|  |  |
| --- | --- |
| Question | |
| **Gradient-recalled echo (GRE) on brain magnetic resonance imaging (MRI) 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:** | Gradient-recalled echo (GRE) on brain magnetic resonance imaging (MRI), assessed within four days after cardiac arrest. |
| **Comparison:** | *None.* |
| **Main outcomes:** | Prediction of good neurological outcome defined as Cerebral Performance Categories (CPC) 1–2 at 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 Unpublished studies, reviews, case reports, case series, studies including less than 10 patients, letters, editorials, conference abstracts, and studies published in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

|  |  |  |
| --- | --- | --- |
| 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 | Gradient-recalled echo (GRE) was investigated in one study [Jang, 2019].  Phase-images of the T2-weighted GRE sequence were assessed at a mean of 74.5 h after ROSC. GRE was measured in three venous structures of the brain, the superior sagittal sinus, the thalamostriate veins, and the cortical veins to assess changes in cerebral venous oxygen content. **The absence of GRE abnormalities** (summary GRE score 0)predicted good outcome at six months **with 100% specificity and 75% sensitivity** (very- low-certainty evidence)  Jinhee Jang, Sang Hoon Oh, Yoonho Nam, et al. Prognostic value of phase information of 2D T2\*-weighted gradient echo brain imaging in cardiac arrest survivors: A preliminary study, Resuscitation, 140:142-149 |  |
| Undesirable Effects How substantial are the undesirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Large ○ Moderate ● Small  ○ Trivial  ○ Varies  ○ Don't know | Brain imaging is usually not available at the bedside. 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 GRE is based only on one study, and it is very low because of the high risk of bias, especially self-fulfilling prophecy and selection bias.  In the included study [Jang, 2019], brain MRI, but not the GRE score, was used for prognostication after CA. GRE values of cases were compared with GRE values determined from ten healthy controls. | Unlike other predictors, such as those based on clinical examination, imaging is not affected by sedation or paralysis and can be assessed blindly.  However, the interpretation of imaging results is operator dependent. |
| 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 | Good outcome is defined as CPC 1-2 in almost all prognostication studies. | 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 | The absence of GRE abnormalities was 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 | The costs of imaging assessment are higher when compared with those of clinical examination. In addition, measurement of GRE requires specific skills. No study assessing savings from prognostication based on imaging has been included in our review. |  |
| 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 | A problem of inequity is possible since prognostic assessment using imaging requires resources and skills that may not be available anywhere, anytime. |  |
| 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 study 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. | MRI cannot be performed at the bedside, which is a major limitation, and it carries additional risks due to the magnetic field, which makes it incompatible with most standard monitoring equipment and with some implanted devices, such as pacemakers/defibrillators. In addition, MRI recording is a relatively long procedure.  An MRI is available in most hospitals in high-income countries, but the skills to assess the severity of HIBI on brain MRI may not be universally available.. |

# Summary of judgements

|  | **Judgement** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **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

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| 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

|  |
| --- |
| Recommendation |
| **We suggest against routine use of GRE on brain MRI to predict good neurological outcome in patients who are comatose after cardiac arrest (weak recommendation, very-low-certainty evidence).** |
| Justification |
| Although the absence of gradient Echo (GRE) abnormalities was associated with good neurological outcome three days after cardiac arrest, the evidence is limited to one study, and the certainty of the evidence is very low. |

|  |
| --- |
| Subgroup considerations |
| None |
| Implementation considerations |

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

|  |
| --- |
| Monitoring and evaluation |
| |  | | --- | | Research priorities | | Further studies are needed to assess the usefulness of GRE abnormalities for assessing HIBI after cardiac arrest.  The influence of comorbidities (e.g., the presence of white matter lesions or brain atrophy) on imaging techniques has not been sufficiently investigated. |   None |