Received: 2 March 2023 | Revised: 16 September 2023 | Accepted: 19 September 2023

DOI: 10.1111/aas.14337

RESEARCH ARTICLE

acta Anaesthesiologica Scandinavica

Outcome prediction in comatose cardiac arrest patients with initial shockable and non-shockable rhythms

Henning Wimmer[1,2] | Stine Håheim Stensønes[3] | Jūratė Šaltytė Benth[2,4] | Christofer Lundqvist[2,4,5] | Geir Ø. Andersen[6] | Tomas Drægni[7] | Kjetil Sunde[2,8] | Espen Rostrup Nakstad[1]

[1]Department of Acute Medicine, Oslo University Hospital, Ullevål, Norway

[2]Institute of Clinical Medicine, University of Oslo, Oslo, Norway

[3]Faculty of Medicine, University of Oslo, Oslo, Norway

[4]Health Services Research Unit, Akershus University Hospital, Nordbyhagen, Norway

[5]Department of Neurology, Akershus University Hospital, Nordbyhagen, Norway

[6]Department of Cardiology, Oslo University Hospital, Ullevål, Norway

[7]Department of Research and Development, Oslo University Hospital, Ullevål, Norway

[8]Department of Anaesthesia and Intensive Care, Oslo University Hospital, Ullevål, Norway

Correspondence
Henning Wimmer, Department of Acute Medicine, Oslo University Hospital, PO Box 4950 Nydalen, 0424 Oslo, Norway.
Email: henning.wimmer@mailbox.org

Abstract

Background: Prognosis after out-of-hospital cardiac arrest (OHCA) is presumed poorer in patients with non-shockable than shockable rhythms, frequently leading to treatment withdrawal. Multimodal outcome prediction is recommended 72 h post-arrest in still comatose patients, not considering initial rhythms. We investigated accuracy of outcome predictors in all comatose OHCA survivors, with a particular focus on shockable vs. non-shockable rhythms.

Methods: In this observational NORCAST sub-study, patients still comatose 72 h post-arrest were stratified by shockable vs. non-shockable rhythms for outcome prediction analyzes. Good outcome was defined as cerebral performance category 1–2 within 6 months. False positive rate (FPR) was used for poor and sensitivity for good outcome prediction accuracy.

Results: Overall, 72/128 (56%) patients with shockable and 12/50 (24%) with non-shockable rhythms had good outcome ($p < .001$). For poor outcome prediction, absent pupillary light reflexes (PLR) and corneal reflexes (clinical predictors) 72 h after sedation withdrawal, PLR 96 h post-arrest, and somatosensory evoked potentials (SSEP), all had FPR <0.1% in both groups. Unreactive EEG and neuron-specific enolase (NSE) >60 μg/L 24–72 h post-arrest had better precision in shockable patients. For good outcome, the clinical predictors, SSEP and CT, had 86%–100% sensitivity in both groups. For NSE, sensitivity varied from 22% to 69% 24–72 h post-arrest. The outcome predictors indicated severe brain injury proportionally more often in patients with non-shockable than with shockable rhythms. For all patients, clinical predictors, CT, and SSEP, predicted poor and good outcome with high accuracy.

Conclusion: Outcome prediction accuracy was comparable for shockable and non-shockable rhythms. PLR and corneal reflexes had best precision 72 h after sedation withdrawal and 96 h post-arrest.

KEYWORDS
hypoxic-ischemic brain injury, late awakening, non-shockable rhythm, out-of-hospital cardiac arrest, prognostication, resuscitation guidelines, withdrawal of life sustaining therapy

Editorial Comment

In a selected ICU cohort of patients still comatose 72 h after cardiac arrest, the authors found signs of more severe hypoxic/ischemic brain injury in those having presented with non-shockable rhythm than in those with shockable first rhythm. This was reflected by lower survival among patients with non-shockable first rhythm whereas prognostic neurological examinations performed equally well in both groups.

1 | INTRODUCTION

Outcome prediction in comatose patients after cardiac arrest (CA) has become a cornerstone of post-resuscitation care. It is currently based on the 2021 European Resuscitation Council (ERC) guidelines,[1] which recommend a multimodal approach to neuroprognostication including clinical assessment, biomarkers, neurophysiology, and imaging initiated in patients still comatose 72 h after CA.[1] This multimodal approach is essential to provide an accurate prognosis based on the severity of hypoxic-ischaemic brain injury. As withdrawal of life-sustaining therapy (WLST) due to presumed poor neurological outcome is the leading cause of in-hospital death after out-of-hospital CA,[2,3] the decision to withdraw intensive care treatment must be soundly based.

Compared with initial shockable rhythms, non-shockable rhythms are associated with worse outcome.[4–6] Non-shockable rhythms are usually related to noncardiac causes of CA or a consequence of prolonged periods without blood flow, leading to more severe brain injury. As a non-shockable rhythm is considered a predictive prehospital factor for poor outcome,[7] and associated with early WLST,[8] self-fulfilling prophecies are likely to be expected.[8] However, the prevalence of good neurological outcome in patients with non-shockable rhythms can vary considerably, depending on factors like age and conversion to shockable rhythm during resuscitation, among others.[9] The current guidelines do not distinguish between shockable and non-shockable rhythms in terms of prognostication,[1] and it remains uncertain how the recommended diagnostic predictors apply to OHCA patients with these different rhythms.

We, therefore, aimed to investigate the prognostic accuracy of the recommended predictors in patients still comatose 72 h after OHCA, stratified by initial shockable vs. non-shockable rhythms. In addition, we assessed the capacity of these predictors in the entire cohort. We hypothesized that outcome prediction would be comparable between patients with shockable and non-shockable rhythms, and that the prognostic predictors would reveal signs of severe brain injury relatively more often in patients with non-shockable rhythms.

2 | METHODS

2.1 | Study population

This was a sub-study of the prospective observational NORCAST trial, which included 259 adult OHCA patients still comatose after return of spontaneous circulation (ROSC), who were admitted to Oslo University Hospital, Ullevål between September 2010 and January 2014. Patients with OHCA following trauma or intracerebral hemorrhage were excluded. All patients received protocol-based intensive care treatment with targeted temperature management at 33°C for 24 h (TTM33) and were deeply sedated with mainly fentanyl and midazolam, regardless of the initial rhythm.[10]

