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Clinical paper

Prediction of good functional outcome decreases diagnostic uncertainty in unconscious survivors after out-of-hospital cardiac arrest

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Abstract

Purpose: To explore modifications of the 2021 European Resuscitation Council/European Society of Intensive Care Medicine (ERC/ESICM) guideline algorithm for neuroprognostication after cardiac arrest to improve its prognostic accuracy.

Methods: Post-hoc analysis of four prospective multicentre studies (TTM, TTM2, KORHN and ProNeCA). We raised the Glasgow Coma Scale motor (GCS-M) inclusion threshold at 72 h after cardiac arrest from the current GCS-M < 4 to GCS-M < 6 (all unconscious patients). Secondly, we included good outcome predictors (GCS-M 4–5, neuron-specific enolase < 17 μg/L, benign electroencephalography patterns ≤ 72 h post-arrest and normal magnetic resonance imaging at 72–168 h post-arrest) in the algorithm. Functional outcome was assessed dichotomously at six months, including modified Rankin Scale 0–3, Cerebral Performance Category 1–2 or Glasgow Outcome Scale 4–5 (no symptoms to moderate disability) as good outcome.

Results: We analysed 3,388 patients, of whom 2,079 had GCS-M < 4 at ≥ 72 h. Of the 874 patients identified by the 2021 ERC/ESICM poor outcome criteria, 870 had poor functional outcome (specificity: 99.6% [95%CI 99.0–99.9]). Using the GCS-M < 6 threshold, 366 more patients entered the algorithm ($N = 2,445$). Seven more patients with poor outcomes were identified, with close to identical specificity. Good outcome predictors thereafter identified 673 patients with potential recovery, of whom 411 (61%) had a good functional outcome at six months. With the updated algorithm, the number of prognosticated patients with an indeterminate prognosis decreased from 1,205/2,079 (58%) to 891/2,445 (36%).

Conclusion: Raising the GCS-M inclusion threshold and adding favourable predictors to the 2021 ERC/ESICM prognostication algorithm reduced prognostic uncertainty without increasing falsely pessimistic predictions.

Keywords: Neurological Prognostication, Cardiac Arrest, Functional Outcome, Good Outcome Prediction, Indeterminate Prognosis

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Introduction

Neurological prognostication in patients who remain unconscious after cardiac arrest is essential for making treatment decisions.[1–4] The European Resuscitation Council and the European Society of Intensive Care Medicine (ERC/ESICM) recommend a multimodal algorithm to predict poor outcome in patients with two or more unfavourable predictors. In validation studies, this algorithm has demonstrated 100% specificity for poor outcome prediction.[1,2,5–8] However, almost half of the prognosticated patients remain with an indeterminate prognosis.[5–8] Some of these patients achieve a good functional outcome at six months.[5,9] Identifying patients with indeterminate prognosis and a potential for neurological recovery might reduce the prognostic uncertainty of the 2021 ERC/ESICM algorithm.[2]

A recent validation study performed in a WLST-permitting cohort with a high proportion of poor outcome showed that an increased threshold for inclusion in the prognostication algorithm from Glasgow Coma Scale motor (GCS-M) < 4 to GCS-M < 6 was feasible, without reduced specificity.[7]

Moreover, in 2022 an ERC/ESICM-endorsed systematic review identified several predictors of good outcome after cardiac arrest, including a GCS-M score 4–5 on day 4, normal blood values of neuron-specific enolase (NSE) $\leq$ 72 h, a continuous or nearly continuous normal-voltage electroencephalogram (EEG) background without periodic discharges or seizures at $\leq$ 72 h, and a lack of diffusion restriction on magnetic resonance imaging (MRI) on day 2–7.[10] Although these predictors are recommended as favourable predictors by a consensus statement from the International Liaison Committee on Resuscitation (ILCOR), they have not yet been incorporated into clinical practice guidelines.[11]

The 2025 ERC/ESICM post-resuscitation care writing group initiated the current study with the aim to explore how the 2021 prognostic algorithm could be improved using previously collected data. We hypothesised that adding criteria of likely favourable prognosis would improve the overall prognostic accuracy.

We evaluated the following potential modifications:

1) Extending the motor score entry criteria of the algorithm to include all unconscious patients (GCS-M < 6). The safety of this approach was evaluated by exploring the risk of reducing the algorithm's specificity (increased rate of false pessimistic predictions).
2) Including favourable predictors to identify patients destined for neurological recovery to reduce the number of patients with an indeterminate outcome.

