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Original paper

Ultra-early short- and middle-latency SSEP accurately predict good and poor outcome after cardiac arrest

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Abstract

Background: Accurate prognostication following cardiac arrest (CA) is crucial for informing clinical decisions. Current guidelines do not recommend a specific time point for recording somatosensory evoked potentials (SSEPs) after CA. We evaluated the ability of ultra-early short- and middle-latency SSEPs to predict good an poor neurological outcome and compared its accuracy with that of other predictors recorded early after CA.

Methods: Prospective single-centre study. Sixty-five comatose adults underwent a multimodal prognostic assessment, including neurophysiological (SSEPs and electroencephalogram [EEG]), clinical (pupillary reflexes and myoclonus), and imaging indices (brain computed tomography [CT]) within 6 h post-CA. Serum neuron-specific enolase (NSE) was sampled 12 h post-CA. We analysed the SSEPs N20 wave amplitude and duration, and the presence of the middle-latency N70 wave. Poor outcome was defined as a Cerebral Performance Category (CPC) of 3–5 at hospital discharge.

Results: A bilaterally absent N20 wave predicted poor outcome with 100[89–100]% specificity and 67[48–82]% sensitivity. Adding low-amplitude (<1.2 μV), prolonged (>10 ms) N20 waves without N70 increased sensitivity to 93[79–99]% without compromising specificity. Conversely, a high-amplitude (>3 μV) N20 wave with normal duration with preserved N70 predicted good outcome with 94[79–99]% sensitivity and 100[89–100]% specificity. SSEPs outperformed all other early prognostic indices for both good and poor outcome prediction. All poor outcome patients had at least two concordant unfavourable predictors.

Conclusions: Ultra-early quantitative assessment of short- and middle-latency SSEPs provides highly accurate prediction of both good and poor neurological outcomes after CA. This approach may enhance early clinical decision-making and warrants validation in larger cohorts.

Keywords: Cardiac arrest, Coma, Prognosis, Somatosensory evoked potentials, Electroencephalogram, Computed tomography, brain

Introduction

Patients who are comatose after resuscitation from cardiac arrest are at high risk of mortality from hypoxic-ischaemic brain injury (HIBI).[1] Accurate prognostication in these patients is crucial for providing proportionate care. The 2021 Guidelines on post-resuscitation care co-issued by the European Resuscitation Council (ERC) and the European Society of Intensive Care Medicine (ESICM) recommend a prognostic algorithm aimed at identifying patients with the most severe HIBI in whom further treatment would be futile.[2] Validation studies demonstrated that the ERC/ESICM prognostic algorithm predicts poor neurological outcome with 100% specificity and a sensitivity above 60%.[3–5] The algorithm is based on a combination of concordant clinical signs and tests collected during the first 72 h after return of spontaneous circulation (ROSC), with a final prognostic judgement made at 72 h or later after ROSC. However, several patients die from HIBI or regain consciousness within 72–96 h after ROSC, before the prognostic assessment can be completed.[6,7]

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Moreover, although an ERC/ESICM-endorsed systematic review published in 2022 has identified reliable predictors of neurological recovery after cardiac arrest,[8] these predictors have not yet been incorporated into the current prognostic algorithm. Predicting both good and poor neurological outcome within 12–24 h after cardiac arrest would increase the sensitivity of the ERC/ESICM prognostic algorithm, reduce prognostic uncertainty, and provide early guidance for patient management.

Somatosensory evoked potentials (SSEPs) are among the most accurate and best-established predictors of neurological outcome after cardiac arrest.[9] The current ERC/ESICM guidelines recommend using the bilateral absence of the SSEP N20 wave to predict poor outcome in patients who are comatose at 72 h or later after ROSC.[2] However, they provide no prognostic guidance on how to interpret a bilaterally present N20 wave. Moreover, there is currently no recommendation on what the best time point is for recording SSEP after cardiac arrest. We previously demonstrated that a bilaterally absent N20 wave accurately predicts poor outcome 12 h after ROSC,[10] and that when the N20 wave is present at this early time point, its amplitude provides additional prognostic information, predicting poor outcome when it is low and good outcome when it is high, therefore yielding a greater accuracy than the conventional dichotomous interpretation based on the presence or absence of the N20 wave.[11,12]

A further approach to improving SSEP accuracy in post-anoxic coma involves evaluating the middle latency (ML) SSEP components, since ML-SSEPs require a greater degree of elaboration of the somatosensory signal within the cerebral cortex than short-latency SSEP. Earlier studies suggested that ML-SEEPs provide further prognostic guidance in comatose resuscitated patients with a preserved N20 wave.[13,14] However, the added value of ML-SSEP versus a quantitative interpretation of short-latency SSEP remains to be investigated.