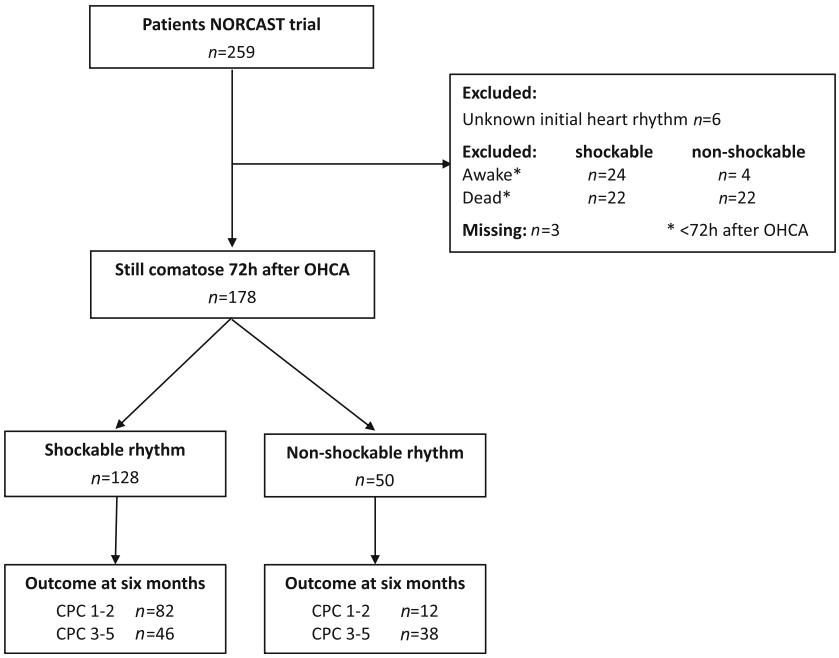
For the present sub-study, patients were classified as shockable or non-shockable according to the first rhythm recorded at the scene. Ventricular tachycardia or fibrillation were defined as shockable, pulseless electrical activity (PEA), and asystole as non-shockable rhythms. For outcome prediction, only patients still comatose (Glasgow Coma Scale [GCS] <9) 72 h after OHCA were included (Figure 1). Patients with an unknown initial rhythm (including ROSC prior to arrival of the emergency medical services) or who died within 72 h after OHCA were excluded (Figure 1).

To assess outcome, we used the cerebral performance category (CPC),[11,12] with a score of 1–2 (none to moderate cerebral disability) as good outcome and 3–5 (severe cerebral disability to death) as poor outcome 6 months after OHCA.[10,13] The highest CPC score within the first 6 months was used as "best CPC score" for patients who regained consciousness but later died from other causes prior to the six-month endpoint. Time to awakening was defined as time from OHCA to GCS ≥9, with late awakening defined as awakening later than 6 days after OHCA based on data from the NORCAST trial where median time to awakening in patients with good outcome was 6 days.[10] WLST was registered when the WLST decision was documented in the medical records. All decisions regarding diagnostics, treatment and WLST were made exclusively by the attending physician.

2.2 | Prognostic predictors

In the NORCAST study, pupillary light reflexes (PLR), corneal reflexes, and GCS were assessed daily. Standard electroencephalography (EEG) and somatosensory evoked potentials (SSEP) were performed in all eligible patients still comatose ≥72 h after sedation withdrawal (Table S1). EEG and SSEP recordings were interpreted independently by two experienced neurophysiologists who were unaware of the patients' medical history. In case of disagreement, a third specialist was consulted. Neuron-specific enolase (NSE) was drawn at admission, 24, 48, 72 h, and 5 and 7 days after OHCA. Results for EEG, SSEP, and NSE were blinded to the treating physicians but could be revealed on request.

FIGURE 1 Study flow chart.



For the present sub-study, we collected the following data from the NORCAST database, adjusted according to the 2021 ERC guidelines[1]; PLR and corneal reflexes 72 and 96 h after OHCA, and 72 h after sedation withdrawal, NSE 24, 48, and 72 h after OHCA, and EEG and SSEP at least 72 h after sedation withdrawal. EEG grading was used as defined in NORCAST.[10,14] Noteworthy, our EEG definition differed slightly from the current guidelines recommendation.[14,15]

EEG grade 1—predominantly post-central alpha-activity mixed with theta-activity.

EEG grade 2—predominantly reactive theta-activity.

EEG grade 3—dominating/substantial delta-activity, or low-amplitude irregular and non-reactive delta-activity.

EEG grade 4—burst suppression, general epileptic activity, status myoclonus, non-reactive activity with low amplitude, alpha-coma and theta-coma.

EEG grade 5—no visible EEG activity during high-sensitivity registration.

Computed tomography (CT) of the brain was not part of the study protocol but could be requested at the discretion of the attending physician. It was therefore performed at different time points. Findings were described as oedema and/or loss of gray-white matter differentiation, which were used to define brain injury. A gray-white-matter ratio was not calculated.

The following predictors were used to assess poor outcome: NSE values >60 μg/L at 24, 48, or 72 h, absent PLR and corneal reflexes 72 and 96 h after OHCA, and 72 h after sedation withdrawal, bilaterally absent SSEP N20 response and EEG grade 4–5 at least 72 h after rewarming, and signs of brain injury on the CT.

We used the same predictors to assess good outcome: Present PLR, corneal reflexes, and SSEP N20 response, an EEG grade 1–2, and "no evidence of brain injury" for brain CT. For NSE, values within normal range (<17 μmol/L) were considered to indicate good outcome, in accordance with previous studies.[1,16,17]

2.3 | Ethics

The Regional Committees for Medical Research Ethics South East Norway approved the NORCAST study (REK-S-O/A-2010/1116a). Informed consent was obtained from relatives shortly after hospital admission, and from all patients who regained decision-making capacity within 6 months.

2.4 | Statistics

Patient characteristics and prognostic predictors are described using frequencies and percentages for categorical variables and mean and standard deviations for continuous variables. Differences between shockable and non-shockable groups were assessed by independent samples *t*-test for continuous and χ^2-test, or Fisher's exact test in case of violated assumptions for χ^2-test, for categorical variables. Two-sided tests were used, and results with *p*-values <.05 were considered statistically significant.

To predict prognostic accuracy, false positive rate (FPR, 1-specificity) for poor outcome and sensitivity for good outcome were calculated with "best CPC score" as outcome parameter. The corresponding 95% confidence interval (CI) was calculated using Wilson's method.[18] Differences in outcome prediction between shockable and non-shockable patients were considered non-significant if there was no overlap in their respective CIs.

For all binary outcome predictors (PLR, corneal reflexes, CT, and SSEP), the accuracy of the FPR in predicting poor outcome is reciprocal to its sensitivity in predicting good outcome.

3 | RESULTS

3.1 | Patient characteristics and outcome

Of the 259 patients enrolled in NORCAST, 178 patients remained comatose 72 h after OHCA and were included in the present substudy (Figure 1, Table 1). Among these, 128 (72%) had initial shockable and 50 (28%) had non-shockable rhythms (Figure 1, Table 1). Compared to the shockable group, non-shockable patients were characterized by more females, fewer witnessed arrests, and more non-cardiac causes of arrest (Table 1). Six-month survival with good outcome was higher in patients with shockable than non-shockable rhythms (64% vs. 24%, $p < .001$; Table 1), which is comparable to the results in all NORCAST patients (64% vs. 22%, respectively, not tabulated). There was no significant difference in good outcome between patients with initial PEA (29%) and asystole (19%) ($p = .411$, not tabulated).