Additionally, we explored whether the current ERC/ESICM recommendation to exert caution when predictors give discordant signals is justified.

Methods

Study design

This was a post-hoc analysis of adults with out-of-hospital cardiac arrest from four studies. Two were randomised trials: the Target Temperature Management after out-of-hospital cardiac arrest (TTM) trial and the Targeted Hypothermia versus Targeted Normothermia after Out-of-Hospital Cardiac Arrest (TTM2) trial. The two other included studies were observational: the Korean Hypothermia Network Prospective Registry 1.0 (KORHN) and the Prognostication of Neurological outcome after Cardiac Arrest (ProNeCA).[12–15] Study designs and results have previously been published.[12–17] An overview of the differences in the study design is presented in eTable 1. We considered all patients with available functional outcome after out-of-hospital cardiac arrest as eligible and included those who were alive after 72 h and had an available GCS-M.

Ethical consent was obtained in all participating countries, including the Regional Ethics Committee of Tuscany (ProNeCA), the Institutional review board (IRB) of Seoul St. Mary's Hospital (KORHN), the Regional Ethics Board at Lund University (TTM) and the Swedish Ethical Review Authority (TTM2).

Predictors

Clinical neurological examination

The patient's best motor response (GCS-M) on day 4 (72–96 h) was used for analysis.[18,19] We performed a sensitivity analysis evaluating the patients' best motor response on day one to five. Pupillary light and corneal reflexes were evaluated on day 4 (72–96 h) or, if unavailable, completed with data from day 5 (96–108 h) post-arrest. The presence of clinical status myoclonus was assessed daily and defined as generalised involuntary sudden jerks with a duration exceeding 30 min and manifested within 72 h.[12–17]

Neuroimaging

Neuroimaging, including computed tomography (CT) and MRI, was performed on clinical indication in the TTM, TTM2 and KORHN studies, except for thirteen sites participating in the prospective TTM2 CT substudy, which routinely investigated unconscious patients (GCS-M < 6) with brain CT at 48 h post-arrest.[12–14,16,17] In the ProNeCA study, results of CT performed at < 24 h were retrospectively reported in 7 out of 13 sites.[15] On-site radiologists qualitatively assessed whether diffuse and extensive anoxic injury was present. Results of neuroimaging were available to treating physicians.

Neurophysiology

In the ProNeCA study, short-latency somatosensory evoked potentials (SSEP) and EEG were routinely performed at 12, 24 and 72 h.[15] In the TTM trial, EEG was mandatory in all patients comatose beyond 48 h. In the TTM2 and KORHN studies, SSEP and EEG were performed on clinical indication. The neurophysiology results were available to the treating physicians.[12–14,16,17]

Biomarkers

NSE values were routinely available for prognostication during TTM, TTM2 and KORHN studies and analysed as per clinical routine at 0–72 h.[12–14,16,17] The ProNeCA study did not include NSE values.[15]

Prognostication

In the 2021 ERC/ESICM guideline algorithm, all patients who do not meet the criteria for a likely poor outcome are considered as having an indeterminate prognosis.[2] In our analysis, we introduced a two-step approach to neurological prognostication, first assessing poor outcome by evaluating unfavourable criteria and thereafter predicting good outcome based on favourable criteria. Finally, patients with neither favourable nor unfavourable predictors were considered to have an indeterminate prognosis.

Prediction of poor functional outcome

Based on the 2021 ERC/ESICM guideline algorithm, poor outcome is likely if at least two of the following signs are present: clinical status myoclonus $\leq$ 72 h, bilaterally absent pupillary light and corneal reflexes at $\geq$ 72 h, bilaterally absent N20 potentials on SSEP $\geq$ 24 h, suppression or burst suppression pattern on EEG at > 24 h, NSE > 60 μg/L at 48 and/or 72 h, and signs of hypoxic-ischaemic brain injury on MRI at day 2–7 and/or on CT at $\leq$ 72 h post-arrest.[2] For this analysis, we considered diffuse and extensive hypoxic-ischaemic brain injury on brain CT up to day 7 as predictive of poor outcome.[4,20,21]

Prediction of good functional outcome

Good outcome prediction was based on at least one of the following criteria in accordance with recent ILCOR recommendations: 1. Motor score (GCS-M 4–5) on day 4; 2. Benign EEG, defined in the current study as continuous, nearly continuous or reactive background on EEG at $\leq$ 72 h; 3. NSE < 17 μg/L at $\leq$ 72 h; 4. Absence of diffusion restrictions and other signs of hypoxic-ischaemic brain injury on MRI at 72–168 h post-arrest.[22]