Based on the encouraging results of our earlier investigation on quantitative analysis of short-latency SSEP at 12 h, we conducted this study to explore whether early quantitative short-latency SSEP and middle-latency SSEP recorded within six hours from ROSC accurately predict both poor and good neurological outcome in patients who are comatose after cardiac arrest. The secondary aim was to compare the accuracy of SSEPs with that of other ERC/ESICM-recommended predictors, including electroencephalogram (EEG), neuron-specific enolase (NSE), and brain computed tomography (CT), when assessed early after cardiac arrest.

Materials and methods

Setting

The study was conducted at the Azienda Ospedaliera Universitaria Careggi. This 1,150-bed teaching hospital serves as a tertiary referral centre for the urban area of Florence (Italy) and a leading referral centre for out-of-hospital cardiac arrest (OHCA). The Careggi Teaching Hospital receives around 150 OHCA cases annually.

Study design and patient selection

This is a prospective, single-centre study conducted in the Emergency Department (ED) and in two Intensive Care Units (ICUs). The study included all consecutive comatose adult patients (Glasgow Coma Scale $\leq$8) who were successfully resuscitated after CA either inside or outside the hospital between 15 May 2024 and 15 May 2025, and who received the first prognostic evaluation within 6 h after CA, as well as the NSE dosage within 12 h after CA. Patients were excluded if they had traumatic or neurological causes of CA, had a pre-existing neurological disability, had regained consciousness or had died before neurophysiological tests could be performed.

A clinical examination was performed within the first 6 h after CA, during suspension of short-acting sedative agents for EEG recording. Neuroimaging and neurophysiological tests were performed as soon as possible after ROSC, either in the ED or upon admission to the ICU. Blood samples for NSE measurement were drawn upon admission to the ICU, as NSE cannot be ordered as a test in the ED of our hospital.

Index test recording and classification

Index test results were interpreted by the attending neurologists participating in this investigation (MS, RC, ML, AC, MS). One neurologist, with specific training in neuroimaging interpretation (MS),[15,16] scored the brain CT, blinded to other index tests.

SSEPs

Short-latency SSEPs were recorded after stimulation of the median nerve on each side, as previously described.[17] The N20 and P25 waves were identified as the major negative and positive peaks, respectively, with latencies of approximately 20 msec and 25 msec from the stimulus, when the cortical response was present. The SSEP cortical response was defined as absent when no reproducible cortical components (N20-P25 amplitudes <0.2 μV from the baseline[18]; could be detected in the presence of the P14 lemniscal wave.

In addition to the amplitude of the N20 SSEP wave, we also evaluated its duration, measured as the difference in latency between the end and the onset of the N20 peak (Fig. 1). This hypothesis was generated by a preliminary analysis of the previously collected data from the ProNeCA multicentre study from our group (Grippo et al., personal communication). An N20 SSEP wave duration of less than 10 ms was scored as normal and classified as a sign of good neurological outcome, regardless of the wave amplitude.

We collected ML SSEP in the same session as the short-latency SSEP, using the same electrode montage (see ESM Appendix 1 for technical details) to detect the presence or absence of the middle-latency (N70) SSEP wave.[19]

EEG

Standard 10-min EEG recordings were initiated as soon as possible after patients arrived in the Emergency Room using the same portable digital machine (NeMus ICU, EBneuro, Florence, Italy) used to record the SSEPs. Ten needle electrodes were placed according to the international 10–20 system, using a reduced bipolar longitudinal montage with Fp2, F4, C4, P4, O2, Fp3, F3, C3, P3, O1. Recordings were acquired with a sampling rate of 128 Hz. During reviewing digital filters (low-pass filter = 30–70 Hz; time constant = 0.1 or 0.3 s; notch filter = 50 Hz) and sensitivity gain (2–10 uV/mm with a standard gain of 7 uV/mm) were adjusted according to interpretation needs[20] The recordings were performed by neurophysiology technicians and interpreted by the neurophysiologists of our Department, who were unaware of the enolase or CT scan results at the time of reporting. EEG and SSEP reporting were made immediately after recording as part of the care process. EEG results were classified according to the 2021 American Clinical Neurophysiology Society (ACNS) terminology.[21] We identified the following EEG patterns:

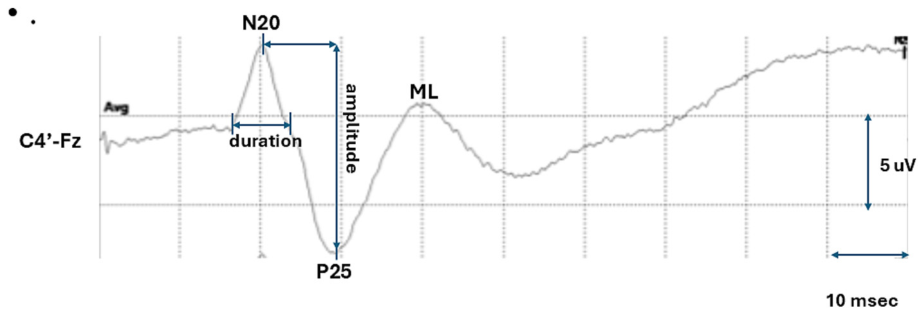

Fig. 1 – Representative record of the right cortical somatosensory evoked potential (SSEP) in a patient from our cohort, recorded with electrodes at C4′ (2 cm posterior to C4). Fz was used as the reference point. The SSEP components are labelled, and the horizontal and vertical lines indicate how the duration and amplitude have been measured. Abbreviations – ML: middle-latency; msec: milliseconds.

continuous or nearly continuous, discontinuous, low-voltage (less than 20 μV), suppression or burst-suppression, and epileptiform discharges. Within the suppression pattern, we separately identified the isoelectric tracings (voltage less than 2 μV). Further details about the EEG classification can be found in the Supplementary Data of the ProNeCA study report.[15,22]

Brain CT

Non-contrast brain CT scans with 4.8 mm slices were acquired using a Siemens SOMATOM X.cite ® system (Siemens Healthineers, Erlangen, Germany). Density measurements (in Hounsfield units, HU) were performed on axial scan, in circular regions of interest (ROIs) measuring 0.6 cm^2 within the grey matter of the putamen (PU) and the caudate nucleus (CN) and the white matter of the posterior limb of the internal capsule (PIC) and the corpus callosum. The severity of brain oedema was measured as the density ratio between grey matter and white matter: GM/WM ratio = (CN + PU)/(CC + PIC) as previously described.[23,24]

NSE

We measured NSE using the electrochemiluminescent immunoassay (ECLIA) kit on the COBAS 8000 modular analyser (Roche Diagnostics, Rotkreuz, Switzerland). The measuring range extended from 0.05 to 370 ng/ml. Samples with values above the measuring range were diluted accordingly. Functional sensitivity was at 0.25 ng/ml, and expected normal values were <17.0 ng/ml. In our laboratory, between-run precision at concentrations of 10.5 and 83.3 ng/ml was 6.8 % and 5.7 %, respectively.

Patient management

Patients were managed according to practises at the Careggi Teaching Hospital. Temperature control aimed at maintaining central body temperature at 36 °C for a minimum of 24 h and preventing fever (central body temperature below 37.7 °C) for up to 72 h after CA. Short-acting sedative agents such as propofol (at a rate of 1–2 mg/kg/h) or, less frequently, midazolam (at a rate of 0.03–0.1 mg/kg/h) were used as needed.

Full intensive care was mandatory until at least 72 h post CA, when clinical and instrumental evaluations were repeated for neurological prognostication, formulated by the consultant neurologist. If a poor outcome was predicted as likely according to the 2021 ERC/ESICM guidelines for post-resuscitation care,[2] the intensive care physician in charge of the patient shifted treatment to palliative care, based on Careggi Hospital's internal protocol. Decisions regarding the withdrawal of life-sustaining treatment were made in agreement with the patient's family and in consideration of the patient's previously expressed wishes, if available, per Italian Law [Advance Directives Act, 22 December 2017]. This protocol for end-of-life care deviates from management standards at the time of the previous multicentre ProNeCA study (data collection period 2016–2018), when WLST was not practised.

Outcome assessment

In surviving patients. neurological outcome was assessed at hospital discharge to home or a rehabilitation facility using the Glasgow-Pittsburgh Cerebral Performance Categories (CPC),[25] defined as follows: CPC 1, no or minor neurological deficits; CPC 2, moderate disability; CPC 3, severe disability; CPC 4, unresponsive wakefulness state; and CPC 5, death. We distinguished patients who died from neurological causes (CPC = 5a) from those who died from non-neurological causes (CPC = 5b).