Time from arrest to sedation withdrawal, and to awakening were similar in both groups (Table 2). Late awakening occurred in 47/95 (49%) patients with shockable and 11/17 (65%) with non-shockable

TABLE 1 Baseline characteristics for patients still comatose ≥72 h after OHCA stratified by initial shockable ($n = 128$) and non-shockable ($n = 50$) rhythms.

Characteristic	Shockable	Non-shockable	*p*-value
Age			
Mean (SD)	61.6 (12.2)	61.2 (15.1)	.860[a]
Median (Q_1–Q_3)	62.0 (56.0–70.0)	64.5 (54.8–72.0)	
Male, *n* (%)	113 (88)	34 (68)	.001[b]
Initial rhythm, *n* (%)			NA
VF	123 (96)	0	
VT	5 (4)	0	
PEA	0	26 (52)	
Asystole	0	24 (48)	
Cause of arrest			<.001[b]
Acute ischaemia	59 (46)	7 (14)	
Chronic ischaemia	50 (39)	11 (22)	
Primary arrhythmia	17 (13)	5 (10)	
Hypoxia	2 (2)	19 (38)	
Other	0	4 (8)	
Unknown	0	4 (8)	
Witnessed arrest	112 (88)	29 (58)	<.001[b]
Bystander CPR*	102 (86)	34 (85)	.912[b]
Time from OHCA to ROSC [min]**			
Mean (SD)	27.5 (17.1)	26.8 (15.5)	.828[a]
Median (Q_1–Q_3)	25.0 (15.5–34.0)	24.5 (18.5–32.8)	
CPC at 6 months			<.001[b]
CPC 1	71 (55)	10 (20)	
CPC 2	11 (9)	2 (4)	
CPC 3	4 (3)	6 (12)	
CPC 5	42 (33)	32 (64)	
Best CPC within 6 months#			<.001[b]
CPC 1	72 (56)	10 (20)	
CPC 2	13 (10)	2 (4)	
CPC 3	13 (10)	8 (16)	
CPC 5	30 (23)	30 (60)	

[a]Independent samples *t*-test.

[b]χ^2-test; OHCA; out-of-hospital cardiac arrest, CPR; cardio-pulmonary resuscitation, ROSC; return of spontaneous circulation, CPC; Cerebral performance category, CPC 1–2 good outcome, CPC 3–5 poor outcome, #Best CPC within 6 months: In total, 14 patients who obtained CPC score 1–3 within the first 6 months after OHCA died prior to six-month follow-up and are tabulated as CPC 5 under "CPC score at six months," *19 missing values, 9 in shockable and 10 in non-shockable rhythm group, **23 missing values, 11 in shockable and 12 in non-shockable rhythm group.

TABLE 2 Clinical outcome data for patients still comatose ≥72 h after OHCA stratified by initial shockable ($n = 128$) and non-shockable ($n = 50$) rhythms.

Characteristic	Shockable *n*/ total (%)	Non-shockable *n*/ total (%)	*p*-value
Days from OHCA to GCS ≥9			
All patients			
n	95	17	
Mean (SD)	7.8 (4.6)	10.5 (8.0)	.198[a]
Median (Q_1–Q_3)	6.0 (5.0–9.0)	7.0 (6.0–11.5)	
Good outcome			
n	84	11	
Mean (SD)	7.4 (4.0)	6.9 (2.0)	.689[a]
Median (Q_1–Q_3)	6.0 (5.0–8.0)	6.0 (6.0–9.0)	
Poor outcome			
n	11	6	
Mean (SD)	10.9 (7.1)	17.0 (10.8)	.179[a]
Median (Q_1–Q_3)	10.0 (5.0–13.0)	15.5 (7.8–24.0)	
Time to sedation withdrawal [days]			
n	125	44	
Mean (SD)	5.4 (7.3)	7.4 (8.2)	.127[a]
Median (Q_1–Q_3)	3 (2.0–6.0)	5 (3.0–9.8)	
Awakening, *n* (%)			.247[b]
Early	48/95 (51)	6/17 (35.3)	
Late	47/95 (49)	11/17 (64.7)	
Late awakening, *n* (%)			.017[c]
CPC 1–2	39/47 (83)	5/11 (45)	
CPC 3–5	8/47 (17)	6/11 (55)	
WLST performed, *n* (%)	31/128 (24)	25/50 (50)	<.001[b]
Days from OHCA to WLST			
n	29	23	
Mean (SD)	14.6 (6.9)	15.2 (14.2)	
Median (Q_1–Q_3)	13.0 (9.0–20.5)	10.0 (6.0–19.0)	.482[d]

[a]Independent samples *t*-test.
[b]χ^2-test.
[c]Fisher's exact test.
[d]Independent samples median test, OHCA; out-of-hospital cardiac arrest, GCS (Glasgow Coma Scale), CPC; Cerebral performance category with 1–2 good outcome and 3–5 poor outcome (best CPC score within 6 months used), Early awakening; GCS ≥9 prior to day six after OHCA, Late awakening; GCS 9 later than day six after OHCA, WLST; withdrawal of life-sustaining therapy.

rhythms (Table 2). Significantly more late awakeners in the shockable vs. the non-shockable group had a good outcome (83% vs. 45%, $p = .017$) (Table 2). WLST was initiated twice as often in non-shockable than in shockable patients (50% vs. 24%, $p < .001$). However, there was no significant difference in median time from OHCA to WLST between the groups (13 vs. 10 days) (Table 2).

The outcome predictors indicated a higher proportion of patients with severe brain injuries in non-shockable than shockable patients (Table 3, Figure 2). NSE, for example, showed a rise and fall pattern in the shockable group, whereas it was continuously increasing from 24 to 72 h with significantly higher mean values at 48 and 72 h in the non-shockable group (Figure 2).

3.2 | Poor outcome prediction

FPR for poor outcome was low (0–0.01) for absent PLR and corneal reflexes 72 h after sedation withdrawal, absent PLR 96 h after OHCA, and bilaterally absent SSEP for both groups. However, CIs were narrow only for absent PLR 96 h after OHCA and 72 h after sedation withdrawal in the shockable group (Table 4a and 4b).[19] In addition, EEG grade 4–5 and NSE values >60 μg/L at 24–72 h showed lower FPRs for shockable than non-shockable patients, with reasonable narrow CIs. Sensitivity was generally low in both groups (7%–64%). The overlapping CIs for all predictors between the groups indicated comparable outcome prediction for patients with shockable and non-shockable rhythms.

TABLE 3 Prognostic predictors for brain injury in still comatose patients ≥72 h after OHCA, stratified by initial shockable ($n = 128$) and non-shockable ($n = 50$) rhythms.