Outcome

The primary outcome was functional outcome at six months, evaluated by blinded trained assessors using the Modified Rankin Scale (mRS), Cerebral Performance Category (CPC) or Glasgow Outcome Scale (GOS).[18,23,24] Good functional outcome was categorised as mRS 0–3 or CPC 1–2 or GOS 4–5 (no symptoms to moderate disability), whereas mRS 4–6, CPC 3–5 and GOS 1–3 (moderate-severe/severe disability to death) were considered as poor functional outcome. Binary assessments of functional outcome as good or poor, based on medical records or telephone interview at six months, were also accepted as primary outcome.[12–17] We performed a sensitivity analysis including moderate-severe/severe disability (mRS 4, CPC 3, GOS 3) as good functional outcome.

Withdrawal of life-sustaining therapy

In the TTM and TTM2 trials, withdrawal of life-sustaining therapy (WLST) was permitted after neurological prognostication when poor outcome was likely according to conservative trial protocol criteria assessed at 96 (TTM2) and 108 h (TTM) post-arrest, respectively (eTable 2).[17] An experienced physician performed neurological prognostication. Decisions about WLST were made at the discretion of the treating physician.[16,17] ProNeCA did not allow for WLST and KORHN had very rare cases of WLST.[14,15]

Statistical analysis

Continuous variables were presented as median with interquartile range (IQR) except for age, which was presented as mean with stan-

