WORKSHEET for Evidence-Based Review of Science for Emergency Cardiac Care

Worksheet author(s)
Tomaso Sanna  
Date Submitted for review: October 01, 2009

Clinical question.

“In adult patients who are comatose after cardiac arrest (prehospital or in-hospital) (P), does the use of electrophysiological studies (I) as opposed to standard care (C), allow accurate prediction of outcome (O) (eg. survival)?”

Is this question addressing an intervention/therapy, prognosis or diagnosis?  
Prognosis

State if this is a proposed new topic or revision of existing worksheet:  
Revision

Conflict of interest specific to this question

Do any of the authors listed above have conflict of interest disclosures relevant to this worksheet?  
No

Search strategy (including electronic databases searched).

- Cochrane Library (Databases: Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects)
  Database search strategy according to PICO format:
  Query 1 “cardiac arrest” OR “heart arrest”
  Query 2 “neurophysiolog**”
  Query 3 “electroencephalograph**”
  Query 4 “somatosensory evoked potentials”
  Query 5 “bispectral index”
  Query 6 2 OR 3 OR 4 OR 5
  Query 7 1 AND 6
  Ö 10 hits (July 28, 2008)

- PubMed
  Database search strategy according to PICO format:
  Query 1 “Heart Arrest”[Mesh] OR “Death, Sudden, Cardiac”[Mesh]
  Query 2 “Electroencephalography”[Mesh]
  Query 3 “Evoked Potentials, Somatosensory”[Mesh]
  Query 4 “Neurophysiology”[Mesh]
  Query 5 “Recruitment, Neurophysiological”[Mesh]
  Query 6 “Transcranial Magnetic Stimulation”[Mesh]
  Query 7 “Recruitment Detection, Audiologic”[Mesh]
  Query 8 2 OR 3 OR 4 OR 5 OR 6 OR 7
  Query 9 1 AND 8
  Ö 484 hits (July 28, 2008)

  -  The results of the Query 9 have been filtered by the “Clinical Queries” tool (category: prognosis; scope: broad, sensitive) and restricted to Ö 84 hits (July 28, 2008)

- Embase (1988-2008)
  Database search strategy according to PICO format:
  Query 1 “cardiac arrest.mp. or exp Heart Arrest”
  Query 2 “neurophysiolog.mp.”
  Query 3 “Evoked Somatosensory Response/ or somato sensory evoked potential*.mp.”
  Query 4 “Electroencephalography/ or Electroencephalogram/ or electroencephal*.mp.”
  Query 5 “Bispectral Index”
  Query 6 “Human [Subjects]”
  Query 71 AND (2 OR 3 OR 4 OR 5)
  Query 87 AND 6 Ö 313 hits (July 28, 2008)

- ECC Endnote Master library

• State inclusion and exclusion criteria
  Inclusion criteria: human studies, non-traumatic cardiac arrest
Exclusion criteria: animal studies, traumatic cardiac arrest, circulatory arrest during surgery with extracorporeal circulation, pediatric cardiac arrest, single-case reports

<table>
<thead>
<tr>
<th>Number of articles/sources meeting criteria for further review:</th>
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</table>

After publication list consolidation, elimination of duplicates, and title analysis, 245 references were considered for further review. During the following steps of the review process, several references were added after manual cross-check of the bibliography of selected publications. The systematic reviews and meta-analyses by Zandbergen et al. 1998 1808-1812 and Wijdicks et al. 2006 203-210 were considered as representative of the relevant scientific evidence published before 1998 on the respective topics. Studies eligible for the worksheet published after 1998 and analyzed in the systematic reviews and meta-analyses by Zandbergen et al. 1998 1808-1812 and Wijdicks et al. 2006 203-210 were appropriately flagged with an asterisk in the “summary of evidence” tables. After analysis of the abstracts and of the publications in extenso, comprehensive analysis was restricted to 56 publications and the 24 publications exactly matching the worksheet topic, as stated in the PICO format (“In adult patients who are comatose after cardiac arrest (prehospital or in-hospital) (P), does the use of electrophysiological studies (I) as opposed to standard care (C), allow accurate prediction of outcome (O) (eg. survival)?”), were eventually included in the worksheet. Of these, 14 were LOE P1 (Inception [prospective] cohort studies [or meta-analyses of inception cohort studies], or validation of Clinical Decision Rule [CDR]), 1 was LOE P2 (Follow up of untreated control groups in RCTs [or meta-analyses of follow-up studies], or derivation of CDR, or validated on split-sample only), 6 were LOE P3 (Retrospective cohort studies), 2 were LOE P4 (Case series) and 1 was LOE P5 (Studies not directly related to the specific patient/population [eg. different patient/population, animal models, mechanical models etc.])
### Summary of evidence

#### Evidence Supporting Clinical Question

<table>
<thead>
<tr>
<th>Good</th>
<th>Evidence</th>
<th>Fair</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Good</strong></td>
<td>Wijdicks et al. 2006 203-210&lt;sup&gt;D&lt;/sup&gt; EEG SSEPs</td>
<td>Fischer et al. 2006 1520-4&lt;sup&gt;D&lt;/sup&gt; BAEPS, MLAEPs, SSEPs, auditory N100, and MMN</td>
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<tr>
<td></td>
<td>Zandbergen et al. 1998 1808-1812&lt;sup&gt;D&lt;/sup&gt; EEG SSEPs</td>
<td>*Gendo et al. 2001 1305-1311&lt;sup&gt;D&lt;/sup&gt; SSEPs</td>
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<td>*Madal et al. 2000 721-6&lt;sup&gt;D&lt;/sup&gt; SSEPs</td>
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<td>Nakabayashi et al. 2001 1210-1214&lt;sup&gt;D&lt;/sup&gt; SSEPs</td>
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<td>Rundgren et al. 2006 836-842&lt;sup&gt;D&lt;/sup&gt; aEEG (Therapeutic hypothermia)</td>
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<td>Sakurai et al. 2006 52-58&lt;sup&gt;D&lt;/sup&gt; ABR (Therapeutic hypothermia)</td>
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<td>Shibata et al. 2005 243-246&lt;sup&gt;D&lt;/sup&gt; EEG (BIS)</td>
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<td>Stammet et al. 2009 437-42&lt;sup&gt;D&lt;/sup&gt; EEG (BIS Therapeutic hypothermia)</td>
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<td></td>
<td>Tainen et al. 2005 1736-40&lt;sup&gt;D&lt;/sup&gt; SSEPs (Therapeutic hypothermia)</td>
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<td>*Young et al. 2005 159-164&lt;sup&gt;D&lt;/sup&gt; SSEPs EEG</td>
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<td>Zandbergen et al. 2006 62-8&lt;sup&gt;D&lt;/sup&gt; SSEPs EEG</td>
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<td>*Zingler et al. 2003 79-84&lt;sup&gt;D&lt;/sup&gt; SSEPs</td>
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<td><strong>Prohl et al. 2007 1230-1237&lt;sup&gt;D&lt;/sup&gt; SSEPs</strong></td>
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<td>Ajisaka 2004 616-8&lt;sup&gt;D&lt;/sup&gt; EEG</td>
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<td>Bauer et al. 2003 283-287&lt;sup&gt;D&lt;/sup&gt; SSEPs</td>
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<td>*Logi et al. 2003 1615-1627&lt;sup&gt;D&lt;/sup&gt; SSEPs, MLAEPs</td>
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<td>Rossetti et al. 2007 255-260&lt;sup&gt;D&lt;/sup&gt; EEG (Therapeutic hypothermia)</td>
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<td>Rothstein 2000 486-497&lt;sup&gt;D&lt;/sup&gt; SSEPs</td>
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<td>Sherman et al. 2000 889-94&lt;sup&gt;D&lt;/sup&gt; SSEPs</td>
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<td><strong>Berkhoff et al. 2000 297-304&lt;sup&gt;D&lt;/sup&gt; EEG</strong></td>
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<td>Thomke et al. 2002 24-31&lt;sup&gt;D&lt;/sup&gt; EEG</td>
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<td>*Zingler et al. 2003 79-84&lt;sup&gt;D&lt;/sup&gt; SSEPs</td>
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</table>

<table>
<thead>
<tr>
<th>Level of evidence</th>
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<tbody>
<tr>
<td>A = Return of spontaneous circulation</td>
</tr>
<tr>
<td>B = Survival of event</td>
</tr>
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<td>C = Survival to hospital discharge</td>
</tr>
<tr>
<td>D = Intact neurological survival</td>
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<tr>
<td>E = Other endpoint</td>
</tr>
</tbody>
</table>

* studies also included in the cited systematic reviews and meta-analyses

LOE P1: Inception (prospective) cohort studies (or meta-analyses of inception cohort studies), or validation of Clinical Decision Rule (CDR)
LOE P2: Follow up of untreated control groups in RCTs (or meta-analyses of follow-up studies), or derivation of CDR, or validated on split-sample only
LOE P3: Retrospective cohort studies
LOE P4: Case series
LOE P5: Studies not directly related to the specific patient/population (e.g. different patient/population, animal models, mechanical models etc.)
### Evidence Neutral to Clinical question

<table>
<thead>
<tr>
<th>Level of Evidence</th>
<th>Good</th>
<th>Fair</th>
<th>Poor</th>
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<tbody>
<tr>
<td>LOE P1: Inception (prospective) cohort studies (or meta-analyses of inception cohort studies), or validation of Clinical Decision Rule (CDR)</td>
<td>Tiainen et al. 2005 1736-40</td>
<td>BAEPs (Therapeutic hypothermia)</td>
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<tr>
<td>LOE P2: Follow up of untreated control groups in RCTs (or meta-analyses of follow-up studies), or derivation of CDR, or validated on split-sample only</td>
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<td>LOE P3: Retrospective cohort studies</td>
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<td>LOE P4: Case series</td>
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<td>LOE P5: Studies not directly related to the specific patient/population (e.g. different patient/population, animal models, mechanical models etc.)</td>
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### Evidence Opposing Clinical Question

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<th>Level of Evidence</th>
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<th>Poor</th>
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<tr>
<td>LOE P1: Inception (prospective) cohort studies (or meta-analyses of inception cohort studies), or validation of Clinical Decision Rule (CDR)</td>
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<tr>
<td>LOE P2: Follow up of untreated control groups in RCTs (or meta-analyses of follow-up studies), or derivation of CDR, or validated on split-sample only</td>
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<tr>
<td>LOE P3: Retrospective cohort studies</td>
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<tr>
<td>LOE P4: Case series</td>
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<tr>
<td>LOE P5: Studies not directly related to the specific patient/population (e.g. different patient/population, animal models, mechanical models etc.)</td>
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</table>
**Somato-sensory evoked potentials**

14 studies were included in the present analysis after careful review. A role of SSEPs to assess prognosis of comatose survivors of cardiac arrest was supported by 9 LOE P1 studies (LOE P1: Inception [prospective] cohort studies [or meta-analyses of inception cohort studies], or validation of Clinical Decision Rule [CDR]); of these, 2 were QOE good and 7 QOE fair 1 LOE P2 study, QOE fair (LOE P2: Follow up of untreated control groups in RCTs (or meta-analyses of follow-up studies), or derivation of CDR, or validated on split-sample only) and 4 LOE P3 studies, QOE fair (LOE P3: retrospective cohort studies); no study was neutral or provided evidence opposing a role of SSEPs to assess prognosis of comatose survivors of cardiac arrest.

The 14 studies included in the present review analyzed the predictive performance at different times of variable combinations of presence, latency, amplitude and amplitude ratio of both short latency SEP peaks (exploring the peripheral-thalamo-cortical pathway) and long latency SEP peaks (exploring cortico–cortical interactions).

The predictive performance of these factors has been extensively analyzed in the following “Citation list” section and is here summarized as follows (for abbreviations see the Abbreviations list at the end of the worksheet):

**Studies in samples not treated with therapeutic hypothermia**

Bauer et al. 2003 283-287
SSEPs were recorded within 72 h after cardiac arrest. The authors did not provide any measure of the predictive performance of their findings. The reviewer has calculated, on the basis of the published data, a sensitivity of 41 % (95% CI 35-47) and a specificity of 100% (95%CI-95-100), i.e. FPR of 0% (95% CI 0-5), for the absence of N20 to predict an unfavorable outcome.