Characteristic	Shockable *n*/total (%)	Non-shockable *n*/total (%)	*p*-value
PLR absent 72 h after OHCA	19/121 (16)	16/48 (33)	.011[a]
PLR absent 96 h after OHCA	9/113 (8)	13/43 (30)	<.001[a]
PLR absent 72 h after sedation withdrawal	4/107 (4)	6/25 (24)	.001[a]
Corneal reflex absent 72 h after OHCA	30/90 (33)	18/31 (58)	.015[a]
Corneal reflex absent 96 h after OHCA	16/87 (18)	14/29 (48)	.001[a]
Corneal reflex absent 72 h after sedation withdrawal	1/39 (3)	2/8 (25)	.071[b]
Bilateral SSEP absent	3/21 (14)	5/13 (38)	.211[b]
EEG grade 4–5	16/61 (26)	14/26 (54)	.013[a]
NSE >60 µg/L 24 h after OHCA	13/119 (11)	12/48 (25)	.021[a]
NSE >60 µg/L 48 h after OHCA	19/124 (15)	20/48 (42)	<.001[a]
NSE >60 µg/L 72 h after OHCA	19/114 (17)	19/48 (40)	.002[b]
Brain injury on CT	12/57 (21)	16/33 (49)	.007[b]

[a]χ^2-test.
[b]Fisher's exact test, OHCA; out-of-hospital cardiac arrest, PLR; pupillary light reflex, SSEP; somatosensory evoked potential, EEG; electroencephalography (both registered 72 h after discontinuation of targeted temperature management at 33°C), EEG grade 4; burst suppression, general epileptic activity, status myoclonus, non-reactive activity with low amplitude, alpha-coma, and theta-coma, EEG grade 5; no visible EEG activity during high-sensitivity registration; NSE; neuron-specific enolase, Brain injury on CT; hypoxic ischemic brain injury on cranial computed tomography (oedema and/or loss of gray-white matter differentiation).

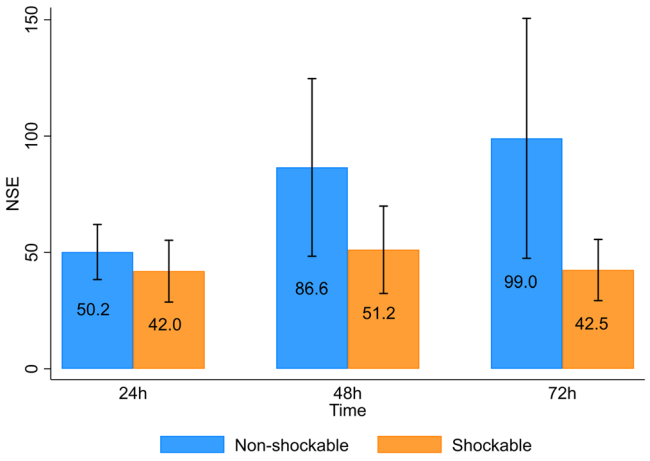


FIGURE 2 NSE values 24, 48, and 72 h after OHCA in patients with initial shockable vs. non-shockable rhythms. NSE; neuron specific enolase, OHCA; out-of-hospital cardiac arrest.

3.3 | Good outcome prediction

There were no substantial differences in sensitivity for predicting good outcome between the shockable and non-shockable groups (Table 4c and 4d). Except for corneal reflexes 72 h after OHCA, all clinical parameters predicted good outcome with high sensitivity (86%–100%) with increasing values over time, but with a wide range in FPRs (0.41–0.93). For NSE, sensitivity was varying from 22% 24 h after OHCA to 69% 72 h after OHCA, but with a low FPR of 0.02 72 h after OHCA. Corresponding to the low FPR for poor outcome, SSEP had a high sensitivity for good outcome prediction in both shockable and non-shockable rhythms, while FPR seemed higher in shockable rhythms (0.73 vs. 0.5). Sensitivity for EEG seemed lower in patients with shockable than non-shockable rhythms (54% vs. 83%). The sensitivity of brain CT was high (94%) for shockable rhythms only. As for poor outcome prediction, no significant differences were found between the groups, as all predictors had overlapping CIs.

3.4 | Outcome prediction for the entire cohort

Poor and good outcome prediction for the entire cohort is shown in Table 5a and 5b. For poor outcome prediction, FPR was 0.01 (CI 0.001; 0.07) for absent PLR 96 h after OHCA, 0 (CI 0; 0.05) for absent corneal reflexes 72 h after sedation withdrawal and 0.02 (CI 0.004; 0.09) for NSE > 60 µg/L at 72 h. All other predictors with a low FPR (0–0.07) showed an upper CI limit >10% (Table 5a).

Good outcome prediction was similar to that of the stratified groups with sensitivities from 88% for corneal reflexes 96 h after OHCA, to 95%–100% for brain CT, SSEP, and PLR and corneal reflexes 72 h after sedation withdrawal. Although sensitivity of NSE increased from 21% 24 h after OHCA to 64% 72 h after OHCA, they were still low (Table 5b).

4 | DISCUSSION

In this NORCAST sub-study, we found that 66% of patients still comatose 72 h after OHCA with initial shockable rhythms and 24% with non-shockable rhythms, survived with good outcome to 6 months. Prediction of poor and good outcome was comparable in both groups.

TABLE 4a Prediction of **poor outcome** ($n = 43$) in patients with initial **shockable rhythms** ($n = 128$), still comatose ≥72 h after OHCA.

Prognostic predictors	*n*	TP	FP	TN	FN	FPR (95% CI)	SENS (95% CI)
PLR 72 h after OHCA	121	11	8	73	29	0.10 (0.05; 0.19)	0.28 (0.15; 0.44)
PLR 96 h after OHCA	113	8	1	74	30	0.01 (0.001;0.08)	0.21 (0.10; 0.38)
PLR 72 h after sedation withdrawal	107	4	0	81	22	0 (0; 0.05)	0.15 (0.05; 0.36)
Corneal reflex 72 h after OHCA	90	15	15	44	16	0.25 (0.15; 0.39)	0.48 (0.31; 0.67)
Corneal reflex 96 h after OHCA	87	9	7	52	19	0.12 (0.05; 0.24)	0.32 (0.17; 0.52)
Corneal reflex 72 h after sedation withdrawal	39	1	0	24	14	0 (0; 0.17)	0.07 (0.003; 0.34)
Bilateral absent SSEP	21	3	0	10	8	0 (0; 0.35)	0.27 (0.07; 0.61)
EEG grade 4 or 5	61	14	2	37	8	0.05 (0.01; 0.19)	0.64 (0.41; 0.82)
NSE >60 μg/L 24 h after OHCA	119	9	3	75	32	0.04 (0.01; 0.12)	0.22 (0.11; 0.38)
NSE >60 μg/L 48 h after OHCA	124	16	3	79	26	0.04 (0.01; 0.11)	0.38 (0.24; 0.54)
NSE >60 μg/L 72 h after OHCA	114	18	1	74	21	0.01 (0.001;0.08)	0.46 (0.30; 0.63)
Brain injury on CT	57	10	2	34	11	0.06 (0.01; 0.20)	0.48 (0.26; 0.70)

TABLE 4b Prediction of **poor outcome** ($n = 38$) in patients with initial **non-shockable rhythms** ($n = 50$), still comatose ≥72 h after OHCA.

