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| QUESTION |
| **Cerebral recovery index (CRI) for prediction of good neurological outcome in adults with cardiac arrest****(Subsection of Prognostication ETD)** |
| **POPULATION:** | Adults who are comatose after resuscitation from cardiac arrest (either in-hospital or out-of-hospital), regardless of target temperature management. |
| **INTERVENTION:** | Cerebral recovery index (CRI) derived from automated quantitative EEG assessed within 24 hours after cardiac arrest.  |
| **COMPARISON:** | *None.* |
| **MAIN OUTCOMES:** | Prediction of good neurological outcome defined as Cerebral Performance Categories (CPC) on hospital discharge or 6 months after cardiac arrest |
| **STUDY DESIGN:** | Prognostic accuracy studies where the 2 x 2 contingency table (i.e., the number of true/false negatives and positives for prediction of good outcome) was reported, or where those variables could be calculated from reported data. are eligible for inclusion. Unpublished studies, reviews, case reports, case series, studies including less than 10 patients, letters, editorials, conference abstracts, and studies published in abstract form were excluded.  |
| **TIMEFRAME:** | An ILCOR review from 2013 and an update from 2020 presented the evidence of predictors of poor neurological outcome after cardiac arrest. More recently, several studies identifying predictors of good neurological outcome after cardiac arrest have been published, therefore an ILCOR evidence review for predictors of good neurological outcome after cardiac arrest is necessary.The most recent search of this systematic review evidence update on neuroprognostication was launched in October 2022. |

# ASSESSMENT

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| ProblemIs the problem a priority? |
| JUDGEMENT | RESEARCH EVIDENCE | ADDITIONAL CONSIDERATIONS |
| ○ No○ Probably no○ Probably yes● Yes○ Varies○ Don't know | Neurologic injury is the most common cause of death in patients with post cardiac arrest syndrome. Most of these deaths occur due to withdrawal of life-sustaining treatment (WLST) based on the prediction of poor neurological outcome. Neurological prognostication after cardiac arrest is of utmost importance to avoid futile treatments for unsalvageable patients but also to minimize the risk of falsely pessimistic prediction and self-fulfilling prophecy. |  |
| Desirable EffectsHow substantial are the desirable anticipated effects? |
| JUDGEMENT | RESEARCH EVIDENCE | ADDITIONAL CONSIDERATIONS |
| ○ Trivial● Small○ Moderate○ Large○ Varies○ Don't know | One study [Tjepkerma-Cloostermans, 2013, R252] investigated the ability of cerebral recovery index (CRI) to predict good outcome at 6 months after CA. In that study, a CRI above 0.57 at 18 h or 0.69 at 24 h predicted good neurological outcome with **100% specificity (sensitivities 65% [44.3–82.8] and 26% [11.1–46.3] respectively).**  | CRI is a summary score which represents a combination of five quantitative EEG features derived from automated quantitative EEG analysis. Each feature is combined into CRI, which ranges from 0 to 1 (the higher, the better). The included study showed that the CRI of patients with good outcome improved faster than did those of patients with poor outcome.  |
| Undesirable EffectsHow substantial are the undesirable anticipated effects? |
| JUDGEMENT | RESEARCH EVIDENCE | ADDITIONAL CONSIDERATIONS |
| ○ Large○ Moderate○ Small○ Trivial○ Varies ● Don't know |  | A falsely optimistic prediction in a patient with poor neurological outcome may potentially lead to futile care being provided. |
| Certainty of evidenceWhat is the overall certainty of the evidence of effects? |
| JUDGEMENT | RESEARCH EVIDENCE | ADDITIONAL CONSIDERATIONS |
| ● Very low○ Low○ Moderate○ High○ No included studies | The certainty of evidence about CRI is very low because of lack of blinding and it is based on only one study.  | CRI is based on an automated and quantitative EEG analysis, which makes the interpretation simpler and more objective. However, the availability of this technique is still limited, and these results need to be validated in a larger patient cohort. |
| ValuesIs there important uncertainty about or variability in how much people value the main outcomes? |
| JUDGEMENT | RESEARCH EVIDENCE | ADDITIONAL CONSIDERATIONS |
| ○ Important uncertainty or variability○ Possibly important uncertainty or variability● Probably no important uncertainty or variability○ No important uncertainty or variability | Almost all prognostic studies included in our review defined good outcome as CPC 1–2.  | There may be interindividual variations in how good neurological outcome is perceived. |
| Balance of effectsDoes the balance between desirable and undesirable effects favor the intervention or the comparison? |
| JUDGEMENT | RESEARCH EVIDENCE | ADDITIONAL CONSIDERATIONS |
| ○ Favors the comparison○ Probably favors the comparison● Does not favor either the intervention or the comparison○ Probably favors the intervention○ Favors the intervention○ Varies○ Don't know | A CRI above 0.57 at 18 h or 0.69 at 24 h predicted good neurological outcome with high specificity after cardiac arrest. However, the evidence is limited to one study. The CRI thresholds for 100% specificity change over time. These thresholds need confirmation from further studies by different groups to ensure reproducibility.  | The interaction between sedation and CRI has not been investigated. |
| Resources requiredHow large are the resource requirements (costs)? |
| JUDGEMENT | RESEARCH EVIDENCE | ADDITIONAL CONSIDERATIONS |
| ○ Large costs○ Moderate costs○ Negligible costs and savings○ Moderate savings○ Large savings○ Varies ● Don't know | No studies addressing this question were identified.  |  |
| Certainty of evidence of required resourcesWhat is the certainty of the evidence of resource requirements (costs)? |
| JUDGEMENT | RESEARCH EVIDENCE | ADDITIONAL CONSIDERATIONS |
| ○ Very low○ Low○ Moderate○ High● No included studies | No studies addressing this question were identified.  |  |
| Cost effectivenessDoes the cost-effectiveness of the intervention favor the intervention or the comparison? |
| JUDGEMENT | RESEARCH EVIDENCE | ADDITIONAL CONSIDERATIONS |
| ○ Favors the comparison○ Probably favors the comparison○ Does not favor either the intervention or the comparison○ Probably favors the intervention○ Favors the intervention○ Varies● No included studies | No studies addressing this question were identified.  |  |
| EquityWhat would be the impact on health equity? |
| JUDGEMENT | RESEARCH EVIDENCE | ADDITIONAL CONSIDERATIONS |
| ○ Reduced● Probably reduced○ Probably no impact○ Probably increased○ Increased○ Varies○ Don't know | CRI is calculated with specific software that is not universally available. The experience in CRI concerns a restricted group of investigators.  |  |
| AcceptabilityIs the intervention acceptable to key stakeholders? |
| JUDGEMENT | RESEARCH EVIDENCE | ADDITIONAL CONSIDERATIONS |
| ○ No○ Probably no● Probably yes○ Yes○ Varies○ Don't know | We have not identified any research that assessed acceptability, but acceptability is likely. |  |
| FeasibilityIs the intervention feasible to implement? |
| JUDGEMENT | RESEARCH EVIDENCE | ADDITIONAL CONSIDERATIONS |
| ○ No○ Probably no○ Probably yes○ Yes○ Varies● Don't know | The equipment and skills required for CRI assessment may represent an obstacle for their implementation.  | CRI has the advantage of being based on an automated and quantitative EEG analysis, which makes the interpretation simpler and more objective.  |