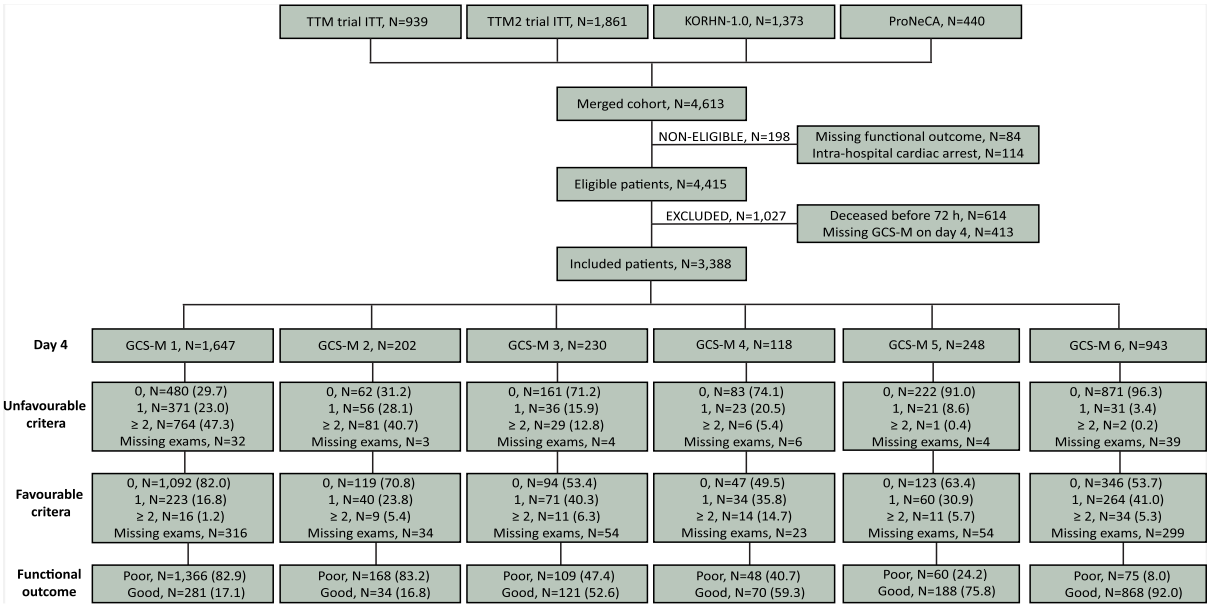

Fig. 1 – Flowchart of patient inclusion, level of consciousness, prognostic criteria and functional outcome. We included all patients with available functional outcome at six months after an out-of-hospital cardiac arrest. Patients who were deceased before 72 h or had missing motor score on day 4 (72–96 h) were excluded. Motor score was defined according to Glasgow Coma Scale Motor (GCS-M) score ranging from 1 "no reaction to pain" up to 6 "awake and obeying commands".[18,19] Unfavourable ERC/ESICM predictors included NSE levels > 60 μg/L at 48 and/or 72 h, highly malignant EEG, bilaterally absent N20 on SSEP, bilaterally absent pupillary light and corneal reflexes, early clinical status myoclonus and hypoxic-ischaemic brain injury on neuroimaging. Favourable predictors included benign EEG $\leq$ 72 h, NSE values < 17 μg/L at $\leq$ 72 h and MRI without diffusion restrictions at 72–168 h. Functional outcome was assessed dichotomously at six months, including modified Rankin Scale 0–3, Cerebral Performance Category 1–2 or Glasgow Outcome Scale 4–5 (no symptoms to moderate disability) as good outcome. Missing exams indicated that none of the examinations listed above were performed. In the flowchart, this category is presented separately for favourable criteria (excluding motor score) and for unfavourable criteria.

dard deviation (SD). We calculated confidence intervals (95%CI) using the Wilson's method. Prognostic accuracies were calculated excluding patients with an indeterminate prognosis, as they did not fit the classification of either positive or negative predictions. Specificity was reported as the proportion of true negatives (predicted and documented good outcomes) among all documented good outcomes. Sensitivity was reported as the proportion of true positives (predicted and documented poor outcomes) among all documented poor outcomes. TTM2 original exam reports were retrospectively monitored as described in the supplement. Analyses were performed using R version 2024.04.2 + 764.

Results

The four cohorts comprised a total of 4,415 eligible patients, of whom we included 3,388 (77%) patients with out-of-hospital cardiac arrest and available functional outcome at six months (Fig. 1). Patients who died before 72 h (*N* = 614) and patients with a missing GCS-M on day 4 (*N* = 413) were excluded. The included patients had a mean age of 61 (SD 14) years, 2,792 (82%) had a presumed cardiac cause of arrest, and a median of 25 (IQR 16–38) minutes to return of spontaneous circulation (eTable 3). At six months, 54% of the included patients had a poor outcome, compared to 77% of the excluded patients (eTable 3). The rate of good outcome survival at six months increased with an improving motor score on day 4, from 17% for patients with no pain reaction (GCS-M 1) to 76% for patients who localized pain (GCS-M 5) (Fig. 1). The prognostic accuracies of individual predictors are presented in eTable 4.

Performance of the 2021 ERC/ESICM algorithm

Among the total 3,388 patients, 1,309 (39%) did not fulfil the entry criteria of the 2021 ERC/ESICM prognostic algorithm, having a GCS-M $\geq$ 4 on day 4 (Fig. 2). Of these, 1,126/1,309 (86%) had a good outcome at six months. Of the remaining 2,079 patients who entered the algorithm, 874 (42%) fulfilled two or more unfavourable criteria and were predicted to have a poor outcome, which occurred in 870 patients (specificity: 99.6% [95%CI 99.0–99.9]). Thus, the 2021 ERC/ESICM guidelines identified poor outcome in 870/3,388 (26%) of the overall cohort. The prognosis remained indeterminate in 1,205 (58%) prognosticated patients, of whom 773 (64%) had a poor outcome at six months (Fig. 2).

Four patients had a falsely pessimistic prediction at 72 h after cardiac arrest (Fig. 2). Three of these were retrospectively evaluated as misclassifications of the original examination reports (eTable 5). The remaining false positive prediction was in a patient with an unreactive suppressed EEG background at 68 h and bilaterally absent corneal and pupillary light reflexes on day 4. The brainstem reflexes recovered by 172 h during a formal trial prognostication when lingering sedation was no longer considered a confounder. This patient's neurological prognosis was not classified as likely poor, neither at trial prognostication nor *a posteriori*. None of these patients had any coexisting favourable predictors (Table 2).

Extending the motor score entry criterion

When we extended the prognostic entry criterion to GCS-M < 6 (all patients who were not awake and obeying commands), 366 more patients (a total of 2,445) entered the algorithm (eFig. 1). Seven additional patients were identified by the poor outcome criteria, without additional falsely pessimistic predictions. On the other hand, the modified entry criteria increased the number of patients with an indeterminate prognosis to a total of 1,564 patients (Table 1).