Prognostic predictors	*n*	TP	FP	TN	FN	FPR (95% CI)	SENS (95% CI)
PLR 72 h after OHCA	48	15	1	11	21	0.08 (0.004; 0.40)	0.42 (0.26; 0.59)
PLR 96 h after OHCA	43	13	0	19	11	0 (0; 0.32)	0.41 (0.24; 0.59)
PLR 72 h after sedation withdrawal	25	6	0	11	8	0 (0; 0.32)	0.43 (0.19; 0.70)
Corneal reflex 72 h after OHCA	31	13	5	4	9	0.56 (0.23; 0.85)	0.59 (0.37; 0.79)
Corneal reflex 96 h after OHCA	29	13	1	6	9	0.14 (0.01; 0.58)	0.59 (0.37; 0.79)
Corneal reflex 72 h after sedation withdrawal	8	2	0	2	4	0 (0; 0.20)	0.33 (0.06; 0.76)
Bilateral absent SSEP	13	5	0	3	5	0 (0; 0.69)	0.50 (0.20; 0.80)
EEG grade 4 or 5	26	13	1	5	7	0.17 (0.01; 0.64)	0.65 (0.41; 0.84)
NSE >60 μg/L 24 h after OHCA	48	10	1	11	26	0.08 (0.00; 0.40)	0.28 (0.15; 0.45)
NSE >60 μg/L 48 h after OHCA	48	18	2	10	18	0.17 (0.03; 0.49)	0.50 (0.33; 0.67)
NSE >60 μg/L 72 h after OHCA	48	18	1	11	18	0.08 (0.004;0.40)	0.50 (0.33; 0.67)
Brain injury on CT	33	16	0	3	14	0 (0; 0.69)	0.53 (0.35; 0.71)

Abbreviations: Brain injury on CT, hypoxic ischemic brain injury on computed tomography (oedema and/or loss of gray-white matter differentiation); CI, confidence interval; EEG, electroencephalography; FN, false negative; FP, false positive; FPR, false positive rate; NSE, neuron-specific enolase; OHCA; out-of-hospital cardiac arrest; PLR, pupillary light reflex; SENS, sensitivity; SSEP, somatosensory evoked potential; TP, true positive; TN, true negative.

TABLE 4c Prediction of **good outcome** ($n = 85$) in patients with initial **shockable rhythm** ($n = 128$), still comatose ≥72 h after OHCA.

Prognostic predictors	*n*	TP	FP	TN	FN	FPR (95% CI)	SENS (95% CI)
PLR 72 h after OHCA	121	73	29	11	8	0.73 (0.56; 0.85)	0.90 (0.81; 0.95)
PLR 96 h after OHCA	113	74	30	8	1	0.79 (0.62; 0.90)	0.99 (0.92; 0.99)
PLR 72 h after sedation withdrawal	107	81	22	4	0	0.85 (0.64; 0.95)	1.00 (0.94; 1.00)
Corneal reflex 72 h after OHCA	90	44	16	15	15	0.48 (0.31; 0.67)	0.75 (0.61; 0.85)
Corneal reflex 96 h after OHCA	87	52	19	9	7	0.68 (0.48; 0.83)	0.88 (0.76; 0.95)
Corneal reflex 72 h after sedation withdrawal	39	24	14	1	0	0.93 (0.66; 1.00)	1.00 (0.83; 1.00)
Bilateral present SSEP	21	10	8	3	0	0.73 (0.39; 0.93)	1.00 (0.66; 1.00)
EEG grade 1 or 2	61	21	2	20	18	0.09 (0.02; 0.31)	0.54 (0.37; 0.70)
NSE <17 μg/L 24 h after OHCA	119	17	1	40	61	0.02 (0.002; 0.14)	0.22 (0.14; 0.33)
NSE <17 μg/L 48 h after OHCA	124	38	4	38	44	0.10 (0.03; 0.24)	0.46 (0.35; 0.58)
NSE <17 μg/L 72 h after OHCA	114	52	3	36	23	0.08 (0.02; 0.22)	0.69 (0.57; 0.79)
No brain injury on CT	57	34	11	10	2	0.52 (0.30; 0.74)	0.94 (0.80; 0.99)

TABLE 4d Prediction of **good outcome** ($n = 12$) in patients with initial **non-shockable rhythms** ($n = 50$), still comatose ≥72 h after OHCA.

Prognostic predictors	*n*	TP	FP	TN	FN	FPR (95% CI)	SENS (95% CI)
PLR 72 h after OHCA	48	11	21	15	1	0.58 (0.41; 0.74)	0.92 (0.60; 0.99)
PLR 96 h after OHCA	43	19	11	13	0	0.46 (0.26; 0.67)	1.00 (0.79; 1.00)
PLR 72 h after sedation withdrawal	25	11	8	6	0	0.57 (0.30; 0.81)	1.00 (0.68; 1.00)
Corneal reflex 72 h after OHCA	31	4	9	13	5	0.41 (0.22; 0.66)	0.44 (0.15; 0.77)
Corneal reflex 96 h after OHCA	29	6	9	13	1	0.41 (0.22; 0.63)	0.86 (0.42; 0.99)
Corneal reflex 72 h after sedation withdrawal	8	2	4	2	0	0.67 (0.24; 0.94)	1.00 (0.20; 1.00)
Bilateral present SSEP	13	3	5	5	0	0.50 (0.20; 0.80)	1.00 (0.31; 1.00)
EEG grade 1 or 2	26	5	1	19	1	0.05 (0.003; 0.27)	0.83 (0.36; 0.99)
NSE <17 μg/L 24 h after OHCA	48	2	1	35	10	0.03 (0.002; 0.16)	0.17 (0.03; 0.49)
NSE <17 μg/L 48 h after OHCA	48	2	5	31	10	0.14 (0.05; 0.30)	0.17 (0.03; 0.49)
NSE <17 μg/L 72 h after OHCA	48	4	6	30	8	0.17 (0.07; 0.34)	0.33 (0.11; 0.65)
No brain injury on CT	33	0	16	14	3	0.53 (0.35; 0.71)	0 (0; 0.69)

TABLE 5a Prediction of **poor outcome** ($n = 81$) in patients comatose ≥72 h after OHCA, irrespective of the initial rhythm.