Fischer et al. 2006 1520-4
Somato-sensory, auditory, and cognitive evoked potentials were recorded in this study at an average timing of 8 days after cardiac arrest. Of note, the authors stated that recordings of evoked potentials were performed when they were expected to be useful. However, all patients in whom SSEPs or MLAEPs were not recorded did not awaken (100% specificity, with FPR as calculated by the ILCOR reviewer respectively of 0 (95% CI 0-8) for the absence of N20 and of 0 (95% CI 0-8) for the absence of MLAEPs). All patients in whom MMN was present awakened (100% specificity). Complete data on sensitivity, specificity, PPV and NPV for all the prognostic variables are reported in the Table 2 of the study, while selected data are reported in the table below. The highest levels of sensitivity for awakening were observed with BAEPs, SEPs N20, SEPs P24, MLAEPs (sensitivity 100%, 95%CI 86-100 for all of them); the highest levels of specificity were observed with MMN (specificity 100%, 95%CI 93-100, i.e. FPR 0 (95%CI 0-7)); the highest levels of PPV was observed with MMN (100%, 95%CI 78-100); the highest levels of NPV were observed with BAEPs, SEPs N20, SEPs P24, MLAEPs (PPV 100%, 95%CI 5-100, 79-100, 78-100, 86-100 respectively).

<table>
<thead>
<tr>
<th>Predictor of awakening</th>
<th>Sensitivity % (95% CI)</th>
<th>Specificity % (95% CI)</th>
<th>Positive predictive value % (95% CI)</th>
<th>Negative predictive value % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BAEP (normal vs abnormal)</td>
<td>100 (96-100)</td>
<td>2 (0-13)</td>
<td>33 (21-46)</td>
<td>100 (5-100)</td>
</tr>
<tr>
<td>SSEPs N20 (normal vs abnormal)</td>
<td>100 (96-100)</td>
<td>31 (18-47)</td>
<td>41 (27-56)</td>
<td>100 (79-100)</td>
</tr>
<tr>
<td>MLAEP (normal vs abnormal)</td>
<td>100 (96-100)</td>
<td>48 (32-64)</td>
<td>48 (32-64)</td>
<td>100 (96-100)</td>
</tr>
<tr>
<td>Auditory N100 (present vs absent)</td>
<td>75 (51-91)</td>
<td>86 (71-95)</td>
<td>71 (48-99)</td>
<td>88 (74-96)</td>
</tr>
<tr>
<td>MMN (present vs absent)</td>
<td>60 (36-81)</td>
<td>100 (93-100)</td>
<td>100 (78-100)</td>
<td>64 (71-93)</td>
</tr>
</tbody>
</table>

Gendo et al. 2001 1305-1311
Both short and long latency evoked potentials were recorded at 4, 12, 24 and 48 hours (48 h in 10 out of 25 pts). The authors report that sensitivity of the N20 peak latency to predict an unfavorable outcome was 6% (95%CI 4-7%) at 4h and 17% (95% CI 13-20%) at 24 hours while specificity was 100% (95%CI 80-100%), i.e. FPR 0 (95%CI 0-20) both at 4 and 24 hours. Sensitivity and specificity of the absence of the N20 component to predict an unfavorable outcome were computed by the reviewer on the basis of the published data: sensitivity 6% (95% CI 1-25%) at 4h and 12% (95%CI 6-
39%) at 24 hours while specificity was 100% (95% CI 65-100%) i.e. FPR 0 (95%CI 0-35), both at 4 and 24 hours. Sensitivity of the N70 peak latency (critical cutoff 130 ms) was 100% (95% CI 80-100%) at 4 hours but decreased to 83% (95% CI 67-100%) at 24 hours while the corresponding specificity was 43% (95% CI 34-51%), i.e. FPR 57 (95%CI 49-66), at 4 hours and increased at 100% (95%CI 80-100%), i.e. FPR 0 (95%CI 0-20), at 24 hours. The predictive performance of the above mentioned criteria at 4, 24 and 48 hours was also assessed in a subset of 10 pts in whom data at 48 hours were available, with possible selection bias. In this subset of pts sensitivity at 4, 24 and 48 hours were respectively 83%, 83% and 100% while the corresponding specificity levels were 50%, 100% and 75%.

Logi et al. 2003 1615-1627
EP studies were not performed in a protocol-specified time window, but “when the contribution of EPs to prognosis was expected to be useful” with a possible assessment bias. With these limitations, SSEPs (grade 1 as opposed to grade 2) had a sensitivity of 47% (10% in case of bilateral absence of cortical components), a specificity of 100% (100% in case of bilateral absence of cortical components), a positive predictive value of 100% and a negative predictive value of 38% to predict an unfavorable outcome.

Madl et al. 2000 721-6
Short- and long-latency SSEPs were recorded within 8 and 24 hrs after cardiac arrest. None of the 46 patients who presented bilateral loss of N20 peaks survived. Of the 113 patients with an N70 peak latency of > 130 msec (n = 32) or an absent N70 peak (n = 81), 112 had an unfavorable outcome. By using a cutoff of 130 msec, the N70 peak latency had a sensitivity of 94%, a specificity of 97%, a positive predictive value of 98%, and a negative predictive value of 82%. The predictive accuracy of the N70 peak latency was significantly higher than the clinical assessment 24 hrs after cardiac arrest (91% vs. 76%, p = .0003).

Nakabayashi et al. 2001 1210-1214
SSEPs were recorded immediately after return of spontaneous circulation (within 3 hours after arrest). Sensitivity and specificity of absence of N20 to predict an unfavorable outcome were calculated by the authors and resulted 81.8 and 100.0 % respectively; 95% CI were not reported and have been calculated from the original data by the ILCOR reviewer and resulted 61-92% and 67-100% respectively, with a i.e. FPR 0 (95%CI 0-33).

Prohl et al. 2007 1230-1237
Short latency (N10, N20) and long-latency (N70) SSEPs were recorded on day 4 after cardiac arrest. The presence of SEP N70 had a significant correlation with a favorable outcome, while the correlation was weaker for N20 or absent for N10. If SEP N70 could be recorded (30 out of 47 examinations), the prediction of a favorable outcome was successful in 87% of patients. A multivariate logistic-regression analysis was performed to assess a possible independent predictive role of age, NSE, S-100B (days 2– 4), CES (days 2 and 4), SEPs N10, N20, and N70, and the interval between cardiac arrest and the first blood sampling. This multivariate logistic-regression analysis resulted in a model in which outcome was explained by NSE at day 4, CES at day 4 but not SSEPs; however, as this analysis was performed in a limited subset of patients, these findings cannot be considered adequate to disprove the results of univariate analysis.

Rothstein 2000 486-497
SSEPs were recorded within 48 hours. Several indicators of predictive performance were reported by the authors: normal N20: sensitivity and positive predictive value for neurological recovery 100% and 36%, respectively; delayed N20: sensitivity and positive predictive value for neurological recovery 33% and 43%, respectively; absent N20: sensitivity and positive predictive value for death of 68% and 100%, respectively. Other indexes of predictive performance have been recalculated by the reviewer on the basis of published data: abnormal N20 (delayed or absent) had a sensitivity of 75% (95%CI 61-85) and a specificity of 83% (95%CI 44-97), i.e. FPR 17 (95%CI 3-56), to predict an unfavorable outcome (persistent neurological impairment, persistent vegetative state, death without awakening); bilateral absence of N20 had a sensitivity of 52% (95%CI 38-66) and a specificity of 100% (95%CI 61-100), i.e. FPR 0 (95%CI 0-39) to predict an unfavorable outcome (persistent neurological impairment, persistent vegetative state, death without awakening); bilateral absence of N20 had a sensitivity of 52% (95%CI 38-66) and a specificity of 100% (95%CI 61-100), i.e. FPR 0 (95%CI 0-39) to predict an unfavorable outcome (persistent neurological impairment, persistent vegetative state, death without awakening).

Sherman et al. 2000 889-94
SSEPs were recorded between 0.5 and 4 days after cardiac arrest in 53 patients, between 5 and 10 days in 17 patients, and between 3 and 4 weeks in 2 patients. Bilateral absence of the N1 (i.e. N20) peak predicted nonawakening with a sensitivity of 55% (95%CI 42-67) and a specificity of 100% (95%CI 63-100), i.e. FPR 0 (95%CI 0-37); bilaterally absent N3 (i.e. N70) predicted nonawakening with a sensitivity of 62% (95%CI 50-75) and a specificity of 100% (95%CI 63-100), i.e. FPR 0 (95%CI 0-37); N3 (i.e. N70) peak latency or ≥ 176 msec predicted nonawakening with a sensitivity of 67% (95%CI 55-79) and a specificity of 100% (95%CI 63-100), i.e. FPR 0 (95%CI 0-37). Higher values of sensitivity and specificity were obtained combining SSEPs results and CSF-CKBB levels.
Wijdicks et al. 2006 203-210
This pooled analysis included 8 studies in which SSEPs were recorded within 3 days from CA. Bilateral absence of N20 response to median nerve stimulation was associated with a pooled FPR for poor outcome of 0.7% (95% CI: 0.1 to 3.7). A few patients have been reported in whom an absent N20 response > 24 h after CA reappeared in successive recordings, all with a poor outcome. Conversely, the presence of the N20 response is not helpful in predicting outcome (pooled sensitivity of 46%)

Young et al. 2005 159-164
SSEPs were recorded between 1 and 3 days after ROSC. The predictive performance of the absence of the N20 component to predict an unfavorable outcome was recalculated by the ILCOR reviewer and resulted in a sensitivity of 57% (95% CI 41-72), and a specificity of 92% (95% CI 65-98), i.e. FPR 8 (95% CI 2-35)

Zandbergen et al. 1998 1808-1812
In this pooled analysis, bilateral absence of early cortical SSEP within the first week was associated with a pooled positive LR of an unfavorable outcome of 12·0 (95% CI 5·3–27·6) and a pooled 95% CI FPR of 0–2 %.

Zandbergen et al. 2006 62-8
SSEPs were recorded at 24, 48 and 72 hours and offered the predictive performance reported in the following table together with the predictive performance of EEG results, which were also studied by the authors.

<table>
<thead>
<tr>
<th>Prognostic factor</th>
<th>False positive rate (95% CI)</th>
<th>Positive likelihood ratio (95% CI)</th>
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<tbody>
<tr>
<td>Bilateral absence N20 at 24 h</td>
<td>0 (0-4)</td>
<td>24 (4-45)</td>
</tr>
<tr>
<td>Bilateral absence N20 at 48 h</td>
<td>0 (0-4)</td>
<td>27 (9-42)</td>
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<tr>
<td>Bilateral absence N20 at 72 h</td>
<td>0 (0-3)</td>
<td>25 (2-90)</td>
</tr>
<tr>
<td>Bilateral absence N20 at 24-72 h</td>
<td>0 (0-3)</td>
<td>23 (2-30)</td>
</tr>
<tr>
<td>EEG no activity ≤ 20 µV at 72h</td>
<td>0 (0-5)</td>
<td>17 (1-27)</td>
</tr>
<tr>
<td>EEG burst suppression pattern 72h</td>
<td>0 (0-15)</td>
<td>5 (0-81)</td>
</tr>
<tr>
<td>EEG status epilepticus 72h</td>
<td>7 (1-24)</td>
<td>1 (0-5)</td>
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</tbody>
</table>

Zingler et al. 2003 79-84
SSEPs were assessed on days 2 and 7 after cardiac arrest. SSEPs with bilateral loss of cortical response (grade 4) were found exclusively in CPC 4–5 (prediction of poor outcome with a specificity of 100%).

Studies in samples (also) treated with therapeutic hypothermia

Tiainen et al. 2005 1736-40
SSEPs and BAEPs were recorded 24 –28 hrs after cardiac arrest. Bilaterally absent N20 predicted permanent coma with a specificity of 100% (95% confidence interval, 92–100%), i.e. FPR 0 (95% CI 0-8). However, the authors reported this level of predictive performance for aggregate data (hypothermic + normothermic pts) but it is debatable whether this approach is entirely acceptable. Specificities and their CIs have then been recalculated for the separate groups by the ILCOR reviewer from the original data. Given the small sample groups, the confidence interval for the specificity of SSEP broadened to 87-100, i.e. FPR 0 (95% CI 0-13) in the hypothermia group and to 82-100, i.e. FPR 0 (95% CI 0-18) in the normothermia group). Three patients (one in the hypothermia group and two in the normothermia group) had bilateral N20 responses but did not awaken. Thus, the sensitivity was 75% (95% CI, 30 –95%) in the hypothermia group and 80% (95% CI, 49 –94%) in the normothermia group

**Electroencephalography**

12 studies were included in the present analysis after careful review. A role of EEG to assess prognosis of comatose survivors of cardiac arrest was supported by 7 LOE P1 studies (LOE P1: Inception (prospective) cohort studies (or meta-analyses of inception cohort studies), or validation of Clinical Decision Rule (CDR)); of these, 2 were QOE good and 4 QOE fair), 2 LOE P3 study, QOE fair (LOE P3: Retrospective cohort studies), 2 LOE P4 studies, QOE fair (LOE P4: Case series); and 1 LOE P5 study, QOE poor (LOE P5: Studies not directly related to the specific patient/population [e.g. different patient/population, animal models, mechanical models etc.]); no study was neutral or provided evidence opposing a role of EEG to assess prognosis of comatose survivors of cardiac arrest
The predictive performance of the different EEG parameters has been extensively detailed in the “Citation list” section and is here summarized as follows:

**Studies in samples not treated with therapeutic hypothermia**

**Ajisaka 2004 616-8**
The authors have found that EEG Hockaday grade, as recorded 72 hours post CA, has a univariate role in predicting prognosis of comatose survivors of cardiac arrest. The authors do not present estimates of sensitivity and specificity, probably because of the small number of patients and the small number of events. However, the ILCOR reviewer has made an estimate of sensitivity and specificity of EEG grades 1 and 2 to predict a favorable outcome (good recovery or mild disability) which resulted 80% (95%CI 49-94) and 91% (95% CI 62-98) i.e. FPR 9 (95%CI 2-38) and calculated sensitivity and specificity of EEG grade 5 to predict an unfavorable outcome (severe disability, vegetative state, death) which resulted 9% (95%CI 1.6-38) and 100% (95% CI 72-100), i.e. FPR 0 (95%CI 0-28).

