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| QUESTION | |
| **Brain computed tomography (CT) 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:** | Grey matter/white matter ratio (GWR), QRA, and ASPECTS-b on brain computed tomography (CT)), assessed within three hours after cardiac arrest. |
| **COMPARISON:** | *None.* |
| **MAIN OUTCOMES:** | Prediction of good neurological outcome defined as Cerebral Performance Categories (CPC) 1-2 at 1 month 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 Unpublished studies, reviews, case reports, case series, studies including less than 10 patients, letters, editorials, conference abstracts, and studies published in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 ability of brain CT performed at one to three hours after ROSC to predict good neurological outcome was assessed in one study [Lee, 2017]. Hypoxic-ischaemic changes due to cardiac arrest were quantified using the density ratio between the grey and white matter (GWR), the quantitative regional attenuation (QRA) score and the Alberta Stroke Program Early CT (ASPECTS-b) score. **A GWR ≥ 1.25 or a QRA ≤ 5** predicted good neurological outcome at 1 month with **77% specificity and 25% sensitivity**. **ASPECTS- b≥15** predicted good neurological outcome with **89% specificity and 75% sensitivity.**  Kyu Sun Lee, Sung Eun Lee, Jun Young Choi, et al. Useful Computed Tomography Score for Estimation of Early Neurologic Outcome in Post-Cardiac Arrest Patients With Therapeutic Hypothermia, Circulation Journal, 2017, Volume 81, Issue 11, Pages 1628-1635  **Grey matter to white matter ratio (GWR)** is the ratio between the densities (measured in Hounsfield units) of the grey matter and the white matter on brain CT. In the normal brain, the grey matter has a higher density than the white matter. The occurrence of brain oedema reduces GWR.  **QRA (Quantitative regional abnormality)** is the sum of hypoattenuations in 12 parenchymal areas on brain CT and is calculated bilaterally (lower scores indicate fewer hypoattenuation, maximum score of 24).  **ASPECTS-b** (The Alberta Stroke Program Early CT Score) provides a semiquantitative assessment of early ischemic changes on brain CT in the middle cerebral artery territory, bilaterally. ASPECTS-b score is calculated by subtracting 1 per each change from the maximum score of 20 points. Lower scores indicate more abnormalities. | In the study from Lee, 2017 CT was performed early, when the discriminative value of GWR for post-CA brain injury is low.  The ASPECTS-b score, was more accurate than GWR or QRA in that study [Lee, 2017]. However, ASPECTS-b has been designed for assessing ischaemic injury from stroke, which is usually unilateral. Brain damage after CA is usually bilateral, which deprives the reader of the CT scan of a contralateral reference when detecting ischaemic changes. The feasibility of the ASPECT-b score after CA is thus uncertain. |
| Undesirable Effects How substantial are the undesirable anticipated effects? | | |
| JUDGEMENT | RESEARCH EVIDENCE | ADDITIONAL CONSIDERATIONS |
| ○ Large ○ Moderate  ●Small  ○Trivial  ○ Varies  ○ Don't know | Brain CT implies exposure to ionizing radiation.  Brain imaging is usually not available at the bedside and requires transportation to a Radiology department. Patients after cardiac arrest are often hemodynamically unstable, and intra-hospital transport may carry additional risk. | A falsely optimistic prediction in a patient with poor neurological outcome may potentially lead to therapeutic obstinacy. |
| 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 for brain CT is very low because of lack of blinding and it is based on only one retrospective study ([Lee, 2017] on 67 participants) investigating good outcome. That study included only patients with CT scan performed within six hours after CA (potential selection bias)  A source of confounding for GWR is represented by the different available methods and sites of measurement. | Unlike other predictors, such as those based on clinical examination, imaging is not affected by sedation or paralysis and can be assessed blindly.  There is no consensus on what the normal levels for GWR are. ASPECT-b score has been designed to assess ischemic injury after stroke. |
| 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 | Almost all prognostic studies included in our review 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 |
| ○ Favours the comparison ○ Probably favours the comparison ● Does not favour either the intervention or the comparison  ○ Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know | A high GWR or QRA or ASPECT-b score is associated with good neurological outcome after cardiac arrest. However, evidence is limited to one study, and both sensitivity and specificity are probably too low to make clinical decisions based on brain CT. |  |
| 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. | The costs of imaging assessment are higher when compared with those of clinical examination. In addition, the measurement of GWR/QRA/ASPECTS-b requires additional calculations and skills. On the other side, undergoing brain CT is routine for most patients who are unconscious after resuscitation and are scheduled for coronary angiography and/or treatment with anticoagulants. |
| 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 | We did not identify any studies specifically assessing costs of imaging for prognostication after cardiac arrest. |  |
| 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 | We did not identify any studies addressing cost-effectiveness. |  |
| 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 | No studies addressing this question were identified. | A problem of inequity is possible, since prognostic assessment using imaging implies resources and skills that may not be universally available. |
| 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 studies assessing acceptability, but 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 | Feasibility was not specifically addressed in any of the studies included in this review. | Imagingstudies used for neuroprognostication after cardiac arrest cannot be performed at the bedside and require transportation to a Radiology Department, with additional clinical and safety risks. A CT scan is likely available in every hospital, at least in high-income countries, but the skills to assess the severity of HIBI on brain CT may not be universally available. |

# 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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| Recommendation |
| * **We suggest against using GWR, QRA, or ASPECTS-b on brain CT to predict good neurological outcome in patients who are comatose after cardiac arrest (weak recommendation, very-low certainty of evidence).** |
| Justification |
| Evidence showing that a high grey matter to white matter ratio (GWR), a low quantitative regional attenuation (QRA) score or a high Alberta Stroke Program Early CT (ASPECTS-b) score predict good neurological outcome after cardiac arrest is limited to one study, and the certainty of evidence is very low. There is a wide heterogeneity of measurement techniques (sites and calculation methods) for GWR. |
| Subgroup considerations |
| None |
| Implementation considerations |

Prognostication based on imaging requires technology and skills that may not be universally available.

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| Monitoring and evaluation |
| |  | | --- | | Research priorities | | A consistent GWR threshold for predicting good neurological outcome after cardiac arrest should be identified.  A standardisation of the methods for GWR calculation is warranted.  The optimal timing for prognostication using brain CT after cardiac arrest is still unknown. Studies assessing serial brain CT after cardiac arrest are desirable. |   None |