Prognostic predictors	*n*	TP	FP	TN	FN	FPR (95% CI)	SENS (95% CI)
PLR 72 h after OHCA	169	26	9	84	50	0.10 (0.05; 0.18)	0.34 (0.24; 0.46)
PLR 96 h after OHCA	156	21	1	85	49	0.01 (0.001;0.07)	0.30 (0.20; 0.42)
PLR 72 h after sedation withdrawal	132	10	0	92	30	0 (0; 0.05)	0.25 (0.13; 0.42)
Corneal reflex 72 h after OHCA	121	28	20	48	25	0.29 (0.19; 0.42)	0.53 (0.39; 0.66)
Corneal reflex 96 h after OHCA	116	22	8	58	28	0.12 (0.06; 0.23)	0.44 (0.30; 0.59)
Corneal reflex 72 h after sedation withdrawal	47	3	0	26	18	0 (0; 0.16)	0.14 (0.04; 0.37)
Bilateral absent SSEP	34	8	0	13	13	0 (0; 0.28)	0.38 (0.19; 0.61)
EEG grade 4 or 5	87	27	3	42	15	0.07 (0.02; 0.19)	0.64 (0.48; 0.78)
NSE >60 μg/L 24 h after OHCA	167	19	4	86	58	0.04 (0.01; 0.12)	0.25 (0.16; 0.36)
NSE >60 μg/L 48 h after OHCA	172	34	5	89	44	0.05 (0.02; 0.13)	0.44 (0.33; 0.55)
NSE >60 μg/L 72 h after OHCA	162	36	2	85	39	0.02 (0.004;0.09)	0.48 (0.36; 0.60)
Brain injury on CT	90	26	2	37	25	0.05 (0.01; 0.19)	0.51 (0.37; 0.65)

Abbreviations: Brain injury on CT, hypoxic ischemic brain injury on computed tomography (oedema and/or loss of gray-white matter differentiation); CI, confidence interval; EEG, electroencephalography; FPR, false positive rate; FP, false positive; FN, false negative; NSE, neuron-specific enolase; OHCA, out-of-hospital cardiac arrest; PLR, pupillary light reflex; SENS, sensitivity; SSEP, somatosensory evoked potential; TP, true positive; TN, true negative.

TABLE 5b Prediction of **good outcome** ($n = 97$) in patients comatose ≥72 h after OHCA, irrespective of the initial rhythm.

Prognostic predictors	*n*	TP	FP	TN	FN	FPR (95% CI)	SENS (95% CI)
PLR 72 h after OHCA	169	84	50	26	9	0.66 (0.54; 0.76)	0.90 (0.82; 0.95)
PLR 96 h after OHCA	156	85	49	21	1	0.70 (0.58; 0.80)	0.99 (0.93; 0.99)
PLR 72 h after sedation withdrawal	132	92	30	10	0	0.75 (0.59; 0.87)	1.00 (0.95; 1.00)
Corneal reflex 72 h after OHCA	121	48	25	28	20	0.47 (0.34; 0.61)	0.71 (0.58; 0.81)
Corneal reflex 96 h after OHCA	116	58	28	22	8	0.56 (0.41; 0.70)	0.88 (0.77; 0.94)
Corneal reflex 72 h after sedation withdrawal	47	26	18	3	0	0.86 (0.63; 0.96)	1.00 (0.84; 1.00)
Bilateral present SSEP	34	13	13	8	0	0.62 (0.39; 0.81)	1.00 (0.72; 1.00)
EEG grade 1 or 2	87	26	3	39	19	0.07 (0.02; 0.21)	0.58 (0.42; 0.72)
NSE <17 μg/L 24 h after OHCA	167	19	2	75	71	0.03 (0.01; 0.10)	0.21 (0.13; 0.31)
NSE <17 μg/L 48 h after OHCA	172	40	9	69	54	0.12 (0.06; 0.21)	0.43 (0.33; 0.53)
NSE <17 μg/L 72 h after OHCA	162	56	9	66	31	0.12 (0.06; 0.22)	0.64 (0.53; 0.74)
No brain injury on CT	90	37	25	26	2	0.49 (0.35; 0.63)	0.95 (0.81; 0.99)

PLR and corneal reflexes had better precision 72 h after sedation withdrawal and 96 h after OHCA than 72 h after OHCA. However, the generalisability of this assumption is undoubtedly reduced by the low number of non-shockable survivors. As expected, the prognostic predictors indicated a higher proportion of patients with severe brain injuries among those with non-shockable than shockable rhythms.

Despite an overall higher mortality in the non-shockable group, almost one-fourth survived with good neurological outcome to 6 months, which is high compared to previous studies.[20–22] The wide range (<0.1%–29%) of good outcome in OHCA patients with non-shockable rhythms reflects the heterogeneity of underlying causes for CA in this group.[9] As non-shockable rhythms are considered predictive for poor outcome, it is more likely to lead to early WLST.[8,23] Decisions on WLST taken as late as median 13 days in the non-shockable group might have contributed to the relatively high survival with good outcome in the present study.

WLST will always interfere with outcome prediction in CA patients.[3,6,24] Interestingly, 20% of patients with good outcome woke up late in a recent study where WLST was not performed.[6] Therefore, early WLST must be based on a reliable prediction of poor prognosis. In the present study, poor outcome prediction showed low FPRs in almost all predictors for the entire cohort. Nevertheless, none of them reached an FPR ≤0.001 which was considered acceptable for WLST according to a survey among health care workers.[25] However, very low FPRs are at the expense of sensitivity, reducing the predictor's clinical usability. As an example, for NSE the current guidelines therefore suggest an FPR of 0.01–0.02 as acceptable in poor outcome prediction.[1] Non-shockable rhythms had higher FPRs at all time points and only NSE 72 h after OHCA in the shockable group had an acceptable FPR of 0.01 for poor outcome prediction, with a relatively low sensitivity of 46%. This is consistent with findings in the TTM sub-study by Stammet et al.[26] They also described a "rise-and-fall" pattern for a good outcome (comparable to our findings for shockable rhythms) and increasing values for poor outcome (comparable to our findings for non-shockable rhythms).[26] Importantly, among patients with non-shockable rhythms with favorable outcome at 6 months, 17% had NSE values >60 μg/L at 48 h. In contrast, a larger retrospective multicentre study described equal outcome prediction for NSE in patients with shockable and non-shockable rhythms.[27] Although the threshold of 60 μg/L at 48 h indicating poor outcome seems to be too low for patients with non-shockable rhythms in the present cohort, this may be solely due to the small sample size and should be interpreted with caution.

In contrast to previous studies,[28] the FPRs for clinical predictors remained high up to 48–72 h after OHCA. This is probably attributed to deep sedation with fentanyl/midazolam and TTM33, which affect metabolism and pharmacokinetics and thereby clearly delay awakening.[10,29–32] Consequently, with contributing factors for late awakening, clinical parameters are more reliable in the later course, such as 72 h after sedation withdrawal, where we found FPR values of zero. Again, wide CIs due to few study patients clearly limit the general validity of the results.

