Soluble TNF receptors are associated with infarct size and ventricular dysfunction in ST-elevation myocardial infarction

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Conflict of interest: None to declare.
Enhanced apoptosis of several cell types and in diverse aspects of cardiovascular disease.

Atherosclerosis
ACS-Reperfusion injury
Congestive heart failure

Predicts mortality\(^1\) and bears prognostic value\(^2\) in ACS and CHF patients.

\(^1\)Circulation. 2005;111:863-870
\(^2\)Eur Heart J 2009;30:789-796
Ischemia-Reperfusion injury

- Vascular leakage
- No reflow phenomenon
- Cell death programs: Apoptosis, necrosis, autophagy-associated cell death
- Transcriptional reprogramming
- Autoimmunity: Autoantibody and complement activation
- Innate and adaptive immune activation

Nat Med 2011;17:1391-401
Objective

• Investigate circulating markers of apoptosis in relation to infarct size, left ventricular dysfunction and remodelling in a STEMI population undergoing PCI.

• Predefined substudy of the F.I.R.E trial¹

¹J Am Coll Cardiol 2009;53:420-9
Methods

STEMI (n=48)
Symptom onset to arrival PCI lab < 6 h

Apoptotic markers pre PCI and 24 h
sTNFR1, sTNFR2, sFas, sFasL (ELISA)

MRI at 5 days and 4 months
LGE, LVEF and volume indices of LV remodelling
Results

- **Baseline variables**
  - Age, year (mean, sd) 61 (11)
  - Anterior infarct location, % 46
  - Symptom onset to PCI, min (median, 25th, 75th perc) 152 (115, 280)

- **Procedural variables**
  - TIMI pre-procedural, %
    - 0 98
    - 1 2
  - TIMI after PCI, %
    - 2 6
    - 3 94

- **Outcome measures**
  - Infarct size at 5 days, g (median, 25th, 75th perc) 35 (14, 53)
  - Infarct size at 4 months, g (median, 25th, 75th perc) 23 (6, 38)
  - LVEF at 5 days, % (median, 25th, 75th perc) 45 (40, 52)
  - LVEF at 4 months, % (median, 25th, 75th perc) 50 (45, 57)
## Results

<table>
<thead>
<tr>
<th></th>
<th>Total LGE at 5 days</th>
<th>Total LGE at 4 months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>sTNFR1</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0h</td>
<td>-0.014</td>
<td>0.037</td>
</tr>
<tr>
<td>24h</td>
<td>0.231</td>
<td>0.358*</td>
</tr>
<tr>
<td>% change</td>
<td>0.412*</td>
<td>0.385*</td>
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<tr>
<td><strong>sTNFR2</strong></td>
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<td></td>
</tr>
<tr>
<td>0h</td>
<td>0.005</td>
<td>0.034</td>
</tr>
<tr>
<td>24h</td>
<td>0.138</td>
<td>0.203</td>
</tr>
<tr>
<td>% change</td>
<td>0.356*</td>
<td>0.369*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>LVEF % at 5 days</th>
<th>LVEF % at 4 months</th>
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</thead>
<tbody>
<tr>
<td><strong>sTNFR1</strong></td>
<td></td>
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</tr>
<tr>
<td>0h</td>
<td>-0.048</td>
<td>-0.177</td>
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<tr>
<td>24h</td>
<td>-0.200</td>
<td>-0.354*</td>
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<tr>
<td>% change</td>
<td>-0.274</td>
<td>-0.375*</td>
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<tr>
<td><strong>sTNFR2</strong></td>
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<td></td>
</tr>
<tr>
<td>0h</td>
<td>-0.017</td>
<td>-0.155</td>
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<tr>
<td>24h</td>
<td>-0.078</td>
<td>-0.253</td>
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<tr>
<td>% change</td>
<td>-0.125</td>
<td>-0.192</td>
</tr>
</tbody>
</table>

* p< 0.05
Results

Infarct size at 4 months

LV ejection fraction at 4 months
Conclusions

• In STEMI patients, sTNFRI at 24 h and the increase in sTNFR1 and sTNFR2 during the first 24 h are associated with the final infarct size and LV dysfunction.

• These data provide further evidence for apoptosis in ischemia-reperfusion injury.