**Berkhoff et al. 2000 297-304**
All of the pts (9/9) with complete ATC had an unfavorable outcome. Two out of five (2/5) pts with incomplete ATC had an unfavorable outcome while 3/5 regained cognition, even though two of them remained dependent in activities of daily living

**Fatovich et al. 2006 207-212**
Case series not intended to assess prognosis in comatose survivors of cardiac arrest, describing a comatose survivor of cardiac arrest whose BIS score was good and recovered thus suggesting a possible role of BIS in assessing prognosis of comatose survivors of cardiac arrest

**Shibata et al. 2005 243-246**
In this study, BIS was recorded in 10 pts who remained comatose after resuscitation from OHCA. The BIS values were significantly lower in the non-surviving group than in the surviving group. Of interest, BIS increased rapidly after about 30 min of ROSC or reached a plateau of >80 in patients who achieved a favorable outcome or moderate disability; it did not increase in patients with unfavorable outcome (permanent vegetative state/dead). The authors could not analyze the recordings within 30 min of ROSC in three patients because of muscular artifacts contamination.

**Thomke et al. 2002 24-31**
It was not possible to calculate sensitivity and specificity as it is not reported by the authors how many pts who were comatose after CA did not show BS-EEG and their outcome. Therefore, it should be considered a case series study (LOE P4) suggesting a role of EEG (burst suppression pattern) to assess the prognosis of pts who remain comatose after cardiac arrest (QOE fair)

**Wijdicks et al. 2006 203-210**
This pooled analysis included 5 studies in which EEG recording was obtained generally within 3 days from CA. Generalized suppression to less than 20 µV, BS pattern with generalized epileptiform activity, or generalized periodic complexes on a flat background are associated with an unfavorable outcome. ATC pattern is not invariably associated to an unfavorable outcome. In this meta-analysis, the pooled FPR for poor outcome of malignant EEG patterns was 3% (95% CI: 0.9% to 11%).

**Young et al. 2005 159-164**
*EEG*: As the authors state “EEG categorization created groups with such small numbers that analysis was problematic”. However, there were no survivors among those few who had generalized epileptiform discharges or who had suppression with voltage less than 20 µV. The predictive performance of the criterion “presence of a pattern 1A or B at EEG” to predict a good outcome (survival) as reported by the authors were: sensitivity 89% and specificity 84%.

**Zandbergen et al. 1998 1808-1812**
EEG recordings with an isoelectric or burst-suppression pattern had a specificity of 100% in five of six relevant studies (pooled positive-likelihood ratio 9·0 [2.5–33.1]; 95%CI pooled false-positive test rate 0·2–5·9%).

**Zandbergen et al. 2006 62-8**
EEG was recorded at 72 hours. The predictive performance of EEG in this sample of patients is reported hereafter, together with data on SSEPs which were also studied by the authors.
Studies in samples (also) treated with therapeutic hypothermia

Rundgren et al. 2006 836-842

In this prospective inception cohort study (LOE P1) 34 consecutive hypothermia-treated cardiac arrest survivors were included. Amplitude-integrated EEG (aEEG) recording was initiated upon arrival at the ICU and continued until the patient regained consciousness or, if the patient remained in coma, no longer than 120 h. The aEEG patterns were classified into the following categories: extremely low voltage (flat; maximum voltage < 5 µV); discontinuous suppression-burst pattern; electrographic status epilepticus with recurrent epileptiform activity; and continuous EEG.

In patients not regaining consciousness, full supportive treatment was continued for at least 72 h after normothermia had been attained. The initial aEEG pattern was flat in 24 patients (71%), 7 patients (20%) showed a continuous aEEG, 2 patients (6%) showed a suppression-burst pattern, and 1 an alpha-coma pattern (3%) (Table 3). All patients with an initial continuous aEEG regained consciousness, whereas the outcome for patients with an initially flat aEEG was mixed and inconclusive. The three patients exhibiting an initial suppression-burst or alpha-coma pattern did not regain consciousness and died in hospital. At normothermia (mean 37 h after cardiac arrest), the aEEG pattern was discriminative for outcome. All 20 patients with a continuous aEEG at this time regained consciousness, whereas 14 patients with pathological aEEG patterns (flat, suppression-burst or status epilepticus) did not regain consciousness and died in hospital. Among the 20 surviving patients, at 6-month follow-up, a best CPC score of 1–2 (good outcome) was found in 18, while one patient had a best CPC score of 3 and one patient (best CPC 3) had died due to cardiac failure. Four patients were contacted by telephone only, and no patient was lost to follow-up. The ILCOR reviewer calculated the predictive performance of a pathological aEEG after restoration of normothermia to assess a poor outcome: sensitivity 100% (95% CI 78-100), specificity 100% (95% CI 84-100), i.e. FPR 0 (95% CI 0-16) Multivariate analysis was not performed. This LOE P1 study support a role for the presence of a pathological aEEG after restoration of normothermia to assess a poor outcome in patients who remain comatose after resuscitation from cardiac arrest who receive therapeutic hypothermia (QOE fair); however, after 72 hours of restoration of normothermia, a clinical neurological examination was performed in combination with bilateral somatosensory evoked potentials (SSEP); in patients with a GCS score of 3 or 4 and/or bilateral lack of cortical response, treatment was considered futile and active care was withdrawn, but this may have biased the results as the role of SSEPs in assessing prognosis of comatose survivors of cardiac arrest receiving therapeutic hypothermia is less robust as compared to comatose survivors of cardiac arrest receiving not therapeutic hypothermia.

Rossetti et al. 2007 255-260

In this retrospective series, PSE (RR= 6.3; 95% CI 2.1, 19.1), rhythm other than VF on emergency team arrival and time to ROSC [<25 vs. >25 min] were associated with an increased risk of dying at univariate analysis. Mortality was also studied using a multivariate logistic model including PSE, type of cardiac rhythm, time to ROSC, and hypothermic treatment. This model was rejected by the Lemeshow goodness of fit test (p= 0.05) and therefore the authors concluded that an independent predictive role of PSE was not demonstrated in the whole study population (receiving and not receiving therapeutic hypothermia). However, a subgroup analysis in pts who received hypothermic therapy, resulted in an acceptable goodness of fit (p=0.24) showing that PSE (OR=14.4; 95% CI 2.8, 74.8) and asystole or PEA on emergency team arrival (OR=6.3; 95% CI 1.2, 32.1) were significantly associated with an increased risk of death, thus generating the hypothesis (to be verified in future research) that PSE in patients receiving therapeutic hypothermia may be predictive of outcome.

Stammet et al. 2009 437-42

In this LOE P1 study, 45 consecutive patients who remained comatose after CA and who were treated with therapeutic hypothermia (TH) were studied with EEG processed to derive the BIS. TH was started as soon as possible after arrival in the hospital; BIS was evaluated on admission to ICU. Post resuscitative outcome was determined by GCS and CPC.
score at the end of ICU stay and by CPC score at 6 months (blinded to BIS). CPC 1 and CPC 2 were regarded as good outcome, whereas CPC 3, 4 and 5 were considered as bad outcome. BIS value of 0 had a positive predictive value of 100% for bad neurological outcome. The negative predictive value was 55%. Confidence intervals for an unfavorable outcome at 6 months were recalculated by the ILCOR reviewer: BIS value of 0 had a sensitivity of 50 % (95%CI 33-67) and a specificity of 100% (95%CI 82-100%), i.e. FPR 0 (95%CI 0-18) to predict an unfavorable outcome. This study supports a role of EEG, as processed to obtain the BIS, to assess the prognosis of comatose survivors of cardiac arrest receiving therapeutic hypothermia, but these findings need to be confirmed by larger series before this prognostic tool could be recommended.

Auditory evoked potentials

**BAEPs:**

3 studies were included in the present analysis after careful review. A role of BAEPs to assess prognosis of comatose survivors of cardiac arrest was supported by 2 LOE P1 studies, QOE fair (LOE P1: Inception (prospective) cohort studies (or meta-analyses of inception cohort studies), or validation of Clinical Decision Rule (CDR)); 1 study was neutral (LOE P1 QOE fair); no study provided evidence opposing a role of BAEPs to assess prognosis of comatose survivors of cardiac arrest.

**Studies in samples not treated with therapeutic hypothermia**

Fischer et al. 2006 1520-4

All patients in whom MLAEPs or SSEPs were abolished did not awaken. (100% specificity, with FPR as calculated by the ILCOR reviewer respectively of 0 (95% CI 0-8) for the absence of MLAEP and of 0 (95% CI-0-8) for the absence of N20). All patients in whom mismatch negativity (MMN) was present awakened (100% specificity). Complete data on sensitivity, specificity, PPV and NPV for all the prognostic variables are reported in the Table 2 of the study and summarized in the table below. The highest levels of sensitivity were offered by BAEPs, SEPs N20, SEPs P24, MLAEPs (sensitivity 100%, 95%CI 86-100 for all of them); the highest levels of specificity were offered by MMN (specificity 100%, 95%CI 93-100), i.e. FPR 0 (95%CI 0-7); the highest levels of PPV was offered by MMN (100%, 95%CI 78-100), the highest levels of NPV were offered by BAEPs, SEPs N20, SEPs P24, MLAEPs (PPV 100%, 95%CI 5-100, 79-100, 78-100, 86-100 respectively);

<table>
<thead>
<tr>
<th>Predictor of awakening</th>
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<th>Positive predictive value % (95% CI)</th>
<th>Negative predictive value % (95% CI)</th>
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<td>MLAEP</td>
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<td>100 (76-100)</td>
<td>94 (71-93)</td>
</tr>
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</table>

**Studies in samples (also) treated with therapeutic hypothermia**

Sakurai et al. 2006 52-58

Therapeutic hypothermia was used in all patients but ABR were recorded immediately after ROSC, before therapeutic hypothermia was initiated. Among the 16 patients with wave V, 8 had a favorable outcome and 8 had an unfavorable outcome. Among the 10 patients lacking ABR wave V all 10 had an unfavorable outcome. The absence of ABR V wave had a sensitivity of 55.6 and a specificity of 100% to predict an unfavorable outcome. Using the data reported by the authors, the reviewer also computed the 95% confidence interval for both sensitivity and specificity, which resulted 34-75 % and 68-100% respectively, i.e. FPR 0 (95%CI 0-32).

Tiainen et al. 2005 1736-40

Brainstem auditory evoked potentials (BAEPs) were recorded 24 –28 hrs after CA. All latencies were significantly longer in hypothermia-treated patients. Within the treatment groups the latencies did not correlate with age, awakening,
or achieving favorable outcome. Moreover, in several cases the presence/absence of at least one waveform at BAEPs was later recognized as a consequence of a hearing deficit. In conclusion, the authors state that in this study the addition of BAEP recording to SEP recording did not increase sensitivity for identifying patients with poor prognosis, as compared with SSEP recording alone; however formal data on the predictive performance of the presence/absence of at least one waveform at BAEPs were not reported and the study was ranked as neutral.

**MLAEPs:**

2 studies were included in the present analysis after careful review. A role of MLAEPs to assess prognosis of comatose survivors of cardiac arrest was supported by 1 LOE P1 studies, QOE fair (LOE P1: Inception (prospective) cohort studies (or meta-analyses of inception cohort studies), or validation of Clinical Decision Rule (CDR)); and 1 LOE P3 study, QOE fair (LOE P3: Retrospective cohort studies); no study was neutral or provided evidence opposing a role of MLAEPs to assess prognosis of comatose survivors of cardiac arrest.