# SUMMARY OF JUDGEMENTS

|  | **JUDGEMENT** |
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| **PROBLEM** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **DESIRABLE EFFECTS** | Trivial | **Small** | Moderate | Large |  | Varies | **Don't know** |
| **UNDESIRABLE EFFECTS** | Large | Moderate | Small | Trivial |  | Varies | **Don't know** |
| **CERTAINTY OF EVIDENCE** | **Very low** | Low | Moderate | High |  |  | No included studies |
| **VALUES** | Important uncertainty or variability | Possibly important uncertainty or variability | **Probably no important uncertainty or variability** | No important uncertainty or variability |  |  |  |
| **BALANCE OF EFFECTS** | Favors the comparison | Probably favors the comparison | **Does not favor either the intervention or the comparison** | Probably favors the intervention | Favors the intervention | Varies | Don't know |
| **RESOURCES REQUIRED** | Large costs | Moderate costs | Negligible costs and savings | Moderate savings | Large savings | Varies | **Don't know** |
| **CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES** | Very low | Low | Moderate | High |  |  | **No included studies** |
| **COST EFFECTIVENESS** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | Favors the intervention | Varies | **No included studies** |
| **EQUITY** | Reduced | **Probably reduced** | **Probably no impact** | Probably increased | Increased | Varies | **Don't know** |
| **ACCEPTABILITY** | No | Probably no | **Probably yes** | Yes |  | Varies | Don't know |
| **FEASIBILITY** | No | Probably no | Probably yes | Yes |  | Varies | **Don't know** |

# TYPE OF RECOMMENDATION

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| Strong recommendation against the intervention | Conditional recommendation against the intervention | Conditional recommendation for either the intervention or the comparison | Conditional recommendation for the intervention | Strong recommendation for the intervention |
| ○  | ● | ○ | ○  | ○  |

# CONCLUSIONS

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| Recommendations |
| We suggest against the use of other EEG metrics, including reduced montage or amplitude integrated EEG, BIS, or EEG-derived indices, to predict good outcome in patients who are comatose after cardiac arrest (weak recommendation, very low-certainty evidence).  |
| Justification |
| In making the recommendation, the ALS TF considered that although a CRI above 0.57 at 18 h or 0.69 at 24 h predicted good neurological outcome with high specificity after cardiac arrest, the evidence is limited to one study. The CRI thresholds for 100% specificity change over time. These thresholds need confirmation from further studies by different groups to ensure reproducibility. CRI is based on specific software that is not universally available.  |
| Subgroup considerations |
| None |
| Implementation considerations |

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| Monitoring and evaluation |
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| Research priorities |
| Studies assessing the reproducibility of CRI are warranted. |

References:

Tjepkema-Cloostermans MC, van Meulen FB, Meinsma G, van Putten MJ (2013) A Cerebral Recovery Index (CRI) for early prognosis in patients after cardiac arrest. Crit Care 17:R252