Although brain CT in the present study was predominantly performed when brain injury was suspected, the FPR was slightly higher in shockable patients than in previous studies (0.06 vs. 0–0.02).[1] Noteworthy, Beekman et al. showed that early CT findings indicating hypoxic brain injury often led to de-escalation of intensive care treatment.[33] Thus, a "biomarker-guided" indication for brain CT could increase its specificity and contribute to a more robust prognostication.[34]

Present PLR and corneal reflexes 72 h after sedation withdrawal and 96 h after OHCA, all were reliable predictors of good outcome prediction. Again, higher accuracy in the later course may be due to sedation effects and TTM33 the first days after OHCA. Sensitivity for EEG and NSE was lower in the present than in previous studies.[16,17,35,36] While different EEG classifications[14,15] or sedation may explain differences for EEG, different NSE levels may be explained by different storage procedures or analysis methods.[17,37,38]

SSEP is generally considered a reliable predictor for both poor and good outcome with high specificity but lower sensitivity.[39,40] While poor outcome prediction was good (with a broad CI, however), we found a lower specificity with a surprisingly high sensitivity in good outcome prediction, compared to previous studies.[40,41] This may be due to a cautious interpretation of bilaterally present N20 responses, with 24% of registrations considered inconclusive in the non-shockable group (Table S1) and the relatively small number of examinations. Recent proposals using SSEP signals as a continuous measure and peak-to-peak analysis instead of the binary absent/present may further improve accuracy.[40]

The analyzes of the entire cohort indicated that none of the predictors were reliable enough to be used alone to predict good outcome. A multimodal approach, as recommended for poor outcome prediction,[1] would clearly increase prediction accuracy, as Vanat et al. recently showed by presenting a new multimodal good outcome prediction score.[42] This may prevent early WLST in late awakeners with potentially good outcome.[6,34,43]

The present study has important limitations. Due to the relatively low number of patients with good outcome in the non-shockable group, the validity of the results is limited. Notably, a broad 95% CI with an upper limit >5%[19] reduces the overall significance considerably, even with an FPR of zero. Thus, these results are not conclusive and should be interpreted with caution since the true FPR value for the population is more uncertain. Nevertheless, there is currently no generally accepted standard for an optimal FPR value. The EEG classification used[10,14] is no longer recommended. Some EEG patterns would be classified differently using the current terminology.[15] EEG classifications according to current guidelines recommendations could have improved accuracy. Of note, sedation may also impact EEG patterns.[44] Brain CT was not a part of the study protocol but requested on clinical indication. This could have resulted in selection bias if performed more often when brain injury was suspected. For bilaterally absent SSEP N20 responses, blinding was lifted in four cases but likely contributed to WLST in only one case. We cannot rule out that this might influence the results due to the low number of SSEPs performed.

5 | CONCLUSIONS

In OHCA patients still comatose 72 h after OHCA, prediction of poor and good outcome was comparable between shockable and

non-shockable rhythms. PLR and corneal reflexes were more accurate 72 h after sedation withdrawal and 96 h after OHCA than earlier after OHCA. However, the generalisability of these results is limited by the relatively small number of patients, especially in the non-shockable group. The outcome predictors indicated a higher proportion of patients with severe brain injury among those with non-shockable than shockable rhythms, reflecting the higher mortality in patients with non-shockable rhythms.

AUTHOR CONTRIBUTIONS

Conceptualization and study design of NORCAST: Espen Rostrup Nakstad, Kjetil Sunde, Geir Ø. Andersen, Christofer Lundqvist, Investigation and data collection: Henning Wimmer, Espen Rostrup Nakstad, Geir Ø. Andersen, Christofer Lundqvist, Data curation, data set construction: Tomas Drægni, Statistical analysis and interpretation: Jūratė Šaltytė Benth, Henning Wimmer, Stine Håheim StensØnes. Drafting of manuscript: Henning Wimmer, Stine Håheim StensØnes, Kjetil Sunde, Espen Rostrup Nakstad, Review and editing: Jūratė Šaltytė Benth, Christofer Lundqvist, Geir Ø. Andersen. All authors have read and approved the final manuscript.

FUNDING INFORMATION

The study was funded departmentally.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Henning Wimmer https://orcid.org/0000-0002-8749-0334
Kjetil Sunde https://orcid.org/0000-0001-9518-5199

REFERENCES

1. Nolan JP, Sandroni C, Bottiger BW, et al. European resuscitation council and European Society of Intensive Care Medicine Guidelines 2021: post-resuscitation care. *Resuscitation*. 2021;161:220-269.
2. Dragancea I, Wise MP, Al-Subaie N, et al. Protocol-driven neurological prognostication and withdrawal of life-sustaining therapy after cardiac arrest and targeted temperature management. *Resuscitation*. 2017;117:50-57.
3. Elmer J, Torres C, Aufderheide TP, et al. Association of early withdrawal of life-sustaining therapy for perceived neurological prognosis with mortality after cardiac arrest. *Resuscitation* 2016;102:127–135.
4. Martinell L, Nielsen N, Herlitz J, et al. Early predictors of poor outcome after out-of-hospital cardiac arrest. *Crit Care*. 2017;21:96.
5. Maupain C, Bougouin W, Lamhaut L, et al. The CAHP (cardiac arrest hospital prognosis) score: a tool for risk stratification after out-of-hospital cardiac arrest. *Eur Heart J*. 2016;37:3222-3228.
6. Lee DH, Cho YS, Lee BK, et al. Late awakening is common in settings without withdrawal of life-sustaining therapy in out-of-hospital cardiac arrest survivors who undergo targeted temperature management. *Crit Care Med*. 2022;50:235-244.
7. Pemberton K, Franklin RC, Bosley E, Watt K. Pre-hospital predictors of long-term survival from out-of-hospital cardiac arrest. *Australas Emerg Care*. 2022;26:184-192. doi:10.1016/j.auec.2022.10.006
8. May TL, Ruthazer R, Riker RR, et al. Early withdrawal of life support after resuscitation from cardiac arrest is common and may result in additional deaths. *Resuscitation*. 2019;139:308-313.
9. Fukuda T, Matsubara T, Doi K, Fukuda-Ohashi N, Yahagi N. Predictors of favorable and poor prognosis in unwitnessed out-of-hospital cardiac arrest with a non-shockable initial rhythm. *Int J Cardiol*. 2014;176:910-5.
10. Nakstad ER, Staer-Jensen H, Wimmer H, et al. Late awakening, prognostic factors and long-term outcome in out-of-hospital cardiac arrest—results of the prospective Norwegian cardio-respiratory arrest study (NORCAST). *Resuscitation*. 2020;149:170-179.
11. Jennett B, Bond M. Assessment of outcome after severe brain damage. *Lancet*. 1975;305:480-484.
12. Brain Resuscitation ClinicalTrial I Study Group. A randomized clinical study of cardiopulmonary—cerebral resuscitation: design, methods, and patient characteristics. *Am J Emerg Med*. 1986;4:72-86.
13. Bossaert LL, Perkins GD, Askitopoulou H, et al. European resuscitation council guidelines for resuscitation 2015: section 11. The ethics of resuscitation and end-of-life decisions. *Resuscitation*. 2015;95:302-311.
14. Bassetti C, Bomio F, Mathis J, Hess CW. Early prognosis in coma after cardiac arrest: a prospective clinical, electrophysiological, and biochemical study of 60 patients. *J Neurol Neurosurg Psychiatry*. 1996;61:610-615.
15. Hirsch LJ, Fong MWK, Leitinger M, et al. American clinical neurophysiology Society's standardized critical care EEG terminology: 2021 version. *J Clin Neurophysiol*. 2021;38:1-29.
16. Sandroni C, D'Arrigo S, Cacciola S, et al. Prediction of good neurological outcome in comatose survivors of cardiac arrest: a systematic review. *Intensive Care Med*. 2022;48:389-413.
17. Moseby-Knappe M, Mattsson-Carlgren N, Stammet P, et al. Serum markers of brain injury can predict good neurological outcome after out-of-hospital cardiac arrest. *Intensive Care Med*. 2021;47:984-994.
18. Wilson EB. Probable inference, the law of succession, and statistical inference. *J Am Stat Assoc*. 1927;22:209-212.
19. Sandroni C, Cariou A, Cavallaro F, et al. Prognostication in comatose survivors of cardiac arrest: an advisory statement from the European resuscitation council and the European Society of Intensive Care Medicine. *Resuscitation*. 2014;85:1779-1789.
20. Andrew E, Nehme Z, Lijovic M, Bernard S, Smith K. Outcomes following out-of-hospital cardiac arrest with an initial cardiac rhythm of asystole or pulseless electrical activity in Victoria, Australia. *Resuscitation*. 2014;85:1633-1639.
21. Frydland M, Kjaergaard J, Erlinge D, et al. Target temperature management of 33 degrees C and 36 degrees C in patients with out-of-hospital cardiac arrest with initial non-shockable rhythm—a TTM sub-study. *Resuscitation*. 2015;89:142-148.
22. Lascarrou JB, Merdji H, Le Gouge A, et al. Targeted temperature Management for Cardiac Arrest with nonshockable rhythm. *N Engl J Med*. 2019;381:2327-2337.
23. Moseby-Knappe M, Westhall E, Backman S, et al. Performance of a guideline-recommended algorithm for prognostication of poor neurological outcome after cardiac arrest. *Intensive Care Med*. 2020;46:1852-1862.
24. Elmer J, Kurz MC, Coppler PJ, et al. Time to awakening and self-fulfilling prophecies after cardiac arrest. *Crit Care Med*. 2023;51:503-512.
25. Steinberg A, Callaway CW, Arnold RM, et al. Prognostication after cardiac arrest: results of an international, multi-professional survey. *Resuscitation*. 2019;138:190-197.
26. Stammet P, Collignon O, Hassager C, et al. Neuron-specific enolase as a predictor of death or poor neurological outcome after out-of-hospital cardiac arrest and targeted temperature management at