Inclusion of favourable predictors

In the new cohort, 736/2,445 (30%) patients entering the algorithm had at least one favourable predictor (eTable 6). Of them, 411

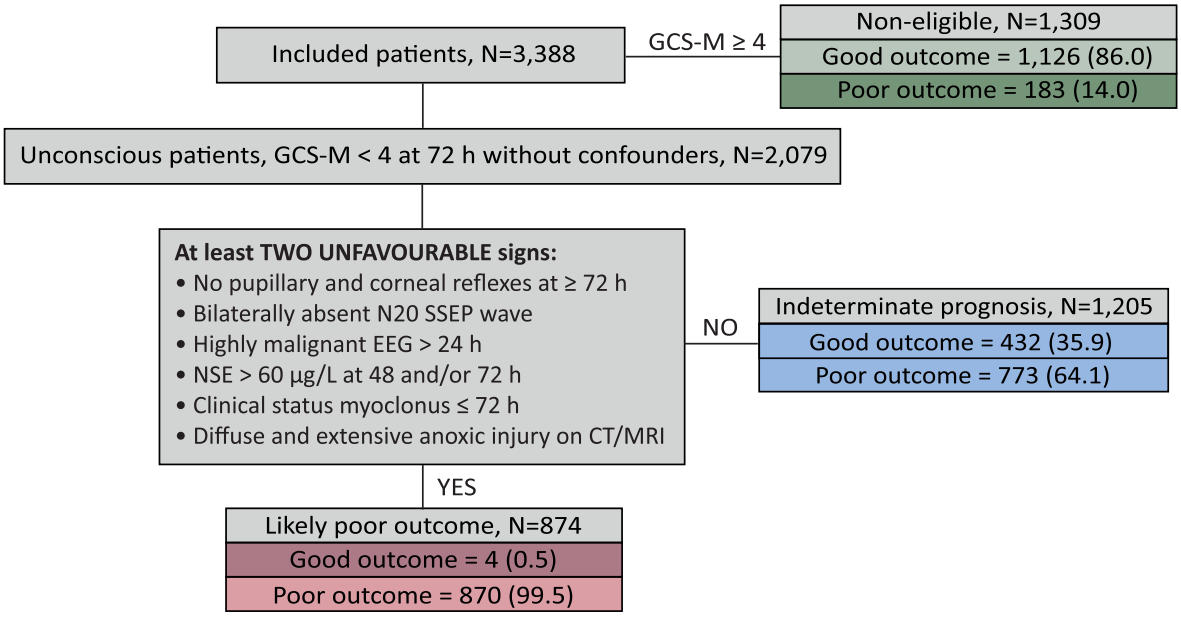

Fig. 2 – Prognostic performance of the 2021 ERC/ESICM algorithm. The 2021 ERC/ESICM guideline algorithm on neurological prognostication. Patients with indeterminate prognosis were not included as likely good outcome prediction (true or false negative patients).

Table 1 – Table of predictive performance for ERC/ESICM modifications.

	TP	FP	TN	FN	Indeterminate prognosis (%)	Correct prognosis (TP + TN, %)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Fig. 2 2021 ERC/ESICM	870	4	1,126	183	1,205 (35.6)	1,996 (58.9)	82.6 (80.2–84.8)	99.6 (99.0–99.9)	99.5 (98.7–99.9)	86.0 (84.0–87.8)
Fig. 3 Optimal modification	877	4	1,279	337	891 (26.3)	2,156 (63.6)	72.2 (69.6–74.7)	99.7 (99.1–99.9)	99.5 (98.8–99.9)	79.1 (77.1–81.1)
Analyses published in the supplementary										
eFig. 1 Extending inclusion to GCS-M < 6	877	4	868	75	1,564 (46.2)	1,745 (51.5)	92.1 (90.2–93.7)	99.5 (98.7–99.9)	99.5 (98.8–99.9)	92.0 (90.1–93.7)
eFig. 2 Adding favourable predictors to 2021 ERC/ESICM	870	4	1,279	344	891 (26.3)	2,149 (63.4)	71.7 (69.0–74.2)	99.7 (99.1–99.9)	99.5 (98.7–99.9)	78.8 (76.7–80.8)
eFig. 3 Evaluating favourable predictors first	814	4	1,279	400	891 (26.3)	2,093 (61.8)	67.1 (64.3–69.7)	99.7 (99.1–99.9)	99.5 (98.7–99.8)	76.2 (74.0–78.2)

Predictive performances of the 2021 ERC/ESICM guideline algorithm on neurological prognostication and the suggested modifications to the algorithm, $N = 3,388$. TP: predicted poor outcome and observed poor functional outcome at six months. FP: predicted poor outcome but good functional outcome was observed at six months. TN: predicted good outcome (including those excluded from neuroprognostication due to motor score level or those with at least one favourable criterion) and observed good functional outcome at six months. FN: predicted good outcome, but poor functional outcome was observed at six months. Prognostic accuracies were calculated excluding patients with an indeterminate prognosis, as they did not fit the classification of either positive or negative predictions. Specificity was reported as the proportion of true negatives (TN) among all documented good outcomes. Sensitivity was reported as the proportion of true positives (TP) among all documented poor outcomes.

