial Infarction

Pre-clinical: Allogeneic 5-aza treated BM-MSC following AMI (Pig)

Group 1 (n=5): Intracoronary route
Group 2 (n=5): Intramyocardial route
Group 3 (n=5): Endocardial route

Sacrificed 30 days after transplantation
Confirmation of cellular engraftment: DiO and DAPI

Procedural safety: no adverse events

### 2. IC vs. IM (epicardial) vs. EC

**Infarc zone engraftment rate of MSCs: IC >> IM & EC**

<table>
<thead>
<tr>
<th></th>
<th>IC</th>
<th>IM</th>
<th>EC</th>
<th>NI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infarcted zone</td>
<td>$85.96 \pm 19.95 \times 10^{-9}$</td>
<td>$12.39 \pm 6.7 \times 10^{-9}$</td>
<td>$8.09 \pm 3.3 \times 10^{-9}$</td>
<td>$0.3 \pm 0.06 \times 10^{-3}$</td>
</tr>
<tr>
<td>Healthy zone</td>
<td>$1 \pm 0.53 \times 10^{-3}$</td>
<td>$0.94 \pm 0.67 \times 10^{-3}$</td>
<td>$0.75 \pm 0.16 \times 10^{-3}$</td>
<td>$0.36 \pm 0.17 \times 10^{-3}$</td>
</tr>
</tbody>
</table>

- The mean number of engrafted cells within the infarct zone was significantly greater after IC infusion than either IM or EC injection.
- Fluorescent cells were not observed in healthy zones of the myocardium or in healthy animals.

3. IC vs. EC

Effects of Adipose Tissue-Derived Stem Cell Therapy After Myocardial Infarction: Impact of the Route of Administration

Pre-clinical: Adipose Tissue-Derived Stem Cell following AMI (Pig)

Group 1 (n=4): intracoronary PBS
Group 2 (n=5): intracoronary ADSCs
Group 3 (n=4): endocardial PBS
Group 4 (n=6): endocardial ADSCs

Sacrificed 21 days after transplantation
Echocardiography and histopathology

Procedural safety: no adverse events

3. IC vs. EC

Infarct zone engraftment rate of ADSCs: IC (80%) = EC (79%)

Neovascularization: IC > EC

<table>
<thead>
<tr>
<th></th>
<th>Intracoronary Administration</th>
<th>Transendocardial Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Culture Medium (Control)</td>
<td>ADSCs n = 5</td>
</tr>
<tr>
<td>Small vessels</td>
<td>141 ± 26</td>
<td>223 ± 40*</td>
</tr>
<tr>
<td>Large vessels</td>
<td>31 ± 4</td>
<td>38 ± 11</td>
</tr>
<tr>
<td>Total number of vessels</td>
<td>172 ± 25</td>
<td>261 ± 40*</td>
</tr>
</tbody>
</table>

3. IC vs. EC

**Improvement of LV function:** IC = EC = control

<table>
<thead>
<tr>
<th></th>
<th>Intracoronary Administration</th>
<th>Transendocardial Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Culture Medium (Control)</td>
<td>n = 4</td>
<td>n = 4</td>
</tr>
<tr>
<td>Culture Medium (ADSCs)</td>
<td>n = 5</td>
<td>ADSCs n = 6</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>49 ± 2*</td>
<td>49 ± 10*</td>
</tr>
<tr>
<td>LVEDV (mL)</td>
<td>27.3 ± 3.9</td>
<td>32.0 ± 4.8</td>
</tr>
<tr>
<td>LVESV (mL)</td>
<td>13.8 ± 1.3*</td>
<td>16.2 ± 2.7*</td>
</tr>
</tbody>
</table>

Both pathways of ADSCs delivery are feasible, producing a similar number of engrafted and differentiated cells, although intracoronary administration was more effective in increasing neovascularization.

4. IC vs. EC

**Comparison of intracoronary and transendocardial delivery of allogeneic mesenchymal cells in a canine model of acute myocardial infarction**

**Pre-clinical: allogeneic BM-MSC at 7 days after AMI (Canine)**

<table>
<thead>
<tr>
<th>Group 1 (n=7)</th>
<th>Intracoronary route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 2 (n=6)</td>
<td>Endocardial route</td>
</tr>
<tr>
<td>Group 3 (n=6)</td>
<td>Control</td>
</tr>
</tbody>
</table>

Sacrificed 21 days after transplantation
Echocardiography and histopathology

**Procedural safety:** 2 dogs died after randomization and IC infusion of MSCs

- Dog 1: extensive **microvascular “plugging”** associated with MSCs
- Dog 2: **intestinal ischemia/infarct**