33 degrees C and 36 degrees C. *J Am Coll Cardiol*. 2015;65:2104-2114.
27. Streitberger KJ, Leithner C, Wattenberg M, et al. Neuron-specific enolase predicts poor outcome after cardiac arrest and targeted temperature management: a multicenter study on 1,053 patients. *Crit Care Med*. 2017;45:1145-1151.
28. Sandroni C, D'Arrigo S, Cacciola S, et al. Prediction of poor neurological outcome in comatose survivors of cardiac arrest: a systematic review. *Intensive Care Med*. 2020;46:1803-1851. doi:10.1007/s00134-020-06198-w
29. Rey A, Rossetti AO, Miroz JP, Eckert P, Oddo M. Late awakening in survivors of Postanoxic coma: early neurophysiologic predictors and association with ICU and long-term neurologic recovery. *Crit Care Med*. 2019;47:85-92.
30. Paul M, Bougouin W, Geri G, et al. Delayed awakening after cardiac arrest: prevalence and risk factors in the Parisian registry. *Intensive Care Med*. 2016;42:1128-1136.
31. Lybeck A, Cronberg T, Aneman A, et al. Time to awakening after cardiac arrest and the association with target temperature management. *Resuscitation*. 2018;126:166-171.
32. Bjelland TW, Klepstad P, Haugen BO, Nilsen T, Dale O. Effects of hypothermia on the disposition of morphine, midazolam, fentanyl, and propofol in intensive care unit patients. *Drug Metab Dispos*. 2013;41:214-223.
33. Beekman R, Maciel CB, Ormseth CH, et al. Early head CT in post-cardiac arrest patients: a helpful tool or contributor to self-fulfilling prophecy? *Resuscitation*. 2021;165:68-76.
34. Lagebrant A, Lang M, Nielsen N, et al. Brain injury markers in blood predict signs of hypoxic ischaemic encephalopathy on head computed tomography after cardiac arrest. *Resuscitation*. 2023;184:109668.
35. Westhall E, Rossetti AO, van Rootselaar AF, et al. Standardized EEG interpretation accurately predicts prognosis after cardiac arrest. *Neurology*. 2016;86:1482-1490.
36. Bongiovanni F, Romagnosi F, Barbella G, et al. Standardized EEG analysis to reduce the uncertainty of outcome prognostication after cardiac arrest. *Intensive Care Med*. 2020;46:963-972.
37. Paus E, Nustad K. Immunoradiometric assay for alpha gamma- and gamma gamma-enolase (neuron-specific enolase), with use of monoclonal antibodies and magnetizable polymer particles. *Clin Chem*. 1989;35:2034-2038.
38. Rundgren M, Cronberg T, Friberg H, Isaksson A. Serum neuron specific enolase—impact of storage and measuring method. *BMC Res Notes*. 2014;7:726.
39. Sandroni C, Grippo A, Westhall E. The role of the electroencephalogram and evoked potentials after cardiac arrest. *Curr Opin Crit Care*. 2023;29:199-207.
40. Benghanem S, Nguyen LS, Gavaret M, et al. SSEP N20 and P25 amplitudes predict poor and good neurologic outcomes after cardiac arrest. *Ann Intensive Care*. 2022;12:25.
41. Scarpino M, Lolli F, Lanzo G, et al. SSEP amplitude accurately predicts both good and poor neurological outcome early after cardiac arrest; a post-hoc analysis of the ProNeCA multicentre study. *Resuscitation*. 2021;163:162-171.
42. Vanat A, Lee JW, Elkhider H, et al. Multimodal prediction of favorable outcome after cardiac arrest: a cohort study. *Crit Care Med*. 2023;51:706-716.
43. Perman SM, Kirkpatrick JN, Reitsma AM, et al. Timing of neuroprognostication in postcardiac arrest therapeutic hypothermia*. *Crit Care Med*. 2012;40:719-724.
44. Sandroni C, Cronberg T, Hofmeijer J. EEG monitoring after cardiac arrest. *Intensive Care Med*. 2022;48:1439-1442.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Wimmer H, Stensønes SH, Benth Jūratė Šaltytė, et al. Outcome prediction in comatose cardiac arrest patients with initial shockable and non-shockable rhythms. *Acta Anaesthesiol Scand*. 2024;68(2):263-273. doi:10.1111/aas.14337