(56%) had a good outcome at six months (eTable 6). The specificity of individual favourable predictors for good outcome ranged from 28% (95%CI 25–31) for normal NSE values to 96% (95%CI 88–99) for MRI without diffusion restrictions (eTable 4). Using these favourable predictors, the number of patients remaining with an indeterminate prognosis was 891/2,445 (36%), compared to 1,205/2,079 (58%) in the 2021 ERC/ESICM algorithm (Figs. 2 and 3). Of these indeterminate patients, 48% lacked NSE samples, 80% were not examined with EEG and 97% had no MRI performed (eTable 7).

In a sensitivity analysis we added favourable predictors to the 2021 ERC/ESICM criteria in all patients with GCS-M < 4. This approach correctly identified 153 previously indeterminate patients with good outcome (eFig. 2, Table 1). Our results were largely consistent even when including moderate-severe/severe neurological deficits as good outcome, with 5/3,313 (0.2%) patients with mRS 4/CPC 3/GOS 3 meeting two or more unfavourable ERC/ESICM criteria (eTable 8).

As an exploratory analysis, we investigated an alternative version of the algorithm by adding the favourable predictors prior to evaluating the unfavourable predictors. This reduced the detection of poor outcome patients from 877 to 814, with an equivalent increase in false negative predictions, reducing the overall prognostic performance (eFig. 3, Table 1). These results were consistent also when evaluating the patients' best motor response in an extended group of patients ($N = 3,784$) with available motor score on day one to five (eTable 9-10).

Patients with discordant predictors

Among 736 patients with at least one favourable predictor in our cohort, 63 also had two or more coexisting unfavourable predictors (eTable 6). All these patients had poor outcome at six months. In 131 patients, one single unfavourable predictor coexisted with at least one favourable predictor (eTable 6, Table 2). Of these patients, 42 (32%) survived with a good outcome at six months (Table 2). The proportion of survival with good outcome was higher in patients who had two coexisting favourable predictors (16/25, 64%) compared to only one (26/104, 25%). In patients with no discordant poor outcome predictors, the proportion of good outcome survival was 83/104 (80%) for patients with two favourable predictors and 269/415 (65%) for patients with one favourable predictor (Table 2).

Discussion

Our results demonstrate that the prognostic uncertainty of the 2021 ERC/ESICM algorithm can be reduced without decreasing its specificity by including all patients who are not awake and obeying commands after 72 h and applying the favourable predictors recommended by ILCOR.[11].

In our study, broadening the entry criteria of the ERC/ESICM algorithm did not reduce its specificity, confirming a recent study from a different multicentre cohort with a high proportion of poor outcome and allowing for WLST.[7] The algorithm's sensitivity for identifying poor outcome did not significantly increase by this approach, since only seven more patients with a poor outcome were identified. This was expected, since the patients entering the algorithm had less severe signs of hypoxic-ischaemic brain injury and, therefore, only a few of them fulfilled the strict criteria for a likely poor outcome. The increase in prognostic yield we observed was almost entirely attribu-