*Perin EC, et al. J Mol Cell Cardiol 2008; 44:486–495*
4. IC vs. EC

Reduction of ischemic area:
EC > control (p=0.03)
IC = control (p=0.08)
EC = IC (p=0.13)

Improvement of LVEF:
EC >> control (p=0.01)
IC = control (p=0.83)
EC = IC (p=0.63)

Perin EC, et al. J Mol Cell Cardiol 2008; 44:486–495
4. IC vs. EC

**Infarct Size:**
EC = IC = control (p>0.05)

**Vascular density:**
EC >> control (p=0.01)
IC = control (p>0.05)
EC = IC (p>0.05)

- EC: safe, higher cell retention with an increased vascularity and greater functional improvement than did the IC group

*Perin EC, et al. J Mol Cell Cardiol 2008; 44:486–495*
5. IM (epicardial) vs. EC

Comparison of Initial Cell Retention and Clearance Kinetics After Subendocardial or Subepicardial Injections of Endothelial Progenitor Cells in a Canine Myocardial Infarction Model

Pre-clinical: EPC following AMI (Dog)

Group 1 (n=7): epicardial route
Group 2 (n=7): endocardial route

Sacrificed 15 days after transplantation
Serial SPECT/CT

Procedural safety: no adverse events

Initial EPC retention rate: IM (57%) = EC (54%) (p=0.53)
Clearance half-life: IM (69hr) = EC (60hr) (p=0.81)

- Subendocardial injections, clinically more practical, show clearance kinetics comparable to those of subepicardial injections and will facilitate the ultimate clinical use of this treatment modality

Intracoronary administration of cardiac stem cells in mice: a new, improved technique for cell therapy in murine models

Qianhong Li • Yiru Guo • Qinghui Ou • Ning Chen • Wen-Jian Wu • Fangping Yuan • Erin O’Brien • Tao Wang • Li Luo • Gregory N. Hunt • Xiaoping Zhu • Roberto Bolli

IC: More homogeneous distribution

Li Q, et al. Basic Res Cardiol 2011;106:849–64
6. IC vs. EC

Li Q, et al. Basic Res Cardiol 2011;106:849–64
Summary and Conclusion

Engraftment ➔ IC ≥ EC=IM

Procedural safety ➔ All methods are relatively safe
IC => microvascular “plugging”

Extracardiac retention of stem cells ➔ EC=IM ≤ IC & IV

Improvement of heart function ➔ IC = EC = IM (?)
<table>
<thead>
<tr>
<th>Trial</th>
<th>Cell</th>
<th>Time of Delivery</th>
<th>Results</th>
<th>F/U</th>
</tr>
</thead>
<tbody>
<tr>
<td>van Ramshorst et al., 2009</td>
<td>Autologous BM-MNC, 1×10⁸ cells, intramyocardial injection</td>
<td>Chronic MI</td>
<td>Modest improvement of summed stress score, LVEF in BMC group at 3 mo, increase of quality of life at 6 mo</td>
<td>3, 6</td>
</tr>
<tr>
<td>Williams et al., 2011</td>
<td>transendocardial, intramyocardial injection of auto BM-MNC (1 or 2×10⁸), or MSC (1 or 2×10⁸)</td>
<td>ICMP</td>
<td>EDV (208.7±20.4 to 167.4±7.32mL), infarct size ↓, regional function ↑ at 3 mo, changes in chamber dimensions not diff at 6 mo</td>
<td>12</td>
</tr>
<tr>
<td>Ahmadi et al., 2012</td>
<td>BM-CD133+BMC, 1.77×10⁶±1.14×10⁶ CD133+ cells, intramyocardial transplantation</td>
<td>Candidate of CABG after MI</td>
<td>Safe, no benefit</td>
<td>60</td>
</tr>
</tbody>
</table>
## Intravenous Delivery in Clinical Trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>Cell</th>
<th>Time of Delivery</th>
<th>Results</th>
<th>F/U</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hare et al., Prochymal, 2009</td>
<td>Allogeneic BM-MSC, 0.5, 1.6, $5 \times 10^6$ cells/kg, iv</td>
<td>1-10 d</td>
<td>EF ↑</td>
<td>12</td>
</tr>
<tr>
<td>Moreira et al., 2011</td>
<td>BM-MNC $1 \times 10^8$, anterograde intra-arterial coronary (IAC) or retrograde intravenous coronary (IVC)</td>
<td>24h &lt; MI, infract size &gt; 10%,</td>
<td>Comparison of cell retention: IAC (16.14%), IVC (4.62%) at 4h, IAC (10.29%), IVC (3.13%) at 24h</td>
<td>24h</td>
</tr>
</tbody>
</table>