The primary endpoint of the current study was the accuracy of short- and middle-latency SSEPs recorded within 6 h of ROSC in predicting both poor (CPC 3–5) and good (CPC 1–2) neurological outcomes at hospital discharge. The secondary aim was to evaluate the prognostic accuracy of other ERC-ESICM predictors.

Ethical approval

The study adhered to ethical principles and guidelines for good clinical practice. Due to logistical constraints, the informed consent was obtained after the ICU admission by the patient's next of kin. In patients who recovered consciousness, deferred consent was obtained. The study was approved by the local ethics committee (Ethics Committee Area Vasta Centro #27241).

Statistical analysis

We calculated descriptive statistics for continuous variables, including mean, median, and interquartile ranges (IQRs). Categorical variables were characterised using proportions. Pearson's chi-square and the Mann-Whitney U tests were used for comparing categorical and continuous variables, respectively.

We stratified the short-latency SSEP based on the amplitude of the N20 wave as absent (less than 0.2 μV), low-amplitude (amplitude at least 0.2 μV but less than 1.2 μV), intermediate amplitude (between 1.2 μV and 3.0 μV) and high amplitude (more than 3.0 μV). Based on our previous studies, we assumed that absent or low amplitudes predicted a poor outcome, and higher amplitudes predicted a good outcome. In patients with a present N20 wave, we investigated whether a normal N20 wave duration, as opposed to a prolonged one, or the presence of an ML N70 wave predicted a good outcome and increased the prognostic accuracy of the amplitude-based N20 classification. For the EEG, we performed a binary comparison between highly malignant patterns (suppression, including isoelectric, and burst suppression) predicting poor outcome per the 2021 ERC/ESICM Guidelines[2] and all other patterns to predict poor outcome, and between benign patterns (continuous and nearly continuous) identified in a previous ERC/ESICM-endorsed systematic review[8] and confirmed in a recent retrospective study on a large multicentre dataset[26] and all other patterns to predict good outcome. Similarly, for the NSE, we reported the accuracy of the recommended 60 ng/mL threshold for predicting poor outvome. Regarding the GM/WM ratio, for which there are no standardised thresholds for poor outcome prediction, we reported the threshold at which the false positive rate (FPR) for poor outcome was 100 %.

We reported the accuracy of all clinical and instrumental tests in predicting poor or good neurological outcomes as sensitivity, specificity, and FPRs (defined as 1-specificity), along with their 95 % confidence intervals (CI), calculated using Jamovi (The jamovi project [2025]. jamovi version 2.6 [Computer Software]). Data reported in the current study are compliant with the Standards for Reporting of Diagnostic Accuracy Studies (STARD) Statement, 2015 version.[27]

Results

During the study period, 123 patients with CA were resuscitated. Of the 98 potentially eligible patients, 65 had their EEGs and SEPs recorded within the first 6 h from CA and were included in the study (Fig. 2). The index tests were recorded at a median of four hours from ROSC (IQR 2–6). The demographic and clinical characteristics of the 65 included patients are presented in Table 1. The median age was 70 years, and 44 (67 %) patients were male. Thirty-two (49 %) patients survived with a good neurological outcome, one (2 %) was discharged in a vegetative state, and 32 (49 %) died. Among non-survivors, eight (12 %) fulfilled the neurological criteria of death, and 24 (37 %) died after WLST, of whom eight became controlled donors after cardiac death (DCD). WLST occurred on days 5–7 after ROSC (median 6 days or 144 h) except for one patient whose treatment was withdrawn on day 4 based on advance directives.

SSEPs

Tables 2 and 3 show the distribution of the N20 SSEP characteristics in patients with poor and good neurological outcomes, respectively. All 22 patients with a bilaterally absent N20 SSEP wave had a poor outcome (FPR 0 % [0–11]; sensitivity 67 % [48–82]). Ten patients exhibited a low-amplitude N20 wave (<1.2 μV). In nine of these patients, the N20 was also prolonged (>10 msec), and was not followed by the ML N70 wave. All these patients had a poor outcome. Adding this pattern to the absence of the N20 wave increased the cumulative sensitivity of early SSEPs for predicting a poor outcome to 93 % [79–99], while maintaining an FPR of 0 % [0–11] (Table 2). In the remaining patient with a low-amplitude N20, the wave duration was not prolonged. This patient had a preserved ML 70 wave and survived with a good neurological outcome (ESM Table 1).

In 23 patients, the N20 SSEP wave amplitude was equal to or greater than 3 μV. In all these patients, the N20 duration was ≤10 msec, and the ML N70 SSEP wave was preserved. All these patients had a good neurological outcome (FPR 0 % [0–10]; sensitivity 72 % [53–86]; Table 3).

