Predicting Neurologic Outcome
After Cardiac Arrest and Hypothermic Treatment by Neuron Specific Enolase

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Neuron-Specific Enolase
- Neuronal form of intracytoplasmatic glycolytic enzyme-enolase
- Half-life 24 hours
- Source: neurons and neuro-ectodermal cells
- Parameter for:
  - Lung- and liver diseases (pneumonia, SCLC)
  - Hemolysis
  - And: neuronal damage as well as damage of blood-brain barrier
- Normal value:
  - < 12.5 ng/ml in adults
  - < 25 ng/ml in children under 1 year
NSE and Neurologic Outcome

Patients with good neurologic outcome

Patients with bad neurologic outcome

Changes of NSE and S 100β after CPR

![Graph showing changes of NSE and S 100β after CPR](image)
NSE Cut-off Value

![Box plot showing NSE (ng/mL) levels for different CPC conditions](image)

- CPC 1-2
- CPC 3
- CPC 4

Median, 25% Percentile, 75% Percentile, 90% Percentile

Days after CPR: 0, 1, 2, 3, 4, 5

Sample sizes: 90, 28, 59, 90, 28, 59, 90, 28, 59, 90, 28, 54
Limitations

- Therapeutic hypothermia was not routinely applied
- Cut-off values of NSE differ between studies
- Many studies have an observation period of only 24 to 48 hours
- Peak NSE values at diverging time-points
- Determination of a mean cut-off value of NSE over the entire observation period rather than values at different time-points
Study Aims

- Defining new NSE cut-off values for good neurologic outcome at different time-points up to 72 hours after cardiac arrest and therapeutic hypothermia.

- Determination of the optimal time-point of blood sampling for prediction of neurologic outcome.
109 comatose survivors of cardiac arrest were initially included, 104 analyzed

Initiation of mild therapeutic hypothermia to 33°C (either invasively or non-invasively) as soon as possible and maintenance for 24 hours

Outcome evaluation at discharge of ICU by assessing cerebral performance category (CPC)
Study Protocol

Time-point of Blood sample Collection (TP) | 0h | 6h | 12h | 24h | 36h | 48h | 72h
--- | --- | --- | --- | --- | --- | --- | ---
INR | X | X | X | X | X | X | X
Clotting Time | X | X | X | X | X | X | X
Creatinine | X | X | X | X | X | X | X
CK/CK-MB | X | X | X | X | X | X | X
Blood Count | X | X | X | X | X | X | X
NSE | X | X | X | X | X | X | X
Cooling modality

61% invasive
39% non-invasive
### Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>All n = 104</th>
<th>CPC 1/2 n = 37 (36%)</th>
<th>CPC 3-5 n = 67 (64%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (±SD)</td>
<td>62±13</td>
<td>54±11</td>
<td>66±12 *</td>
</tr>
<tr>
<td>Male Gender (n/%)</td>
<td>78/75</td>
<td>26/70</td>
<td>52/78</td>
</tr>
<tr>
<td>Body mass index, kg/m² (±SD)</td>
<td>28±4</td>
<td>26±3</td>
<td>29±4 *</td>
</tr>
<tr>
<td>History of Diabetes (n/%)</td>
<td>34/33</td>
<td>4/11</td>
<td>30/45 *</td>
</tr>
<tr>
<td>Recent Symptoms (n/%)</td>
<td>56/54</td>
<td>18/49</td>
<td>38/57</td>
</tr>
<tr>
<td>Out of hospital-SCA (n/%)</td>
<td>84/81</td>
<td>34/92</td>
<td>50/75 *</td>
</tr>
<tr>
<td>Bystander witnessed SCA (n/%)</td>
<td>92/89</td>
<td>34/92</td>
<td>58/78</td>
</tr>
<tr>
<td>Bystander CPR (n/%)</td>
<td>60/58</td>
<td>19/51</td>
<td>41/61</td>
</tr>
<tr>
<td>Initial Rhythm VF/VT (n/%)</td>
<td>69/66</td>
<td>29/78</td>
<td>40/60</td>
</tr>
<tr>
<td>Admission via External ED (n/%)</td>
<td>38/37</td>
<td>13/35</td>
<td>25/37</td>
</tr>
<tr>
<td>Inhospital Pressors (n/%)</td>
<td>86/83</td>
<td>29/78</td>
<td>57/85</td>
</tr>
<tr>
<td>Acute Myocardial Infarction (n/%)</td>
<td>60/58</td>
<td>20/54</td>
<td>40/60</td>
</tr>
<tr>
<td>SCA to ROSC, min (±SD)</td>
<td>31±24</td>
<td>26±14</td>
<td>34±27</td>
</tr>
</tbody>
</table>


*p<0.05 (univariate analysis)
Time Course NSE Good vs Impaired Neurologic Outcome

![Graph showing the time course of NSE (ng/mL) for CPC 3-5 and CPC 1-2 categories.](image-url)

- CPC 3-5
- CPC 1-2
NSE at 72 h

P<0.001

good vs. bad neurologic outcome
ROC-Curves

<table>
<thead>
<tr>
<th>TP</th>
<th>AUC</th>
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<tbody>
<tr>
<td>0</td>
<td>0.603</td>
</tr>
<tr>
<td>6</td>
<td>0.708</td>
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<tr>
<td>12</td>
<td>0.686</td>
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<tr>
<td>24</td>
<td>0.715</td>
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<tr>
<td>36</td>
<td>0.744</td>
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<tr>
<td>48</td>
<td>0.814</td>
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<tr>
<td>72</td>
<td>0.934</td>
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## NSE Cut-off Values

<table>
<thead>
<tr>
<th>Time-point (h)</th>
<th>Cut-off (ng/ml)</th>
<th>Specificity</th>
<th>Sensitivity</th>
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<tbody>
<tr>
<td>0</td>
<td>42.5</td>
<td>100</td>
<td>13.4</td>
</tr>
<tr>
<td>6</td>
<td>41.0</td>
<td>100</td>
<td>25.8</td>
</tr>
<tr>
<td>12</td>
<td>43.5</td>
<td>100</td>
<td>25.4</td>
</tr>
<tr>
<td>24</td>
<td>35.5</td>
<td>100</td>
<td>37.5</td>
</tr>
<tr>
<td>36</td>
<td>36.5</td>
<td>100</td>
<td>41.5</td>
</tr>
<tr>
<td>48</td>
<td>46.5</td>
<td>100</td>
<td>41.3</td>
</tr>
<tr>
<td>72</td>
<td>29.0</td>
<td>100</td>
<td>62.5</td>
</tr>
</tbody>
</table>
Conclusions

- NSE cut-off values at the assessed time-points are lower as compared to the results of former studies, since in former studies, therapeutic hypothermia was not routinely applied.

- NSE at 72 hours after cardiac arrest has the greatest predictive power regarding neurologic outcome with a cut-off of 29 ng/ml