**Studies in samples not treated with therapeutic hypothermia**

Logi et al. 2003 1615-1627

EP studies were not performed in a protocol-specified time window, but “when the contribution of EPs to prognosis was expected to be useful” with a possible assessment bias. With this limitation, MLAEPs (grades 1 and 2 opposed to grade 3) had a sensitivity of 40% (37% in case of bilateral absence of cortical components), a specificity of 64% (100% in case of bilateral absence of cortical components), a PPV of 71% and NPV of 32% to predict an unfavorable outcome.

Fischer et al. 2006 1520-4

All patients in whom SSEPs or MLAEPs were abolished did not awaken. (100% specificity, with FPR as calculated by the ILCOR reviewer respectively of 0 (95% CI 0-8) for the absence of N20 and of 0 (95% CI 0-8) for the absence of MLAEP).). All patients in whom MMN was present awakened (100% specificity). Complete data on sensitivity, specificity, PPV and NPV for awakening of all the prognostic variables are reported in the Table 2 of the study and are summarized in the table below. The highest levels of sensitivity were offered by BAEPs, SEPs N20, SEPs P24, MLAEPs (sensitivity 100%, 95%CI 86-100 for all of them); the highest levels of specificity were offered by MMN (specificity 100%, 95%CI 93-100); the highest levels of PPV was offered by MMN (100%, 95%CI 78-100); the highest levels of NPV were offered by BAEPs, SEPs N20, SEPs P24, MLAEPs (PPV 100%, 95%CI 5-100, 79-100, 78-100, 86-100 respectively).

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<tr>
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<td>BAEP</td>
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<td>33 (21-46)</td>
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<td>(normal vs abnormal)</td>
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<tr>
<td>MLAEP</td>
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<td>(normal vs. absent)</td>
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<tr>
<td>Auditory N100</td>
<td>75 (51-91)</td>
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<tr>
<td>MMN</td>
<td>60 (36-81)</td>
<td>100 (63-100)</td>
<td>100 (78-100)</td>
<td>84 (71-93)</td>
</tr>
<tr>
<td>(present vs. absent)</td>
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</table>

**Studies in samples (also) treated with therapeutic hypothermia**

None

**Auditory N100 and mismatch negativity**

1 study was included in the present analysis after careful review. A role of auditory N100 and mismatch negativity to assess prognosis of comatose survivors of cardiac arrest was supported by 1 LOE P1 study, QOE fair (LOE P1: Inception (prospective) cohort studies (or meta-analyses of inception cohort studies), or validation of Clinical Decision Rule (CDR)); no study was neutral or provided evidence opposing a role of MLAEPs to assess prognosis of comatose survivors of cardiac arrest.

**Studies in samples not treated with therapeutic hypothermia**
Fischer et al. 2006 1520-4
All patients in whom SSEPs or MLAEPs were abolished did not awaken, (100% specificity), with FPR as calculated by the ILCOR reviewer respectively of 0 (95% CI 0-8) for the absence of N20 and of 0 (95% CI 0-8)).. All patients in whom MMN was present awakened (100% specificity for awakening). Complete data on sensitivity, specificity, PPV and NPV for awakening of all the prognostic variables are reported in the Table 2 of the study and are summarized in the table below. The highest levels of sensitivity were offered by BAEPs, SEPs N20, SEPs P24, MLAEPs (sensitivity 100%, 95%CI 86-100 for all of them); the highest levels of specificity were offered by MMN (specificity 100%, 95%CI 93-100); the highest levels of PPV was offered by MMN (specificity 100%, 95%CI 78-100); the highest levels of NPV were offered by BAEPs, SEPs N20, SEPs P24, MLAEPs (PPV 100%, 95%CI 5-100, 79-100, 78-100, 86-100 respectively).

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<tr>
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<td>MMN (present vs. absent)</td>
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<td>100 (63-100)</td>
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Studies in samples (also) treated with therapeutic hypothermia
None

Acknowledgements:
Andrea Scapigliati, MD
Catholic University of the Sacred Heart
Rome, Italy

Citation List

Study design: not unambiguously characterized as prospective and therefore ranked as retrospective (LOE P3)
Study population: 21 comatose survivors of cardiac arrest
Sedative treatment: not stated
Hypothermia: not stated
EP study/ies under evaluation: EEG performed within 72 h after CPR. EEG findings were classified according to the five Hockaday grades
Other prognostic factors assessed: Brain CT scan findings
Outcome assessed: The Glasgow outcome scale (GOS) applied 3 months after CPR was used for prognosis.
Evidence of treatment bias: not stated whether treatment was affected by EEG results
Results: Of the nine patients with grade 1 and 2 EEGs, eight had a good outcome (5 recovered satisfactorily and 3 remained moderately disabled). Of the eight patients with grade 4 and 5 EEGs, 7 had a poor outcome (3 died and 4 remained in a persistent vegetative state). On the other hand, there was no correlation between early CT features and prognosis except for 2 severe cases
Multivariate analysis: No multivariate analysis was performed
Cut off proposed and corresponding predictive performance: not applicable
Conclusions and quality of evidence: In this study (LOE P3), the authors have found that EEG grade, as recorded 72 hours post CA, has a univariate role in predicting prognosis of comatose survivors of cardiac arrest. The authors do not propose estimates of sensitivity, specificity probably because of the small number of patients and the small number of events. However, the ILCOR reviewer has made an estimate of sensitivity and specificity of EEG grades 1 and 2 to predict a favorable outcome (good recovery or mild disability) which resulted 80% (95%CI 49-94) and 91 % (95% CI 62-98, i.e. FPR 9 (95%CI 2-38)) and of sensitivity and specificity of EEG grade 5 to predict an unfavorable outcome (severe disability, vegetative state, death) which resulted 9% (95%CI 1,6-38) and 100 % (95% CI 72-100), i.e. FPR 0 (95%CI 0-
In conclusion the study supports a role of EEG pattern (Hockaday grade) at 72 h after to assess prognosis of comatose survivors of cardiac arrest (QOE fair).


Study design: not unambiguously prospective and therefore ranked as retrospective (LOE P3)
Study population: 305 comatose patients after cardiopulmonary resuscitation (in-hospital 70 and out-of-hospital 235). Patients with traumatic cardiac arrest, exsanguinations and intoxication and patients who awoke within 24 h after cardiac arrest were excluded
Sedative treatment: not stated
Hypothermia: not stated
EP study/ies under evaluation: SEPs were recorded within 72 h after cardiac arrest. The authors measured the short latency SEP peaks N9, P15, N20, P25 and the long latency SEP peaks N35 and N70.
Other prognostic factors assessed: none
Outcome assessed: The authors used the CPC score to assess cerebral performance outcome (unclear timing). Patients with CPC = 2 were classified as having a favorable outcome without hypoxic-ischemic brain damage, whereas patients with CPC > 2 were classified as having a poor outcome with hypoxic-ischemic brain damage
Evidence of treatment bias: not stated whether treatment was affected by EP study results
Results: Two hundred and thirty-two patients showed a CPC outcome score of > 2 and were therefore classified as having hypoxic-ischemic brain damage. One hundred and seventy-four of these patients died, 35 patients remained in a persistent vegetative state and 23 patients showed severe cerebral disability. The remaining 73 patients were classified as having a favorable outcome without hypoxic-ischemic brain damage with a CPC of ≤ 2. Patients with hypoxic-ischemic brain damage (n = 232) showed a decrease of detectable peaks along the thalamo-cortical afferent pathway: N13, P15, N20, P25 and N70 peaks were detectable in 99%, 63%, 59%, 55% and 44% patients, respectively; the decrease of detectable SEP peaks was statistically significant between the cervical cord (N13) and the thalamus (P15) and primary sensory cortex (N20, P25; P = 0.005); a further significant decrease of detectable peaks was seen between the short-latency cortical SEP peaks (N20, P25) and the long-latency SEP peaks (N35, N70; P = 0.032). Cortical N20 and P25 peaks were preserved in all 73 patients with favorable outcome, whereas in the poor outcome group (n=232) 95 and 104 patients, respectively, had lost these peaks. Furthermore, in patients with hypoxic-ischemic brain damage and detectable SEP peaks, P15, N20, P25, N35 and N70, peak latencies were prolonged (P < 0.05) and N20 and N70 amplitudes were decreased (P < 0.05) compared with patients without hypoxic-ischemic brain damage. Regarding long-latency SEPs in the patients with hypoxic-ischemic brain damage, N35 and N70 peaks were detectable in only 104 and 102 patients, respectively out of 232; in any case, peak latencies and amplitudes of long-latency potentials, if present, were significantly different between the two outcome groups
Multivariate analysis: No multivariate analysis was performed
Cut off proposed and corresponding predictive performance: Sensitivity and specificity have not been reported by the authors. The reviewer has calculated, on the basis of the published data, a sensitivity of 41 % (95% CI 35-47) and a specificity of 100% (95%CI-95-100, i.e. FPR 0 (95%CI 0-5)) for the absence of N20 to predict an unfavorable outcome. Conclusions and quality of evidence: The study provides evidence that the extent of hypoxic-ischemic brain damage in cardiac arrest survivors increases along the afferent sensory pathway. The reviewer has calculated, on the basis of the published data, a sensitivity of 41 % (95% CI 35-47) and a specificity of 100% (95%CI-95-100, i.e. FPR 0 (95%CI 0-5)) for the absence of N20 to predict an unfavorable outcome. In conclusion the study supports a role of SSEPs to assess prognosis of comatose survivors of cardiac arrest (QOE fair)


Study design: A retrospective analysis of a previously published series. Patients were included in the present analysis if they exhibited an alpha or theta pattern at EEG; only the outcome of pts with alpha or theta pattern at EEG is presented and therefore the study was ranked LOE P4
Study population: 14 patients who remained comatose after resuscitation from cardiac arrest and presented an alpha or theta pattern at EEG (alpha-theta coma, ATC)
Sedative treatment: not stated
Hypothermia: not stated, generally not used at the time of original study (Bassetti et al. 1996 610-615)
**EP study/ies under evaluation:** EEG for alpha or theta patterns; Patients with normally reactive and normally (occipitally) distributed predominant alpha, alpha-theta or theta EEG activities were not considered. Patients with associated factors likely to affect the EEG such as metabolic disorders, head trauma or drug-induced coma were also excluded. ATC was classified as *complete ATC* (with a monotonous, continuous, frontally distributed, areactive EEG) and *incomplete ATC* (not monotonous, posteriorly accentuated or partially reactive EEG tracings)

**Other prognostic factors assessed:** GCS and brainstem reflexes

**Outcome assessed:** the best cerebral performance achieved at any time over a follow-up period of 1 year. Good outcome was defined by the reappearance of cognition corresponding to a GOS score of 3-5. Bad outcome was defined by a persistent vegetative state or death (GOS 1-2).

**Evidence of treatment bias:** it was a retrospective analysis whose result were obviously not available during ICU stay and therefore absence of treatment bias can be assumed

**Results:** All of the pts (9/9) with complete ATC had an unfavorable outcome. Two out of five (2/5) pts with incomplete ATC had an unfavorable outcome while 3/5 regained cognition, even though two of them remained dependent in activities of daily living. Extracting data also from the original study by Bassetti et al. 1996 610-615, the ILCOR reviewer estimated FPR at 0% (95%CI 0-25).

**Multivariate analysis:** not performed

**Cut off proposed and corresponding predictive performance:** non provided

**Conclusions:** This LOE P4 study supports a role of EEG (alpha theta coma pattern) to predict prognosis of comatose survivors of cardiac arrest (QOE fair)


**Study design:** Case series collected to assess a possible role of BIS in monitoring the quality of resuscitation; the use of BIS was not intended to prognosticate comatose survivors of cardiac arrest. (LOE P5)

**Study population:** convenience sample of 21 OHCA and 1 cadaver. Only 1 pt remained comatose after cardiac arrest.

**Sedative treatment:** not stated

**Hypothermia:** no

**EP study/ies under evaluation:** BIS as recorded during resuscitation efforts for OHCA

**Other prognostic factors assessed:** no

**Outcome assessed:** survival and neurological outcome

**Evidence of treatment bias:** no

**Results:** only 1 pts remained comatose after ROSC, his BIS score was good and recovered.

**Multivariate analysis:** not performed

**Conclusion and quality of evidence:** this study (LOE P5) describes a single case of a comatose survivor of cardiac arrest whose BIS score was good and recovered thus suggesting a possible role of BIS in assessing prognosis of comatose survivors of cardiac arrest (QOE poor)


**Study design:** Prospective inception cohort study (LOE P1)

**Study population:** Sixty-two consecutive patients still comatose 24 hrs after cardiopulmonary resuscitation of out-of-hospital cardiac arrest. Brain-dead patients were excluded

**Sedative treatment:** No sedatives were being administered at the time of the EP recordings

**Hypothermia:** No patient was under hypothermic therapy at the time of the EP recordings. It is unclear whether pts were treated with hypothermia in other phases of ICU stay

**EP study/ies under evaluation:** somatosensory, auditory, and cognitive evoked potentials were recorded within an average period of 8 days after cardiac arrest. Of note, the authors stated that recordings of evoked potentials were performed when they were expected to be useful. For BAEPs grades 1 and 2 were considered as normal. For MLAEPs grades 1, 2, and 3 were considered as normal. N100 was graded as present or absent, and MMN was also graded as present or absent. For SEPs, grades 1 and 2 were considered as normal.