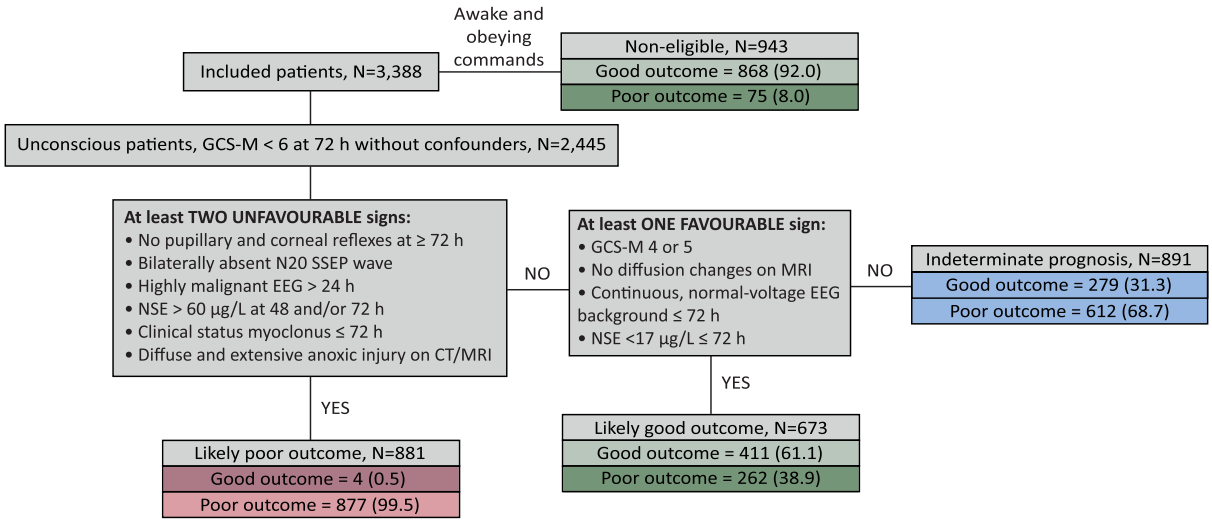

Fig. 3 – Modification of the 2021 ERC/ESICM guideline algorithm for neurological prognostication by including all unconscious patients (GCS-M < 6) and predictors of likely good outcome. Favourable predictors included benign EEG ≤ 72 h, NSE values < 17 µg/L at ≤ 72 h, MRI without diffusion restrictions at 72–168 h and GCS-M 4–5 on day 4. This algorithm first evaluated criteria for likely poor outcome and thereafter evaluated predictors for likely good outcome.

ted to the algorithm's enhanced ability to predict good outcomes in patients previously assigned to the indeterminate group, thereby reducing the prognostic uncertainty. This was achieved both when extending the entry criteria to include GCS-M 4–5 and when evaluating NSE, MRI and EEG among patients with GCS-M < 4.

Of the 736 prognosticated patients with at least one favourable predictor in our cohort, 44% nevertheless had a poor outcome at six months. One third of the ICU-mortality after a cardiac arrest depends on causes other than brain injury, such as cardiogenic shock or multiple organ failure.[25–27] Part of these deaths may even occur after an initial neurological recovery.[28,29] Confounding from extracerebral causes of death is likely one reason why the prediction of good functional survival is rarely 100% accurate. In the 2022 review informing the ILCOR recommendations, the specificity of the most reliable favourable predictors was 80% with a sensitivity above 40% in most studies.[10] In our cohort, EEG and MRI exceeded these standards whereas normal NSE values had a very high sensitivity and a correspondingly low specificity for good outcome.

Achieving a zero false positive rate is less important for good outcome prediction, as it does not entail a risk of treatment withdrawal.[30] Current guidelines advocate that all unconscious patients who do not fulfil criteria for poor outcome should be observed and re-evaluated. Previous studies, nevertheless, indicate an excess mortality among patients with WLST outside of guideline recommendations, and studies including matched controls in non-WLST cohorts suggest that some of these may have survived with good outcome if treatment had continued.[31–34] This demonstrates the clinical importance of reducing the number of patients with indeterminate prognosis. Potential treatment implications of favourable predictors may include avoiding WLST despite delayed awakening, thereby strengthening adherence to guidelines and protecting patients from inadequate treatment withdrawal.

Interestingly, our analysis showed that the specificity for good outcome prediction varied based on the balance between coexisting favourable and unfavourable predictors. The 2021 ERC/ESICM guidelines recommend caution when favourable and unfavourable predictors coexist, indicating a potential for recovery, but this strategy has not previously been validated.[2] Our study showed that patients with two concordant unfavourable predictors had poor outcome regardless of any coexisting discordant favourable predictor indicating potential recovery. Conversely, the presence of one or more coexisting favourable predictor in patients with only one unfavourable sign was often followed by neurological recovery.

Based on the high specificity of the unfavourable predictors, we recommend a two-step approach: first, prognosticate a likely poor outcome, and then, for the remaining patients without signs of irreversible severe hypoxic-ischaemic brain injury, evaluate favourable predictors to reduce the diagnostic uncertainty. The correctness of this approach is confirmed by our exploratory analysis, showing that prognosticating good outcome first reduced the overall sensitivity. Confirming previous studies, a dose–response relationship in the rate of good outcome was observed among favourable predictors, indicating an additive chance for recovery.[9,35] The highest good outcome rate and specificity for good outcome prediction was found in patients with two or more concordant favourable predictors without coexisting unfavourable predictors.