Ten patients exhibited an intermediate N20 wave amplitude (between 1.2 and 3 μV). In seven of these patients, the duration of the N20 wave was normal and the ML N70 wave was present; all these patients survived with a good neurological outcome. The remaining three patients exhibited a prolonged N20 wave. In two of these patients, the N70 ML wave was absent, and one of these patients died. In the remaining patient, the N70 ML wave was present, and this patient survived with a good neurological outcome (ESM Table 1).

Overall, the combined presence of a normal-duration N20 wave and an N70 ML wave predicted a good outcome with 94 % [79–99] sensitivity and a 0 % [0–10] FPR (Table 3).

Other prognostic indices (Table 4)

Seven patients had an early status myoclonus, and all had poor outcome (FPR 0 % [0–11]); sensitivity 21 % [9–39]. Both a bilaterally absent pupillary light reflex and a GM/WM < 1.21 on brain CT predicted poor outcome with 0 % FPR [95 %CI: 0–11 %]. Their sensitivities were 88 % and 45 %, respectively. An NSE above 46 ng/mL predicted poor outcome with 0 % FPR [95 %CI: 0–11 %] and 79 % [95 %CI: 61–91 %] sensitivity. The scatterplots of the GM/WM and NSE are presented in ESM Figs. 1 and 2, respectively.

A burst-suppression pattern on the EEG predicted a poor outcome with 100 % specificity. However, seven patients with a suppressed EEG background recovered (FPR 22 % [9–40]. All patients with a continuous or nearly continuous EEG background experienced neurological recovery (FPR for good outcome: 0 % [0–10]; sensitivity: 69 % [50–84]).

The concordance of unfavourable SSEP patterns with other unfavourable signs having 0 % FPR is shown in the ESM Table 2. All 32 patients with a poor outcome had at least two concordant signs; fourteen patients had three signs, and thirteen patients had four signs.

Discussion

Our study shows that neurological outcome can be accurately predicted within six hours of cardiac arrest using somatosensory evoked potentials, and that combining a quantitative assessment of the N20 SSEP wave (amplitude and duration), with the detection of the middle-latency N70 SSEP wave provides greater sensitivity for predicting poor outcomes than the standard dichotomous classification of the N20 SSEP wave as either absent or present. This combined approach also predicts neurological recovery with high sensitivity and specificity. Overall, ultra-early SSEPs were more accurate than any other prognostic test at the same timepoint after ROSC in our study.

Few other previous studies had investigated the ability of short-latency SSEPs to predict neurological outcome within 6 h after cardiac arrest. One study from Nakabayashi et al.[28] showed that the bilateral absence of the N20 wave at a median of 65 min from ROSC was 100 % specific for poor outcome. The study included only 30 patients and did not provide a quantitative evaluation of SSEP. Another study from our group, including 41 patients, showed that an absent or low-voltage (<1.2 μV) N20 wave within 6 h after ROSC predicted poor neurological outcome at 6 months with 100 % [81–100] specificity.[29] However, our current study, conducted on a larger