**Other prognostic factors assessed:** clinical variables age, GCS score on admission, pupillary light reflex on the day of EP recordings

**Outcome assessed:** the patients were followed for 12 months and classified as awake or nonawake (permanent vegetative state or death). In more detail, one year after the onset of coma, all patients were evaluated and classified according to the GOS (1, death; 2, permanent vegetative state; 3, severe disability; 4, moderate disability; 5, good recovery); the authors also added two additional categories: the minimally conscious and patients who awoke and then died in the follow-up phase, who were referred as “unrelated deaths.” In the statistical analysis, the authors classified
as “awake” at 12 months those patients who, 1 yr after coma onset, were awake with complete recovery or moderate or severe disability as well as minimally conscious patients and unrelated deaths. Patients in a permanent vegetative state or whose death was related to the coma were classified as “unawake”.

Evidence of treatment bias: the authors recognize the possibility that the results of electrophysiological studies may have affected treatment decisions

Results: The time between coma onset and the recording of EPs ranged between 1 and 56 days (mean 8.1 ± 10.7 days).

Univariate analysis: All patients in whom SSEPs or MLAEPs were abolished did not awaken (100% specificity, FPR as calculated from the ILCOR reviewer 0 (95% CI 0-7) to predict a poor outcome). All patients in MMN was present awakened (100% specificity). Complete data on sensitivity, specificity, PPV and NPV for awakening of all the prognostic variables are reported in the Table 2 of the study, while a selection of results is reported in the table below. The highest levels of sensitivity for awakening were offered by BAEPs, SEPs N20, SEPs P24, MLAEPs (sensitivity 100%, 95%CI 86-100 for all of them); the highest levels of specificity were offered by MMN (specificity 100%, 95%CI 93-100); the highest levels of PPV was offered by MMN (100%, 95%CI 78-100); the highest levels of NPV were offered by BAEPs, SEPs N20, SEPs P24, MLAEPs (PPV 100%, 95%CI 5-100, 79-100, 78-100, 86-100 respectively);

Multivariate analysis: On the decision tree, the awakening/nonawakening explicative variables were, by order of importance, MMN, pupillary reactivity, and somatosensory evoked potentials

Cut off proposed and corresponding predictive performance: see above

Conclusions and quality of evidence: The present study LOE P1 supports a predictive role of BAEPs, MLAEPs, SEPs, auditory N100, and MMN to assess the neurological prognosis of pts comatose after resuscitation from cardiac arrest (QOE fair).


Study design: Prospective inception cohort study (LOE P1) designed to assess the time course of SSEP during the first 48 hours of ICU stay in pts who remain comatose after cardiac arrest.

Study population: Twenty-five patients who remained comatose after cardiac arrest

Sedative treatment: All patients received midazolam and fentanyln

Hypothermia: pts were unambiguously kept normothermic

EP study/ies under evaluation: SSEPs. Both short and long latency evoked potentials were recorded at 4, 12, 24 and 48 hours (48 h in 10 out of 25 pts). Reported latencies and amplitudes are mean of averaged values for right side and left side stimulation. It is unclear how unilateral peak absence was managed.

Other prognostic factors assessed: None

Outcome assessed: best CPC score within 6 months. CPC 1-2 were defined as a favorable outcome, CPC 3-5 as unfavorable outcome.

Evidence of treatment bias: It was not unambiguously stated whether results of SSEP affected treatment.

Results: Clinical outcome was favorable in 7 out of 25 pts and unfavorable in the other 18 (14 died and 4 remained in a persistent vegetative state)

Univariate analysis: The authors report that the presence, latency and amplitude of the explored components of SSEP changed at different study times. In more detail, N13 was present at 4, 12 and 24 hours in all 25 pts; N20 was present in 24 out of 25 pts at 4 h, in 22 at 12 and 24 hours; all patients with absent N20 component at any study time had an unfavorable course (2 deaths, 1 persistent vegetative state); of interest, N20 latencies presented a progressive shortening, meaning an improvement of conduction time, over the study times (4, 12 and 24 hours).

Multivariate analysis: Not performed
Cut off proposed and corresponding predictive performance: The authors report that sensitivity of the N20 peak latency to predict an unfavorable outcome was 6% (95% CI 4-7%) at 4h and 17% (95% CI 13-20%) at 24 hours while specificity was 100% (95% CI 80-100%, i.e. FPR 0 (95% CI 0-20)) both at 4 and 24 hours. Sensitivity and specificity of the absence of the N20 component to predict an unfavorable outcome were computed by the reviewer on the basis of the published data: sensitivity 6% (95% CI 1-25%) at 4h and 12% (95% CI 6-39%) at 24 hours while specificity was 100% (95% CI 65-100%, i.e. FPR 0 (95% CI 0-35)) both at 4 and 24 hours. Sensitivity of the N70 peak latency (critical cutoff 130 ms) was 100% (95% CI 80-100%) at 4 hours but decreased to 83% (95% CI 67-100%) at 24 hours while the corresponding specificity was 43% (95% CI 34-51%, i.e. FPR 57 (95% CI 49-66)) at 4 hours and increased at 100% (95% CI 80-100%, i.e. FPR 0 (95% CI 0-20)) at 24 hours. The predictive performance of the above mentioned criteria at 4, 24 and 48 hours was also assessed in a subset of 10 pts in whom data at 48 hours were available, with possible selection bias. In this subset of pts sensitivity at 4, 24 and 48 hours were respectively 83%, 83% and 100% while the corresponding specificity levels were 50%, 100% and 75%.

Conclusions and quality of evidence. The present prospective inception cohort study (LOE P1) supports a role of SSEP (N20 and N70 components) to assess prognosis of comatose survivors of cardiac arrest (QOE fair)


Study design: not explicitly prospective and therefore ranked as retrospective cohort study on consecutive comatose pts admitted to ICU (LOE P3)

Study population: heterogeneous, not only cardiac arrest (cardiac arrest 49 pts, traumatic brain injury 22 pts, stroke 45 pts, complications of neurosurgery 12 pts and encephalitis 3 pts)

EP study/ies under evaluation: SEPs and MLAEPs; The authors classified SEPs in 3 categories defined as follows: grade (1) normal SEPs, at least on one side; grade (2) bilateral amplitude reduction; grade (3) bilateral absence of cortical responses. MLAEPs were classified as: (1) normal, (2) isolated delay of Pa latency without Na–Pa amplitude reduction, (3) Na–Pa amplitude reduction (4) no Pa detected. Of interest, EP studies were not performed in a protocol-specified time window, but "when the contribution of EPs to prognosis was expected to be useful" with a possible assessment bias

Outcome assessed: GOS at 3 months

Evidence of treatment bias: not explicitly stated that treatment was not affected by results of EP studies

Results: Results in different pts groups are presented. For the purposes of our analysis, we will focus on comatose pts after cardiac arrest (49 out of 131 pts).

Univariate analysis: 29/49 had grade 1 SEPs (59.2%) and 11 of them recovered, 16/49 had grade 2 (32.6%) and 4/49 had grade 3 SEPs (8.2%) and none of them recovered. 22/49 (44.9%) had grades 1 or 2 MLAEPs and 7 of them recovered; 14/49 (28.5%) had grade 3 MLAEPs and 4 of them recovered, 13/49 (26.5%) had grade 4 MLAEPs and none recovered.

Multivariate analysis: not performed

Cut off proposed and corresponding predictive performance: SSEPs (grade 1 as opposed to grade 2) had a sensitivity of 47% (10% in case of bilateral absence of cortical components), a specificity of 100% (100% in case of bilateral absence of cortical components), a positive predictive value of 100% and a negative predictive value of 38% to predict an unfavorable outcome. MLAEPs (grades 1 and 2 opposed to grade 3) had a sensitivity of 40% (37% in case of bilateral absence of cortical components), a specificity of 64% (100% in case of bilateral absence of cortical components), a PPV of 71% and NPV of 32% to predict an unfavorable outcome.

Conclusions and quality of evidence: This LOE P3 study supports a role of SEPs and MLAEPs to assess prognosis of comatose survivors of cardiac arrest (QOE fair)


Study design: Prospective inception cohort study (LOE P1)

Study population: 162 pts who remained comatose after resuscitation from cardiac arrest (51 in-hospital, 111 out-of-hospital)

Sedative treatment: At the time of evoked potential measurement, 91 patients were sedated continuously by midazolam and fentanyl or sufentanyl.

Hypothermia: Patients who were hypothermic (body temperature of <35°C [95°F]) were excluded from the study

EP study/ies under evaluation: SSEPs. Short- and long-latency sensory evoked potentials were recorded within 8 and 24 hrs after cardiac arrest.
Other prognostic factors assessed: Clinical judgment of experienced emergency physician on the basis of data available at three time intervals after cardiac arrest. Initially, prehospital data including age, underlying diseases, presumed cause of cardiac arrest, approximate time between recognition of collapse and calling the emergency medical system, initial, electrocardiographic rhythm, time interval from collapse to basic life support and advanced life support, time from collapse to return of spontaneous circulation, medication during resuscitation, number of electrical defibrillations, and heart rate, and the blood pressure and Glasgow Coma Scale score at arrival in the emergency department (PRED 1). Subsequently, the physicians received additional detailed clinical and laboratory data that were obtained within 1 hr after the patient's arrival at the emergency department (heart rate, rhythm, blood pressure, ventilation mode, urinary output, Glasgow Coma Scale score, pupillary responses, and medical treatment and laboratory data including lactate and blood gas analysis) (PRED 2). During the third step, the physicians predicted the outcome after assessing clinical and laboratory data acquired 24 hrs after cardiopulmonary resuscitation (PRED 3).

Outcome assessed: the final outcome was assessed within 6 months after cardiac arrest. CPCs 1 and 2 were considered a favorable outcome, and CPCs 3-5 were considered a bad outcome. The best CPC score achieved within 6 months was used for analysis.

Evidence of treatment bias: not explicitly stated whether results of electrophysiological studies affected treatment

Results: Within 6 months after cardiopulmonary resuscitation, 36/162 of the cardiac arrest survivors (22%) had a favorable outcome (CPC 1-2), whereas the remaining 126 patients (78%) died (n = 105; CPC 5), remained in a persistent vegetative state (n = 15; CPC 4), or had severe neurologic disabilities (n = 6; CPC ).

Univariate analysis: Forty-six patients had a bilateral loss of cortical sensory evoked potential N20 peaks. None of these 46 patients survived. Of the 113 patients with an N70 peak latency of > 130 msec (n = 32) or an absent N70 peak (n = 81), 112 had an unfavorable outcome. By using a cutoff of 130 msec, the N70 peak latency alone had a sensitivity of 94%, a specificity of 97%, a positive predictive value of 98%, and a negative predictive value of 82%. The predictive accuracy of the N70 peak latency was significantly higher than the clinical assessment 24 hrs after cardiac arrest (91% vs. 76%, p = .0003).

Multivariate analysis: Not performed

Conclusions and quality of evidence: This LOE P1 study provides evidence in favor of SSEPs (N20-N35-N70) to assess prognosis of comatose survivors of cardiac arrest (QOE fair).


Study design: prospective inception cohort study (LOE P1)
Study population: 30 patients who remained comatose after resuscitation from out-of-hospital cardiac arrest
Sedative treatment: use of vecuronium was allowed if required to abolish artifacts
Hypothermia: no
EP study/ies under evaluation: SSEPs recorded immediately after return of spontaneous circulation (within 3 hours after arrest)
Other prognostic factors assessed: GCS score, spontaneous breathing, light reflex
Outcome assessed: Patients were assessed for recovery of consciousness for up to 1 month after cardiac arrest.
Evidence of treatment bias: It was not explicitly stated whether results of SSEP affected treatment
Results: In the initial study all 30 patients showed the Erb's point potential and the N11-13 component, while only 12 (40%) showed cortical activity. Patients were assessed neurologically for recovery of consciousness until 1 month after cardiac arrest. Of these 12 patients 8 recovered consciousness within 10 days, while all patients without cortical activity died without opening their eyes. Sensitivity and specificity of absence of N20 to predict a favorable outcome were calculated by the authors and resulted 81.8 and 100.0 % respectively; 95% CI were not reported and have been calculated from the original data by the reviewer and resulted 61-92% and 67-100%, respectively i.e. FPR 0 (95%CI 0-33).