*Kim YS and Ahn Y, Korean Circ J 2012;42:71–9*
## Intracoronary Delivery in Clinical Trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>Cell</th>
<th>Time of Delivery</th>
<th>Results</th>
<th>F/U</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meyer et al., BOOST trial, 2009</td>
<td>Autologous BMC, 24.6×10⁸</td>
<td>5 d</td>
<td>EF ↑</td>
<td>61</td>
</tr>
<tr>
<td>Tendera et al., REGENT trial, 2009</td>
<td>BM-MNC (1.78×10⁸), CD34+ (1.9×10⁶)</td>
<td>PCI after 12h</td>
<td>EF ↑</td>
<td>6</td>
</tr>
<tr>
<td>Beitnes et al., ASTAMI trial, 2009</td>
<td>BMC, 7×10⁷</td>
<td>4-7 d</td>
<td>Safe, exercise time ↑, no other effects</td>
<td>36</td>
</tr>
<tr>
<td>Assmus et al., REPAIE-AMI, 2010</td>
<td>Auto BMC, 236±174×10⁶</td>
<td>3-7 d after reperfusion</td>
<td>Still safe</td>
<td>24</td>
</tr>
<tr>
<td>Gnijek et al., 2010</td>
<td>BMC, 2.34±1.2×10⁹</td>
<td>4-6d after PCI</td>
<td>No differences in EF, LVEDV, LVESV, and spiroergometric stress test</td>
<td>6, 12</td>
</tr>
<tr>
<td>Arnold et al., TECAM study, 2010</td>
<td>BM-MNC, 97.6±61.4×10⁶</td>
<td>STEMI, &lt;9±3d of reperfusion</td>
<td>No difference in stenosis, plaque volume</td>
<td>9</td>
</tr>
<tr>
<td>Strauer et al., STAR-heart study 2010</td>
<td>BMC, 6.6±3.3×10⁷</td>
<td>Chronic HF EF&lt;35% (mean post MI interval: 8.5 yr)</td>
<td>Haemodynamics, exercise capacity, oxygen uptake, LV contractility, long-term mortality↑ in BMC group</td>
<td>3, 12, 60</td>
</tr>
<tr>
<td>Seth et al., ABCD Trial, 2010</td>
<td>BM-MNC</td>
<td>DCMP EF&lt;35%</td>
<td>EF ↑, ESV ↓ at 6 mo</td>
<td>36</td>
</tr>
<tr>
<td>Traverse et al., 2010</td>
<td>auto BMC 1×10⁸</td>
<td>STEMI</td>
<td>EF ↑, LVEDP ↓</td>
<td>6</td>
</tr>
<tr>
<td>Mansour et al., COMPARE-AMI, 2011</td>
<td>CD133+ HSC, 1×10⁷</td>
<td>3~7 d after PCI</td>
<td>Safe, EF ↑</td>
<td>12</td>
</tr>
<tr>
<td>Hirsch et al., HEBE trial, 2011</td>
<td>BM 296±164×10⁶ or peripheral MNC 287±137×10⁶</td>
<td>IC 4-7 d after MI</td>
<td>No difference</td>
<td>4</td>
</tr>
<tr>
<td>Penn et al., 2011</td>
<td>Allo MultiStem, 2×10⁷, 6×10⁷, 1×10⁸</td>
<td>2-5 d after AMI</td>
<td>EF ↑, LV stroke volume ↑</td>
<td>4</td>
</tr>
<tr>
<td>Bolli et al., SCIPIO, 2011</td>
<td>CSCs, 1 million</td>
<td>EF&lt;40%, CABG, ICMP</td>
<td>EF ↑, Infarct size ↓</td>
<td>12</td>
</tr>
<tr>
<td>Solheim et al., 2011</td>
<td>BM-MNC 68×10⁸</td>
<td>6d after the STEMI</td>
<td>No changes in prothrombotic markers</td>
<td>3</td>
</tr>
<tr>
<td>Roncalli et al., BONAMI trial, 2011</td>
<td>auto BMC</td>
<td>9.3 d after STEMI</td>
<td>Myocardial viability ↑</td>
<td>3</td>
</tr>
<tr>
<td>Malik et al., CADUCEUS, 2012</td>
<td>Autologous cardiosphere, 12.5 ~ 25 million</td>
<td>2-4wk after MI</td>
<td>Scar mass ↓, viable heart mass ↑, regional contractility ↑, no changes in EDV, ESV, LVEF</td>
<td>6</td>
</tr>
</tbody>
</table>
Thank you for your attentions!

3rd Gwangju-Boston Joint Cardiology Symposium

Date: 25th - 26th May, 2012
Venue: Deok-Jae Hall/Myung-Hak Hall,
Chonnam National University Medical School, Gwangju