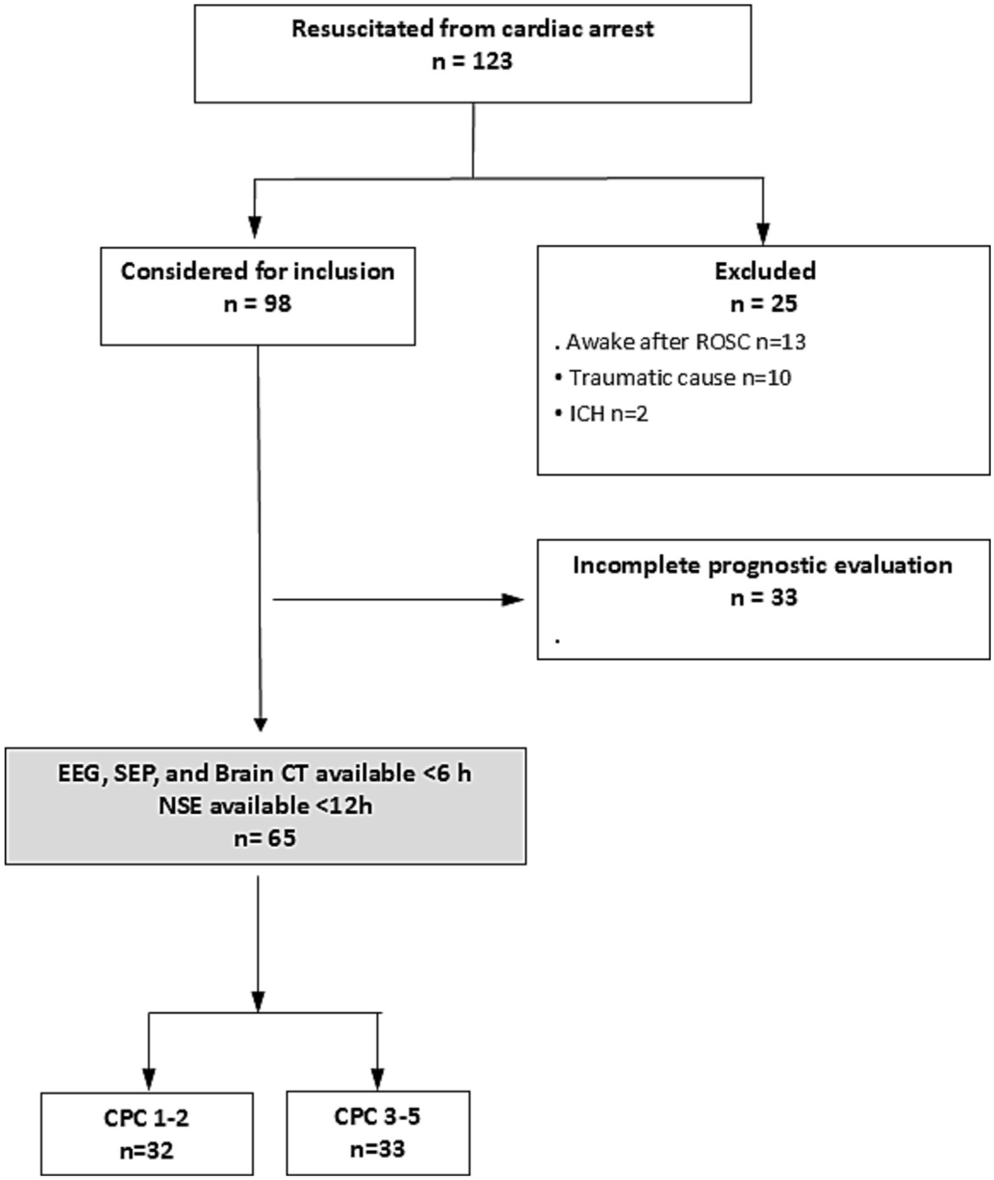

Fig. 2 – Flow-chart of study inclusion.

population, showed that an N20 wave below 1.2 μV was compatible with neurological recovery in at least one patient. In this patient, the N20 wave duration was not prolonged, and the ML N70 wave was present, suggesting that assessing these additional components helps avoid a falsely pessimistic prediction.

Our study is the first to investigate the duration of the N20 SSEP wave for prognostication after cardiac arrest, based on a preliminary analysis of our ProNeCA database. We speculated that an increased N20 wave duration, coupled with a reduction in its amplitude, reflects a desynchronization of its generators, resulting in a reduced summation of their action potential. While this hypothesis deserves further investigation, the unfavourable significance of the prolongation of the N20 wave is confirmed by its association with poor outcome and the absence of the following ML N70 wave in our study.

The rationale of assessing the presence of the ML N70 wave in patients with HIBI is that, while the short-latency SSEPs reflect the functional status of the central sensory pathway between the corticomedullary junction and the sensory cortex, middle-latency SSEPs reflect the more complex activity of associative areas of the cortex (most likely, the second sensory [SII] area),[30] and are likely more sensitive to HIBI. Consequently, the absence of ML-SEP waves can indicate severe HIBI in patients with preserved short-latency SSEPs. This finding was first described in studies conducted in the early 2000s. These studies showed that in patients with preserved N20 but bilaterally absent N70 waves, the outcome was almost invariably poor.[13,14] However, they also described cases of neurological recovery with this pattern.[13,31] Another reason for caution is that the N70 wave may be absent or exhibit prolonged latency (>100 msec) immediately after ROSC and recover in the subsequent 12–24 h.[32] Finally, the interrater reliability of ML-SSEP after cardiac arrest is lower than that of short-latency SSEP.[33] For this reason, we suggest that the absence of the N70 wave be interpreted in light of the short-latency SSEP pattern; in our study, no falsely pessimistic prediction occurred when a concordant low-voltage and prolonged

N20 confirmed the unfavourable signal from a bilaterally absent N70 wave. Notably, despite this restrictive interpretation, the sensitivity for a poor outcome of this pattern remained 93 %.