Multivariate analysis: Not performed

Conclusions and quality of evidence: The present LOE P1 study supports a role of SSEPs in assessing prognosis of comatose survivors of cardiac arrest (QOE fair).

Study design: retrospective observation of consecutive comatose survivors of cardiac arrest, including subjects treated with hypothermia (LOE P3).

Study population: 107 pts extracted from a population of 166 consecutive comatose survivors of cardiac arrest (selection criteria: EEG available)

Sedative treatment: neuromuscular blockade and pharmacologic sedation with midazolam and fentanyl were used (at least in pts in whom therapeutic hypothermia was used); 42 pts also received antiepileptic drugs (data extracted from table 1)

Hypothermia: 63 subjects were treated with therapeutic hypothermia (38+25, extracted from Table 1)

EP study/ies under evaluation: EEG, analyzed for the presence of SE. SE was defined by prolonged (>5 minutes) spontaneous or stimulus-induced occurrence of repetitive or rhythmic focal or generalized spikes, sharp waves, spike and waves, or rhythmic waves evolving in amplitude, frequency, or field. Although periodic epileptiform discharges (PEDs) and burst-suppression represent controversial patterns the authors considered spontaneous burst-suppression with epileptiform bursts and PEDs as electrographic SE, since these features are often associated with myoclonus in post anoxic patients

Other prognostic factors assessed: age, gender, type and length of cardiac arrest, occurrence of circulatory shock, presence of therapeutic hypothermia

Outcome assessed: Survival and neurologic outcome according to the CPC were assessed at hospital discharge. Outcomes were assessed in a blinded fashion.

Evidence of treatment bias: not specified whether treatment was affected by EEG results

Results: 87 (77%) patients had a poor outcome and 20 (23%) had an excellent or moderate outcome.
Univariate analysis: In univariate analysis, PSE (RR = 6.3; 95% CI 2.1, 19.1), rhythm other than VF on emergency team arrival (RR = 2.3; 95% CI 1.1, 4.6), and time to ROSC [<25 vs. >25 min] (RR = 2.2; 95% CI 1.2, 4.2) were associated with an increased risk of dying. Hypothermic treatment (RR = 0.8; 95% CI 0.6, 1.1) was non-significantly associated with a more favorable outcome.

Multivariate analysis: Mortality was studied using a multivariate logistic model including PSE, type of cardiac rhythm, time to ROSC, and hypothermic treatment. This model was rejected by the Lemeshow goodness of fit test (p = 0.05) and therefore the authors concluded that an independent predictive role of PSE was not demonstrated in the whole study population (receiving and not receiving therapeutic hypothermia). However, a subgroup analysis in pts who received hypothermic therapy, resulted in an acceptable goodness of fit (p = 0.24) showing that PSE (OR = 14.4; 95% CI 2.8, 74.8) and asystole or PEA on emergency team arrival (OR = 6.3; 95% CI 1.2, 32.1) were significantly associated with an increased risk of death, thus generating the hypothesis (to be verified in future research) that PSE in patients receiving therapeutic hypothermia may be predictive of outcome.

Cut off proposed and corresponding predictive performance: n.a.

Conclusions and quality of evidence: The study was a retrospective cohort study (LOE P3). Cases were selected from a consecutive series of comatose survivors of cardiac arrest according to the availability of EEG. However, clinical characteristics of pts with EEG were significantly different compared to those of pts in whom EEG was not available, and the results of this study cannot be extrapolated to the whole population of comatose survivors of cardiac arrest. Moreover, even if PSE appeared to be predictive of death at univariate analysis, a multivariate logistic regression including all univariate predictors failed to confirm an independent predictive role of PSE, which was observed only in a subgroup analysis of pts in whom therapeutic hypothermia was used. In conclusion the study suggests a possible role of PSE to assess prognosis of comatose survivors of cardiac arrest, but this finding need to be confirmed (QOE fair).


Study design: not unambiguously characterized as prospective, therefore ranked as a retrospective cohort study (LOE P3). Includes an extensive review of the literature.

Study population: 50 patients who remained comatose for at least 6 hours after resuscitation from cardiac arrest but with preserved brainstem reflexes at the outset. Pts in whom SSEPs results could be altered by an underlying neurological disease were excluded.

Sedative treatment: not stated

Hypothermia: not stated

EP study/ies under evaluation: SSEPs (median nerve stimulation recorded within 48 hours); SSEPs were classified as delayed if prolonged over 3SD of the mean.

Other prognostic factors assessed: None

Outcome assessed: neurological recovery and death

Evidence of treatment bias: treatment was not affected by SSEPs recording results

Results: Univariate analysis: Patients were grouped in G1 (recovery of consciousness 6 pts [2 of them died after recovery of consciousness ]), G2 (persistence of neurologic impairment, 9 pts) and finally G3 (death without awakening/persistent vegetative state, 35 pts). In G1 5/6 pts had normal SSEPs; 1/6 pts showed a mild unilateral delay in the N20 peak. In G2 6/9 pts had normal SSEPs; 3/9 pts had unilateral or bilateral delays in the N20 peak. In G3 5/35 pts had normal SSEPs; 7/35 had unilateral or bilateral delays in the N20 peak; 23/35 had bilateral absence of N20. Of note, all pts with bilateral absence of N20 died.

Multivariate analysis: Not performed

Cut off proposed and corresponding predictive performance: Several indicators of predictive performance were reported by the authors: normal N20: sensitivity and positive predictive value for neurological recovery 100% and 36%, respectively; delayed N20: sensitivity and positive predictive value for neurological recovery 33% and 43%, respectively; absent N20: sensitivity and positive predictive value for death of 68% and 100%, respectively. Other indexes of predictive performance have been recalculated by the reviewer on the basis of published data: abnormal N20 (delayed or absent) had a sensitivity of 75% (95%CI 61-85) and a specificity of 83% (95%CI 44-97, i.e. FPR 27 (95%CI 3-56)) to predict an unfavorable outcome (persistent neurologic impairment, persistent vegetative state, death without awakening); bilateral absence of N20 had a sensitivity of 52% (95%CI 38-66) and a specificity of 100% (95%CI 61-100, i.e. FPR 0 (95%CI 0-39)) to predict an unfavorable outcome (persistent neurological impairment, persistent vegetative state, death without awakening)

Conclusions and quality of evidence: This retrospective cohort study (LOE P3) supports a predictive role of SSEPs (N20 component) to assess the prognosis of comatose survivors of cardiac arrest (QOE fair).

Study design: prospective inception cohort study (LOE P1)
Study population: 26 patients resuscitated from out-of-hospital cardiac arrest. It was not explicitly stated that the patients were comatose, but they were most likely so as they were treated with therapeutic hypothermia.

Sedative treatment: All patients were sedated by intravenous midazolam and buprenorphine with adjustment of the doses as needed for the management of mechanical ventilation. To prevent shivering, paralysis was induced by a continuous infusion of pancuronium

Hypothermia: therapeutic hypothermia was used in all patients but ABR were recorded immediately after ROSC, before therapeutic hypothermia was initiated

EP study/ies under evaluation: auditory brainstem response (ABR) wave V

Other prognostic factors assessed: cardiac etiology, VF/VT as the initial rhythm, and the presence of a witness during the arrest

Outcome assessed: the primary outcome was a favorable neurological outcome with hospital discharge or transfer, defined as a CPC of 1 (good recovery) or 2 (moderate disability) on a five-category scale. The other three categories, namely, 3 (severe disability), 4 (a vegetative state), and 5 (death), were defined as an unfavorable outcome.

Evidence of treatment bias: no.

Results: a population of 26 patients fulfilled the study protocol requirements and could be tested by ABR measurement. Eight patients died because of brain death and 1 patient died from pneumonia after 57 days of unconsciousness following cardiac arrest.

Univariate analysis: Among the 16 patients with wave V, 8 had a favorable outcome and 8 had an unfavorable outcome. Among the 10 patients lacking ABR wave V all 10 had an unfavorable outcome. The absence of ABR V wave had a sensitivity of 55.6 and a specificity of 100% to predict an unfavorable outcome. Using the data reported by the authors, the reviewer also computed the 95% confidence interval for both sensitivity and specificity, which resulted 34-75% and 68-100% respectively, i.e. FPR 0 (95%CI 0-32).

Multivariate analysis: not performed.

Cut off proposed and corresponding predictive performance: see above (results, univariate analysis).

Conclusions and quality of evidence: The present LOE P1 study support a role for the absence of V wave at auditory brainstem response recording to assess the prognosis of comatose patients resuscitated after cardiac arrest (QOE fair).


Study design: retrospective cohort study (LOE P3).

Study population: 72 pts who remained comatose after resuscitation from cardiac arrest.

Sedative treatment: Not stated.

Hypothermia: not stated, presumably not used.

EP study/ies under evaluation: SSEPs. In this article, cortical N1 is synonymous with N19 or N20 and N3 with N70. Determination of all latencies was completed without the knowledge of patient outcome. Peaks were counted as present if the amplitude was at least 0.3 µV, were obtained in a repeated recording, and were clearly distinguishable. When responses were absent, an arbitrarily long value (longer than any recorded latency) was used in subsequent analyses. SSEPs were recorded between 0.5 and 4 days after cardiac arrest in 53 patients, between 5 and 10 days in 17 patients, and between 3 and 4 weeks in 2 patients.

Other prognostic factors assessed: Levels of CKBB as determined on cerebrospinal fluid obtained by lumbar puncture.

Outcome assessed: outcome defined as awakening (ability to follow command, to use comprehensible speech or both).

Evidence of treatment bias: The results of CKBB or SEP testing (N1 i.e. N20 component) were judged to have influenced decisions about the level of medical support in 22 of 43 patients who died in the hospital. Of the 29 patients who survived to discharge, 5 were judged to have had decisions about support influenced by these tests. Nor physicians neither patients were aware of long latency SEPs (N3 i.e. N70).

Results: Six patients awakened and were discharged, 1 patient awakened but died before discharge, 43 died during the hospitalization without awakening, and 22 were discharged without awakening. At the most recent follow-up of the 22 patients discharged without awakening, 2 patients could not be contacted for additional follow-up (discharged at 18 and 22 days after arrest). Five patients remained unconscious (at a follow-up of 6, 17, 31, 36, and 48 months), 14 patients died without awakening, and 1 patient awoke approximately 6 weeks after arrest. Based on this information, the patients were classified as having awakened (n = 8) or as not having awakened (n = 64).

Univariate analysis: Bilateral absence of the N1 (i.e. N20) peak predicted nonawakening with a sensitivity of 55% (95%CI 42-67) and a specificity of 100% (95%CI 63-100, i.e. FPR 0 (95%CI 0-37)); bilaterally absent N3 (i.e. N70) predicted nonawakening with a sensitivity of 62% (95%CI 50-75) and a specificity of 100% (95%CI 63-100, i.e. FPR 0 (95%CI 0-37)); N3 (i.e. N70) peak latency or ≥ 176 msec predicted nonawakening with a sensitivity of 67% (95%CI 55-79) and a specificity of 100% (95%CI 63-100, i.e. FPR 0 (95%CI 0-37)). Higher values of sensitivity and specificity were obtained combining SSEPs results and CSF-CKBB levels.

Multivariate analysis: not performed.

Cut off proposed and corresponding predictive performance: see above the “Results” section.

Conclusions and quality of evidence: This LOE P3 study supports a role of SSEPs (N20 and N70 components) in assessing prognosis (neurological outcome and survival) of comatose survivors of cardiac arrest (QOE fair).


Study design: prospective inception cohort study (LOE P1).

Study population: 10 pts who remained comatose after resuscitation from OHCA.
Sedative treatment: no sedation before electrophysiologic assessment; vecuronium was administered before electrophysiologic assessment to avoid muscular artifacts.

Hypothermia: not used

EP study/ies under evaluation: EEG, as processed to derive the bispectral index. BIS was evaluated after ROSC in the emergency room and on admission to ICU

Other prognostic factors assessed: none

Outcome assessed: the post resuscitative outcome was determined on discharge from the ICU using the GOS and included good recovery (G), moderate disability (MD), severe disability (SD), and permanent vegetative state/death (D).

Evidence of treatment bias: it was not unambiguously stated that treatment was not affected by the results of BIS, but it is very unlikely so.

