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| QUESTION | |
| **Bispectral index (BIS) 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:** | Bispectral index (BIS) 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 Unpublished studies, reviews, case reports, case series, studies including less than 10 patients, letters, editorials, conference abstracts, and studies published in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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| Problem Is 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 Effects How substantial are the desirable anticipated effects? | | |
| JUDGEMENT | RESEARCH EVIDENCE | ADDITIONAL CONSIDERATIONS |
| ○ Trivial ● Small  ○ Moderate ○ Large ○ Varies ○ Don't know | The predictive value of BIS was evaluated in three studies [Park, 2018; Seder, 2010; Leary, 2010]. In one study [Park, 2018] the outcome was defined at 6 months after CA and in two studies [Seder, 2010; Leary, 2010] on hospital discharge.  In two studies, a **BIS value greater than 21 at 1–3 h** [Park, 2018] after ROSC **or 24 at 3–6 h** after ROSC [Seder, 2010] predicted good neurological outcome **with 94% [79.8–99.3] and 86% [73.3–94.2] specificity**, respectively (sensitivities 88% [61.7–98.4] and 94%, [83.1–98.7] respectively).  In one study [Leary, 2010], the ability of BIS to predict good neurological outcome **at 24 h** from ROSC was assessed at different BIS thresholds. **Specificity increased from 41% [25.6–56.7] at BIS 30 to 92.9% [80.5–98.5]at BIS 60**. **Sensitivities decreased from 95%** **[75.1–99.9] to 20% 20 [5.7–43.7],** respectively.  Park JH, Oh JH, Choi SP, Wee JH (2018) Neurologic outcome after out-of- hospital cardiac arrest could be predicted with the help of bispectral- index during early targeted temperature management. Scand J Trauma Resusc Emerg Med 26:59  Seder DB, Fraser GL, Robbins T, Libby L, Riker RR (2010) The bispectral index and suppression ratio are very early predictors of neurological outcome during therapeutic hypothermia after cardiac arrest. Intensive Care Med 36:281–288  Leary M, Fried DA, Gaieski DF, Merchant RM, Fuchs BD, Kolansky DM, Edelson DP, Abella BS (2010) Neurologic prognostication and bispectral index monitoring after resuscitation from cardiac arrest. Resuscitation 81:1133–1137 | BIS value greater than 21 or 24 had high specificity at 2-5 h from ROSC in two studies [Park, Seder], but its accuracy was lower at 24 h [Leary], possibly reflecting a partial recovery of EEG background activity in patients with poor outcome.  BIS is quantitative trend analysis tool based on a few EEG channels. BIS is based on a proprietary technology that returns a single number from zero (corresponding to an isoelectric EEG) to 100 (‘full consciousness |
| Undesirable Effects How substantial are the undesirable anticipated effects? | | |
| JUDGEMENT | RESEARCH EVIDENCE | ADDITIONAL CONSIDERATIONS |
| ○ Large ○ Moderate ○ Small ○ Trivial ○ Varies  ○ Don't know | None known. | A falsely optimistic prediction in a patient with poor neurological outcome may potentially lead to the delivery of futile care. |
| Certainty of evidence What 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 favorable BIS threshold is very low because of lack of blinding and low precision. |  |
| Values Is 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 | All prognostic studies defined good outcome as CPC 1–2. | There may be interindividual variations on how good neurological outcome is perceived. |
| Balance of effects Does 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 | High BIS values within 24h from ROSC predict good neurological outcome after cardiac arrest. However, the optimal BIS threshold has yet to be identified. The evidence is limited to three studies. | BIS does not enable a morphological assessment of the original EEG signals, so the identification of superimposed activity is not possible.  The interaction of sedation on the reliability of BIS for predicting good outcome has yet to be investigated. |
| Resources required How 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 resources What 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 effectiveness Does 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 |  |
| Equity What 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 | Specific equipment is needed to assess BIS. This may not be available everywhere, which can reduce equity. | Presumably, using BIS is simpler than using a full -montage EEG |
| Acceptability Is 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 the acceptability of BIS. However, acceptability is likely. |  |
| Feasibility Is the intervention feasible to implement? | | |
| JUDGEMENT | RESEARCH EVIDENCE | ADDITIONAL CONSIDERATIONS |
| ○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know | The equipment required for BIS may represent an obstacle to its implementation. | Interpretation of BIS does not require a specialist compared to full montage EEG. |

# 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. |
| Justification |
| In recommending against using BIS, the ALS TF considered that, although aery-low-quality evidence from three studies shows that high BIS values within 24h from ROSC predict good neurological outcome after cardiac arrest, the evidence is limited to three studies. Moreover, the optimal BIS threshold has yet to be identified. BIS analysis is made on a limited number of leads and is based on a proprietary algorithm preventing a direct and more complete EEG morphology analysis, even if the raw EEG signal is displayed. |
| Subgroup considerations |
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| Implementation considerations |

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| Monitoring and evaluation |
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| Research priorities |
| The interference of sedation on BIS deserves investigation.  A consistent threshold for predicting good outcome using BIS should be identified. |