Our study showed that a bilaterally present N70 SSEP wave predicts neurological recovery, confirming earlier studies.[13,32] However, these studies also reported falsely optimistic predictions. One potential reason was that these studies classified as N70 waves delayed electrical potentials recorded as late as 182 msec. Evidence shows that these delayed potentials are associated with poor neurological outcome.[13,14] For this reason, we restricted the time window for ML-SEP to 100 msec. Notably, all patients with a present N70 wave had neurological recovery in our study, and all but one exhibited favourable N20 SSEP wave features, suggesting that this concordance should also be considered when predicting a good outcome with ultra-early SSEPs.

While the unfavourable SSEP patterns we identified were 100% specific for poor outcome, the EEG suppressed background exhibited a 12% FPR. This result confirms evidence from previous studies[29] showing that a "highly malignant" EEG is not a reliable sign in the early hours after cardiac arrest and suggests that SSEPs should be preferred instead. In addition, SSEP was also the most sensitive among unfavourable predictors with 100% specificity. Interestingly, all patients with a poor outcome in our study exhibited two or more of these predictors, indicating a strong concordant predictive signal. This is particularly important, given the difficulties in accurately predicting prognosis in such an early phase after ROSC. Although the evolutive nature of HIBI forbids prognostication during this phase,[34] an early and reliable assessment of the severity of HIBI may help stratify patients for neuroprotective strategies, avoiding the opposite extremes of the spectrum, where interventions would be either futile or unnecessary.

Some important limitations of our study should be acknowledged. Firstly, this is a preliminary study, and its results should be considered as hypothesis-generating. Although the combined short- and middle-latency SSEP patterns were the most accurate predictors among those we investigated, further studies are necessary to confirm these findings. Another reason for caution is that the sample size of our preliminary study is small, as shown by the wide confidence interval around its point estimates. Studies in larger cohorts have shown that, even if very accurate, SSEP may occasionally yield falsely pessimistic predictions,[35] even if in some cases this result was due to inaccurate reading of the SSEP record.[36] Secondly, there are

Table 1 – Characteristics of the study population (n = 65).

Variable	
Age, years median (IQR)	70 (19)
Gender, male, *n* (%)	44 (67)
Out-of-hospital, *n* (%)	41 (63)
Witnessed, *n* (%)	60 (92)
CA duration, minutes median (range)	20 (6–60)
Initial rhythm, *n* (%)	
VF/pVT	20 (30.7)
PEA	22 (34.4)
Asystole	18 (28.1)
Unknown	3 (4.2)
GCS at ICU admission, median (range)	3 (3–8)
CPC at ICU Discharge, *n* (%)	
CPC 1	19 (29.7)
CPC 2	13 (20.0)
CPC 3	0 (0)
CPC 4	1 (1.5)
CPC 5a (death by neurological criteria)	8 (12.3)
CPC 5b (WLST)	24 (36.9)

Abbreviations: CA, cardiac arrest; CPC, Cerebral Performance Category; GCS, Glasgow Coma Scale; ICU, intensive care unit; IQR, interquartile range; PEA, pulseless electrical activity; pVT, pulseless ventricular tachycardia; VF, ventricular fibrillation; WLST: withdrawal of life-sustaining treatment.

Table 2 – Accuracy of the SSEP patterns for poor outcome prediction.

SSEP pattern	TP	FP	TN	FN	Sensitivity % (95 %CIs)	False positive rate % (95 %CIs)
Bilaterally absent N20 wave	22	0	32	11	67 (48–82)	0 (0–11)
N20 wave amplitude <1.2 μV, dur > 10 msec, ML absent	31	0	32	2	93 (79–99)	0 (0–11)
N20 wave amplitude 1.2–3.0 μV, dur > 10 msec, ML absent	32	1	31	1	97 (84–99)	3 (1–17)

Note: The table shows a sensitivity analysis exploring the different combinations of N20 amplitude with duration and absence of the ML-SEP wave.

Abbreviations: CIs: Confidence Intervals; FN: false negatives; FP: false positives; ML: middle-latency; dur = duration; SSEP: somatosensory evoked potentials; TN: true negatives; TP: True positives.

Table 3 – Accuracy of the SSEP patterns for neurological recovery.