Results: The BIS values were significantly lower in the non-surviving group than in the surviving group. Of interest, BIS increased rapidly after about 30 min of ROSC or reached a plateau of >80 in patients who achieved a favorable outcome or moderate disability; it did not increase in patients with unfavorable outcome (permanent vegetative state/dead). The authors could not analyze the recordings within 30 min of ROSC in three patients because of muscular artifacts contamination.

Multivariate analysis: not performed

Cut off proposed and corresponding predictive performance: none provided

Conclusions and quality of evidence: This LOE P1 study supports a role of EEG, as processed to obtain the BIS, to assess the prognosis of comatose survivors of cardiac arrest (QOE fair)


Study design: prospective inception cohort study (LOE P1)

Study population: 45 consecutive patients who remained comatose after CA and who were treated with therapeutic hypothermia were included

Sedative treatment: Sedation was done by a standardized protocol using Midazolam and Fentanyl. To avoid shivering and muscular artifacts on the BIS monitoring a continuous infusion of cisatracurium was used.

Hypothermia: all patients were treated with therapeutic hypothermia (TH). TH was started as soon as possible after arrival in the hospital “either in the catheterisation-laboratory or in the ICU”

EP study/ies under evaluation: EEG, as processed to derive the bispectral index. BIS was evaluated on admission to ICU. EEG was systematically performed on days 2 and 4 and repeated if necessary.

Other prognostic factors assessed: Short latency N20 Somatosensory evoked potentials (SSEP) were generally done on day 3 after CA, after rewarming and stopping of neuromuscular blockade. Neuron specific enolase (NSE) was dosed on day 2

Outcome assessed: the postresuscitative outcome was determined by GCS and CPC score at the end of ICU stay and by CPC score at 6 months (blinded to BIS). CPC 1 and CPC 2 were regarded as good outcome, whereas CPC 3, 4 and 5 were considered as bad outcome

Evidence of treatment bias: No therapeutic limitation was decided for any patient unless clinical signs of bad outcome were present (fixed pupils at day 3, seizures or no motor response at day 5 after stopping of sedation) and/or absent SSEP and/or major signs of hypoxic brain damage on CT-Scan or MRI. Neurophysiological testing as well as neuroimaging studies were performed and interpreted by physicians unaware of BIS values.

Results: 14 patients presented BIS values of zero (0) during their ICU stay. At 6 months 11 patients were dead, 1 remained comatose and 2 had severe neurological sequelae (CPC3). No patient of this group had good neurological outcome or improved his neurological outcome between ICU and 6-month follow-up. 31 patients had BIS values higher than 0. At 6 months of those, 11 died, none remained comatose, 3 had bad neurological outcome (CPC3) and 17 had no or minor neurological sequelae (CPC1-2).

Multivariate analysis: not performed

Cut off proposed and corresponding predictive performance: a BIS value of 0 had a positive predictive value of 100% for bad neurological outcome. The negative predictive value was 55%. Confidence intervals for an unfavorable outcome at 6 months were recalculated by the ILCOR reviewer: BIS value of 0 had a sensitivity of 50% (95%CI 33-67) and a specificity of 100% (95%CI 82-100%, i.e. FPR 0 (95%CI 0-18))

Conclusions and quality of evidence: This LOE P1 study supports a role of EEG, as processed to obtain the BIS, to assess the prognosis of comatose survivors of cardiac arrest receiving therapeutic hypothermia (QOE fair)

Study design:  Case series (LOE P4)
Study population: 24 consecutive patients who developed a BS pattern at EEG within 24 hours after cardiopulmonary resuscitation. Twenty-one of the patients were outpatients and three were inpatients.
Sedative treatment: At the time of the initial EEG, none of the patients was on drugs on doses that would produce a BS pattern. On the first day, phenytoin and/or benzodiazepines (diazepam, clonazepam, lorazepam, midazolam) or valproic acid were used to suppress myoclonic jerks in most patients. Thus, EEG 2 was usually performed after the administration of these drugs, and in two patients during the administration of intravenous benzodiazepine
Hypothermia: not explicitly stated whether pts were treated with therapeutic hypothermia
EP study/ies under evaluation: The study was actually designed to assess the time course of BS pattern at EEG in comatose pts after cardiac arrest, or in other words to investigate transitions from BS-EEG to other EEG patterns during hospital stay. However, the prognostic significance of BS pattern was investigated as a consequence. EEG (EEG 1) was recorded 5 to 24 hours after resuscitation (day 1). Subsequent EEGs were recorded on day 2 (EEG 2), on day 3 to day 4 (EEG 3), on day 5 to day 6 (EEG 4), and on day 7 to day 8 (EEG 5). The BS pattern was diagnosed according to the Guidelines of the International Federation of Clinical Neurophysiology, and according to Niedermeyer and Lopes da Silva’s Electroencephalography; the authors fixed the duration of isoelectric or low-amplitude interburst intervals to at least 1 second to exclude patients with generalized periodic epileptiform discharges.
Other prognostic factors assessed: none
Outcome assessed: Neurological outcome
Evidence of treatment bias: It was not explicitly stated whether the presence of BS-EEG has influenced treatment
Results: All the comatose patients after CA included in this study with a BS-EEG at 24 hours after the event died or remained in a persistent vegetative state.
Multivariate analysis: not performed
Cut off proposed and corresponding predictive performance: It was not possible to calculate sensitivity and specificity as it is not reported by the authors how many pts who were comatose after CA did not show BS-EEG and their outcome
Conclusions and quality of evidence: This case series study (LOE P4) supports a role of EEG (BS pattern) to assess the prognosis of pts who remain comatose after cardiac arrest (QOE fair)


Study design:  Prospective, randomized, controlled trial (LOE P1) (A sub study of the European Hypothermia After Cardiac Arrest study)
Study population: Sixty consecutive patients (aged 18 –75 yrs) resuscitated from out-of-hospital ventricular fibrillation and comatose at 24 hrs after cardiac arrest randomly assigned either to therapeutic hypothermia of 33°C or normothermia. All included pts were aged 18 –75 yrs, suffered a witnessed cardiac arrest, ventricular fibrillation or nonperfusing tachycardia was as the initial cardiac rhythm, there was a presumed cardiac origin of the arrest, an estimated interval of 5–15 mins from collapse to the first attempt at resuscitation by emergency medical personnel was verified, and an interval of <60 mins from collapse to restoration of spontaneous circulation (ROSC)
Sedative treatment: Sedation and analgesia were accomplished with administration of midazolam and fentanyl. To avoid shivering, pancuronium was initially used.
Hypothermia: Patients randomized to normothermia were allowed to rewarm passively to normothermia and were then kept normothermic. Those randomized to hypothermia treatment were actively cooled externally to a core target temperature of 33°C (range, 32–34°C) with a cooling device.
EP study/ies under evaluation: SSEPs and BAEPs were recorded 24 –28 hrs after cardiac arrest.
Other prognostic factors assessed: none
Outcome assessed: the primary end point was the recovery of consciousness, defined as ability to obey verbal command, and the secondary outcome was favorable outcome at 6 months after cardiac arrest, as assessed by the Pittsburgh Outcome Scale. The neurologic outcome was dichotomized as good (CPC 1 and 2) or poor (CPC 3, 4, and 5). The SEP and BEAP recordings were all analyzed retrospectively as a block. The physician analyzing SEPs and BAEPs was blinded to the treatment and outcome for the patient.
Evidence for treatment bias: The SSEP and BAEP results did not affect the decision to withdraw treatment
Results: Forty-five patients recovered consciousness (26 in the hypothermia group and 19 in the normothermia group; p <0 .04). At 6 months after cardiac arrest, the outcome was favorable for 77% (n 23) of the hypothermia treated
Evidence of treatment bias: of 60 patients (30 in the hypothermia group and 27 in the normothermia group). Patients and 50% (n 15) of the normothermia-treated patients (p<0.03). SSEP and BAEP could be analyzed in 57 out of 60 patients (30 in the hypothermia group and 27 in the normothermia group).

Univariate analysis:
SSEP. The amplitudes of N20 responses were comparable in the two treatment groups and did not correlate with outcome; The cortical N20 responses were bilaterally absent in 11 patients, of which three were in the hypothermia group and eight in the normothermia group. None of these patients regained consciousness. Bilaterally absent cortical N20 responses predicted permanent coma with a specificity of 100% (95% CI 92-100%, i.e. FPR 0 (95% CI 0-8)). However, the authors reported this level of predictive performance for aggregate data (hypothermic + normothermic pts) but it is debatable whether this approach is entirely acceptable. Specificities and their CIs have then been recalculated for the separate groups by the ILCOR reviewer from the original data. Given the small sample groups, the confidence interval for the specificity of SSEP broadened to 87-100 in the hypothermia group, i.e. FPR 0 (95% CI 0-13) and to 82-100 in the normothermia group, i.e. FPR 0 (95% CI 0-18)). Three patients (one in the hypothermia group and two in the normothermia group) had bilateral N20 responses but did not awaken. Thus, the sensitivity was 75% (95% CI, 30–95%) in the hypothermia group and 80% (95% CI, 49–94%) in the normothermia group.

BAEPs. All latencies were longer in hypothermia-treated patients. Within the treatment groups the latencies did not correlate with age, awakening, or achieving favorable outcome. Moreover, in several cases the presence/absence of at least one waveform at BAEPs was later recognized as a consequence of a hearing impairment. In conclusion, the authors state that in this study the addition of BAEP recording to SEP recording did not increase sensitivity for identifying patients with poor prognosis, as compared with SEP recording alone; however formal data on the predictive performance of the presence/absence of at least one waveform at BAEPs were not reported.

Multivariate analysis: No formal multivariate analyses have been performed.

Cut off proposed and corresponding predictive performance: see above the univariate analysis section.

Conclusions and quality of evidence: The LOE P1 study supports a role of SSEPs (presence/absence of the cortical N20 component) to assess the outcome of comatose survivors of cardiac arrest also if treated with therapeutic hypothermia (QOE fair). The authors also state that the adjunct of the results of BAEPs does not add any predictive advantage over SSEP also because of several altered responses caused by pre-existing hearing deficit, but do not report data on the predictive performance of BAEPs alone so that evidence on this topic was rated as neutral.

Wijdicks et al. 2006 203-210

Study design: Systematic review of the literature and meta-analysis (LOE P1). Studies were ranked in class I to IV of decreasing strength of evidence.

Study population: not applicable.

Sedative treatment: see individual studies.

Hypothermia: see individual studies.

EP study/ies under evaluation: EEG, SSEPs, auditory and visual evoked potentials. For the purposes of the meta-analysis, EEG categories have been collapsed into two categories to allow for comparisons and statistical analyses: malignant and benign or uncertain. Most malignant categories include suppression, burst-suppression, alpha and theta pattern coma and generalized periodic complexes.

Other prognostic factors assessed: see individual studies.

Outcome assessed: see individual studies.

Evidence of treatment bias: see individual studies.

Results: This pooled analysis included 8 studies in which SSEPs were recorded within 3 days from CA. Bilateral absence of N20 response to median nerve stimulation was associated with a pooled FPR for poor outcome of 0.7% (95% CI: 0.1 to 3.7). A few patients have been reported in whom an absent N20 response > 24 h after CA reappeared in successive recordings, all with a poor outcome. Conversely, the presence of the N20 response was not helpful in predicting outcome (pooled sensitivity of 46%). Although it has been suggested that the presence of later responses (N35 and N70) predicts outcome, according to the opinion of the authors of this meta-analysis this topic has been insufficiently examined. This pooled analysis included 5 studies in which EEG recording was obtained usually within 3 days from CA. Generalized suppression to less than 20 µV, BS pattern with generalized epileptiform activity, or generalized periodic complexes on a flat background are associated with an unfavorable outcome. ATC pattern is not invariably associated to an unfavorable outcome. In this meta-analysis, the pooled FPR for poor outcome of malignant EEG patterns was 3% (95% CI: 0.9% to 11%).

Other evoked (brainstem auditory and visual) and event-related potential tests have not been thoroughly tested for their prognostic value in anoxic-ischemic encephalopathy. In one study, the MLAEAEs were absent in all 13 patients who died or remained in a persistent vegetative state (sensitivity 34% [95% CI: 19-49], FPR = 0.

Conclusions and quality of evidence: the LOE P1 study supports a role of EEG and SSEPs to assess prognosis of comatose survivors of cardiac arrest (QOE good).