An important limitation in our cohort includes that none of the studies were designed for the examination of favourable predictors. We presume that a higher prognostic accuracy would be achieved in a better-examined cohort. This reinforces the ERC/ESICM recommendation to re-evaluate indeterminate patients to reduce diagnostic uncertainty, rather than to observe passively. Other limitations include that WLST was permitted during the TTM trials using similar criteria to those in the current ERC/ESICM guidelines and that follow-up routines differed between the original studies.

Conclusions

Our study showed that broadening the entry criteria of the 2021 ERC/ESICM algorithm for neuroprognostication after cardiac arrest to include all unconscious patients (GCS-M < 6) and adding good out-

Table 2 – Functional outcome based on present unfavourable and favourable predictors for prognosticated patients.

		Unfavourable predictors Likely poor outcome for ≥ 2 predictors					
		0	1	2	3	4	5
Favourable predictors Likely good outcome for ≥ 1 predictor	0	Good: 251 (49%) Poor: 264 (51%) (*N* = 515)	Good: 28 (7%) Poor: 348 (93%) (*N* = 376)	Good: 4[A] (1%) Poor: 392 (99%) (*N* = 396)	Good: 0% Poor: 258 (100%) (*N* = 258)	Good: 0 (0%) Poor: 124 (100%) (*N* = 124)	Good: 0 (0%) Poor: 40 (100%) (*N* = 40)
	1	Good: 269 (65%) Poor: 146 (35%) (*N* = 415)	Good: 26 (25%) Poor: 78 (75%) (*N* = 104)	Good: 0 (0%) Poor: 45 (100%) (*N* = 45)	Good: 0 (0%) Poor: 12 (100%) (*N* = 12)	Good: 0 (0%) Poor: 5 (100%) (*N* = 5)	
	2	Good: 83 (80%) Poor: 21 (20%) (*N* = 104)	Good: 16 (64%) Poor: 9 (36%) (*N* = 25)	Good: 0 (0%) Poor: 1 (100%) (*N* = 1)			
	3	Good: 17 (74%) Poor: 6 (26%) (*N* = 23)	Good: 0 (0%) Poor: 2 (100%) (*N* = 2)				

Descriptive table of functional outcome based on the number of favourable and unfavourable predictors in all prognosticated patients (GCS-M < 6, *N* = 2,445). Favourable predictors included benign EEG ≤ 72 h, NSE values < 17 μg/L at ≤ 72 h, MRI without diffusion restrictions at 72–168 h and GCS-M 4 or 5 on day 4. Unfavourable predictors included NSE values > 60 μg/L at 48 and/or 72 h, highly malignant EEG, bilaterally absent N20 on SSEP, bilaterally absent pupillary light and corneal reflexes, early clinical status myoclonus and hypoxic-ischaemic brain injury on neuroimaging. [A] Three of these patients were at retrospective monitoring identified as cases of misclassification of original exam reports. The fourth patient, a 70-year-old male with 21 min to return of spontaneous rhythm after a witnessed cardiac arrest with bystander cardiopulmonary resuscitation, had unreactive supressed background on electroencephalogram at 68 h and absent brainstem reflexes on day 4. The brain stem reflexes had recovered during formal trial-prognostication at 172 h. None of these patients were classified as likely poor, neither at trial prognostication nor a posteriori.

come prediction reduces the number of patients with an indeterminate prognosis without increasing the risk of falsely pessimistic prediction. Moreover, it confirmed the current recommendation to exercise caution in patients with one unfavourable predictor and at least one discordant favourable predictor.

Conflict of interest (COI)

BKL: Honorarium from BD for a lecture. CH: Research funding from The Danish Heart Association, honorarium from BD for lectures and vice president of ESC. CRo: Lecture fees from BD. FST: Lecture fees from ZOLL and BD. JK: Research funding from the NovoNordisk Foundation outside the submitted work. JN: Editor-in-Chief Resuscitation (paid an honorarium by Elsevier). MPW: Served on advisory boards for DRW diagnostics and Clinical Expert NICE Advice Service. TP: Lecture fees from BD. TC, CS, GL, AC, JN are members of the 2025 ERC/ESICM post-resuscitation care writing group. No other conflicts of interest were reported.

CRediT authorship contribution statement

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

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