SSEP pattern	TP	FP	TN	FN	Sensitivity % (95 %CIs)	False positive rate % (95 %CIs)
N20 wave amplitude >3.00 μV, duration <10 msec; ML present	23	0	33	9	72 (53–86)	0 (0–10)
N20 wave amplitude 1.2–3.0 μV, duration <10 msec; ML present	29	0	33	3	91 (75–98)	0 (0–10)
N20 present (any amplitude), duration <10 msec; ML present	30	0	33	2	94 (79–99)	0 (0–10)

Note: The table shows a sensitivity analysis exploring the different combinations of N20 amplitude with duration and presence of the ML-SEP wave.

Abbreviations: CIs: Confidence Intervals; FN: false negatives; FP: false positives; ML: middle-latency; dur = duration; SSEP: somatosensory evoked potentials; TN: true negatives; TP: True positives.

Table 4 – Accuracy of other prognostic indices.

	TP	FP	TN	FN	Sensitivity % (95 %CIs)	False positive rate % (95 %CIs)
Poor outcome prediction						
Clinical examination						
Absent pupillary light reflex	29	0	32	4	88 (72–96)	0 (0–11)
Status myoclonus	7	0	32	26	21 (9–39)	0 (0–11)
NSE						
NSE > 60 ng/mL	22	0	32	11	70 (51–84)	0 (0–11)
Electroencephalogram						
Burst suppression	11	0	32	22	33 (18–52)	0 (0–11)
Suppressed background	22	7	25	11	67 (48–82)	22 (9–40)
Brain CT						
GM/WM ratio <1.21	15	0	32	18	45 (28–63)	0 (0–11)
Good outcome prediction						
EEG						
Continuous or Nearly Continuous	22	0	33	10	69 (50–84)	0 (0–10)

Abbreviations: CT: computed tomography; EEG: Electroencephalogram; GM/WM: grey matter/white matter density ratio; NSE: neuron-specific enolase.

no normative data on the duration of the N20 SSEP wave, and the 10-msec threshold we established was based on a retrospective analysis of our database. Thirdly, recording SSEP in the first hours after ROSC requires the immediate availability of skilled personnel and may be technically challenging due to time pressure and the interference from clinical procedures. This may severely limit the reproducibility of our results. Fourthly, all studies on ML-SSEP after cardiac arrest, including the present one, have been conducted in patients under sedation, and a suppressive effect on ML-SSEP by sedative drugs, similarly to what occurs with volatile anaesthetics,[37] cannot be ruled out. Fifthly, we only have CPC at hospital discharge in our study. Measuring outcome at this early time point may have prevented us from observing late recovery in survivors with poor functional outcome at hospital discharge (CPC 3 or 4). Though this has been observed mainly in patients with CPC 3[38] (not present in our study), this may occasionally occur in patients with CPC 4 as well.[39] Finally, although our hospital guidelines mandate full intensive care support in patients who are comatose during the first 72 h after ROSC, the clinical staff was not blinded to the results of predictive tests. Consequently, we cannot completely exclude that this may have affected their management, causing a self-fulfilling prophecy and biassing the results towards a higher specificity. This is especially important in consideration that neurological recovery in HIBI may occasionally occur late.[40] However, time to awakening in our cohort was longer that the median time reported in other major studies, including those on late awakeners.[41]

In conclusion, we showed that ultra-early prognostication of good and poor outcome after cardiac arrest based on a combination of short- and middle-latency SSEP patterns, including the amplitude and duration of the N20 SSEP wave, is feasible and accurate. However, our preliminary results will require confirmation from larger studies.

CRediT authorship contribution statement

Maenia Scarpino: Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Andrea Nencioni:** Validation, Investigation, Data curation, Conceptualization. **Pasquale Bernardo:** Supervision, Methodology, Investigation, Data curation, Conceptualization. **Manuela Bonizzoli:** Validation, Investigation, Data curation, Conceptualization. **Peiman Nazerian:** Validation, Investigation, Data curation, Conceptualization. **Benedetta Piccardi:** Validation, Methodology, Investigation, Data curation. **Riccardo Carrai:** Validation, Supervision, Methodology, Formal analysis, Conceptualization. **Claudio Sandroni:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Formal analysis. **Antonello Grippo:** Writing – review & editing, Writing – original draft, Validation, Supervision, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Cecilia Agostini:** . **Flavia Caniato:** . **Annalisa Cassardo:** . **Antonella Cramaro:** . **Maria Lombardi:** . **Cristina Mei:** . **Michele Ombrosi:** . **Marta Silvestri:** . **Maddalena Spalletti:** .

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: 'Claudio Sandroni is member of the Editorial Board of *Resuscitation*. The remaining authors have no conflict of interest to disclose'.

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Appendix A. Supplementary material

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