Study design: prospective inception cohort (LOE P1)
Study population: 75 comatose survivors of cardiac arrest (both in-hospital and out-of-hospital)
Sedative treatment: pts declared brain dead or on continuous sedative treatment were excluded from analysis
Hypothermia: unambiguously no
Prognostic EP study/ies under evaluation: SSEPs and EEG recorded between 1 and 3 days after ROSC. SSEPs were classified in four categories according to the pattern of abnormalities: category (1) [all the short- and long-latency components from N20 to N60 were detectable]; category (2) [persistence of only the short-latency components (N20, P22, P27, N30, and N33)]; category (3) [persistence of only N20]; category (4) [bilateral absence of all cortical responses]; EEG was classified according to Young GB 1997.
Other prognostic factors assessed: neurological examination recorded between 1 and 3 days after ROSC
Outcome assessed: death in hospital or GOS at 3 months
Evidence for treatment bias: it was not unambiguously stated that treatment was not affected by the results of EEG or SSEPs
Results: Outcomes were grouped into two categories: those who died without recovery of consciousness (none remained in a vegetative state beyond 2 months) and those who recovered awareness.
Univariate analysis: SSEP. The potential for an assessment bias was found, as SSEPs were recorded only in 47 out of 75 pts. An asymmetry of SSEP over the two hemispheres was not observed in the study population. The N20 response of the SSEP was absent in 20 patients, 1 of whom recovered awareness; of the 26 patients in whom N20 response of the SSEP was present, 11 died. The predictive performance of the absence of the N20 component to predict an unfavorable outcome was recalculated by the ILCOR reviewer and resulted in a sensitivity of 57% (95%CI 41-72), and a specificity of 92% (95% CI 65-98), i.e. FPR 8 (95% CI 2-35)). EEG: As the authors state “EEG categorization created groups with such small numbers that analysis was problematic”. However, there were no survivors among those few who had generalized epileptiform discharges or who had suppression with voltage less than 20 µV. The predictive performance of the criterion “presence of a pattern 1A or B at EEG” to predict a good outcome (survival) as reported by the authors were: sensitivity 89% and specificity 84%.
Multivariate analysis: not performed
Cut off proposed and corresponding predictive performance: as above stated
Quality of evidence: This LOE P1 study supports a role of SSEPs and EEG to assess the prognosis of comatose survivors of cardiac arrest (QOE fair)


Study design: Systematic review and pooled analysis (LOE P1)
Study design: From Medline (since 1966) and Embase (since 1982) databases the authors searched for studies concerning patients older than 10 years with anoxic-ischaemic coma in which findings from early neurological examination, electroencephalogram (EEG), or somato-sensory evoked potentials (SSEP) were related to poor outcome—defined as death or survival in a vegetative state. The authors selected prognostic factors with a specificity of 100% for poor outcome in all studies, and expressed the overall prognostic accuracy of these variables as pooled positive-likelihood ratios and as 95% CIs of the pooled false-positive test rates.
Hypothermia: not stated
EP study/ies under evaluation: EEG and SSEPs
Other prognostic factors assessed: findings at neurological examination
Outcome assessed: see individual studies
Results: In 33 studies, 14 prognostic variables were studied, three of which had a specificity of 100%: absence of pupillary light reflexes on day 3 (pooled positive-LR 10·5 [95% CI 2·1–52·4]; 95% CI pooled FPR 0–11·9%); absent motor response to pain on day 3 (pooled positive-LR 16·8 [3·4–84·1]; 0–6·7%); and bilateral absence of early cortical SSEP within the first week (pooled positive LR 12·0 [5·3–27·6]; 0–2·0%). EEG recordings with an isoelectric or burst-suppression pattern had a specificity of 100% in five of six relevant studies (pooled positive-LR 9·0 [2·5–33·1]; 95%CI pooled FPR 0·2–5·9%). For the 11 SSEP studies, results did not significantly differ between studies in which the treating physicians were or were not masked from the test result, prospective and retrospective studies, studies with short and long follow-up periods, and studies with high or low overall poor outcome.
Conclusions and quality of evidence: This systematic review (LOE P1) supports a role of EEG (isoelectric or BS pattern) and SSEPs (bilateral absence of early cortical SSEP within the first week) to assess prognosis of comatose survivors of cardiac arrest (Quality of evidence: good)


**Study design:** Prospective (inception) cohort study (LOE P1).

**Study population:** 407 adult comatose survivors of CA.

**Sedative treatment:** Within the first 24 hours post CPR, sedatives and muscle relaxants were stopped. When this was not possible, propofol was used as the standard sedative, and this medication was stopped shortly before clinical assessment and EEG recording. Morphinomimetics and benzodiazepines were avoided as much as possible.

**Therapeutic hypothermia:** Therapeutic hypothermia was introduced during the study and used in a very limited number of pts, and a confounding effect cannot be excluded

**EP study/ies under evaluation:** SSEPs at 24, 48 and 72 hours, and EEG at 72 h. The results for the N20 were evaluated for each side separately and classified as absent (only in the presence of a cervical potential), present or the recording was judged to be technically insufficient. For statistical analysis, the authors classified as “SSEP absent” the situation in which N20 was absent on both sides and “SSEP not absent” all the remaining combinations of left and right recordings. EEG was coded using the classification of Hockaday et al. In addition, the presence or absence of a burst-suppression pattern and of epileptiform activity (absent, sporadic, frequent, status epilepticus) was annotated.

**Other prognostic markers evaluated:** clinical characteristics, NSE and S-100 sampled at 24, 48 and 72 hours after CPR.

**Outcome evaluated:** neurological outcome (Glasgow outcome scale at 1 month and at 1 year in survivors). Outcome was registered after 1 month using the Glasgow Outcome Scale. Poor outcome was defined as either death or persisting unconsciousness after 1 month. In patients who died, the probable cause of death was registered. In surviving patients, 1-year outcome was assessed by telephone contact with the patient, a family member, or the general practitioner of the patient

**Results:**

*Univariate analysis.*

All patients unconscious at 72 h with bilateral absence of N20 at any time had a poor outcome (95% CI of false positive rate 0-3%); All patients unconscious a 72 h with NSE>33 µg/ml (but a blood sample was available only in 231/305) at any time had a poor outcome (95% CI of false positive rate 0-3%); pts with bilateral absence of N20 or NSE>33 µg/ml overlapped only partially; all pts with bilateral absence of N20 or NSE>33 µg/ml had a poor outcome (95% CI 0-2%). In pts without absent N20 and NSE not > 33 µg/ml, a small number of pts with poor outcome could be identified with EEG (burst suppression or no voltage > 20 µV).

In conclusion, 252 out of 356 pts with poor outcome could be predicted with these 3 variables in the first 3 days after CPR.

The predictive performance of electrophysiological variables in the subgroup of pts who were evaluated (see original study for details), is summarized in the following table.

<table>
<thead>
<tr>
<th>Prognostic factor</th>
<th>False positive rate (95% CI)</th>
<th>Positive likelihood ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilateral absence N20 at 24 h</td>
<td>0 (0-4)</td>
<td>29 (2-454)</td>
</tr>
<tr>
<td>Bilateral absence N20 at 48 h</td>
<td>0 (0-4)</td>
<td>27 (2-427)</td>
</tr>
<tr>
<td>Bilateral absence N20 at 72 h</td>
<td>0 (0-3)</td>
<td>25 (2-394)</td>
</tr>
<tr>
<td>Bilateral absence N20 at 24-72 h</td>
<td>0 (0-3)</td>
<td>25 (2-383)</td>
</tr>
<tr>
<td>EEG no activity ≥ 20 µV at 72h</td>
<td>0 (0-5)</td>
<td>17 (1-272)</td>
</tr>
<tr>
<td>EEG burst-suppression pattern 72h</td>
<td>0 (0-15)</td>
<td>5 (0-81)</td>
</tr>
<tr>
<td>EEG status epilepticus 72h</td>
<td>7 (1-24)</td>
<td>1 (0-5)</td>
</tr>
</tbody>
</table>

Treating physicians were blinded for the results of the first and second day SSEP and for all blood tests. Absence of SSEP at 72 hours was considered a sufficiently reliable predictor of poor outcome to allow its use for treatment decisions and the result of 72-hour SSEP testing was therefore made available to the treating physicians. Treatment could be modified according to the results of neurological examination, SSEP at 72 h and EEG.
Multivariate analysis: not performed

Conclusions and quality of evidence: Comparison groups were clearly defined. Outcome was assessed in the same way. Blood samples were not available in many enrolled pts, so that a detection bias cannot be excluded. Treatment could be modified according to the results of neurological examination, SSEP at 72 h and EEG. Therapeutic hypothermia was introduced during the study and used in a limited number of pts, and a confounding effect cannot be entirely excluded. The univariate predictive performance of clinical variables, SSEP, NSE and S100-B was assessed with derivation of a clinical decision rule, which however deserves a prospective validation. The study therefore has been ranked as supportive of a role of SSEP and EEG to assess neurological outcome in comatose survivors of cardiac arrest (LOE P1, fair).

Zingler et al. 2003 79-84. "Early prediction of neurological outcome after cardiopulmonary resuscitation: A multimodal approach combining neurobiochemical and electrophysiological investigations may provide high prognostic certainty in patients after cardiac arrest." European Neurology 49(2): 79-84.

Study design: Prospective inception cohort study (LOE P1).

Study population: 27 consecutive comatose survivors of either in or out-of-hospital cardiac arrest.

EP study under evaluation: SSEP as assessed on days 2 and 7. SEPs were classified by four grades of increasing severity: grade 1 = bilateral normal cervical and cortical responses, grade 2 = pathological diminished amplitude ratio N20/P25 –N13 < 1.14 or prolonged central conduction time > 7.2 ms, grade 3 = unilateral loss of cortical response and grade 4 = BLCR

Sedative treatment: most were sedated and anesthetized

Hypothermia: hypothermic pts were excluded; therapeutic hypothermia was not used

Other prognostic factors under investigation: GCS and standardized neurological examination, NSE and S100 levels as assessed on blood samples collected on days 1, 2, 3 and 7 after cardiac arrest.

Outcome assessed: neurological outcome at 2, 4 and 12 weeks after cardiac arrest (bad outcome defined as best CPC score during f.u. ≥ 3 vs. good outcome defined as best CPC score <3 during 6 months f.u). SSEPs latencies and amplitudes were assessed without knowledge of pt's outcome.

Evidence of treatment bias: it is not explicitly stated whether SSEPs results affected treatment

Results: 10 patients (37%) regained consciousness (CPC 1–3), and 17 patients (63%) had a poor neurological outcome and remained unconscious (CPC 4–5). Forty SEP recordings were obtained (22 at 48h and 18 at 7 days). The calculation of Spearman's correlation coefficients (r) revealed a high association between SEP grades and CPC scores of patients. Repeated SEP recordings particularly provided additional prognostic information for patients with SEP grade 1–3, because both improvement and deterioration of SEP findings occurred between the first and the second SEP. SEPs with BLCR grade 4 were found exclusively in CPC 4–5 (prediction of poor outcome with a specificity of 100%). None of the patients who regained consciousness showed a BLCR pattern.

Conclusions and quality of evidence: Comparisons groups were clearly defined, outcomes were measured in the same way and follow up of pts was complete. Even though at univariate analysis SSEPs results appeared to be predictive of outcome, a multivariate analysis of its independent predictive role was not performed. Notably, SSEPs were not recorded in all patients, and the possibility of an assessment bias cannot be excluded. However, the study has been ranked as supportive of a predictive role of SSEPs to assess survival and neurological outcome in comatose survivors of cardiac arrest. (LOE P1, QOE fair)


ABBREVIATION LIST

aEEG: amplitude-integrated EEG
ABR: auditory brainstem response
ATC: alpha theta coma
BAEP: brainstem auditory evoked potential
BIS: bispectral index
BLCR: bilateral loss of cortical responses
BS-EEG: burst suppression pattern at electroencephalography
CA: cardiac arrest
CEP: cortical evoked potentials
CES: clinical examination score
CI: confidence interval
CPC: cerebral performance category
CPR: cardiopulmonary resuscitation
CSF-CKBB: concentration of creatinkinase isoenzyme BB in the cerebrospinal fluid
EEG: electroencephalogram
EP: electrophysiological
FPR: false positive rate
GCS: Glasgow coma scale
GOS: Glasgow outcome scale
LOE: level of evidence
MF: median frequency
MLAE: middle latency auditory evoked potentials
MMN: mismatch negativity
NPV: negative predictive value
NSE: neuron specific enolase
OHCA: out of hospital cardiac arrest
PEA: pulseless electrical activity
PPV: positive predictive value
PSE: persistent status epilepticus
QOE: quality of evidence
ROSC: recovery of spontaneous circulation
SD: standard deviation
SE: status epilepticus
SEF: spectral edge frequency
SEP: sensory-evoked potentials
SSEP: somato-sensory evoked potential