The characteristics of patients with bilateral absent evoked potentials after post-anoxic brain damage: A multicentric cohort study

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Abstract

Objectives: Patients with bilateral absence of cortical response ($N20_{ABS}$) to somatosensory evoked potentials (SSEPs) have poor neurological outcome after cardiac arrest (CA). However, SSEPs are not available in all centers. The aim of this study was to identify predictors of $N20_{ABS}$.

Methods: Retrospective analysis of institutional databases (2008–2015) in three ICUs including all adult admitted comatose patients undergoing SSEPs between 48 and 72 h after CA. We collected clinical (i.e. absence of pupillary reflexes, PLR, myoclonus and absent or posturing motor response and myoclonus on day 2–3), electroencephalographic (EEG; i.e. unreactive to painful stimuli; presence of a highly malignant patterns, such as burst-suppression or flat tracings) findings during the first 48 h, and the highest NSE levels on the first 3 days after CA. Unfavorable neurological outcome (UO) was assessed at 3 months using the Cerebral Performance Categories of 3–5.

Results: We studied 532 patients with SSEPs, including 143 (27%) without $N20_{ABS}$; UO was observed in 334 (63%) patients. Median time to SSEPs was 72 [48–72] h after CA. No patient with absent PLR and myoclonus during the ICU stay had N20 present; similar results were observed with the combination of absent PLR, myoclonus and any EEG pattern (i.e. unreactive or highly malignant). Similar results were observed in the subgroup of patients where NSE was available (n = 303). In a multivariate logistic regression, non-cardiac etiology of arrest, unreactive EEG to painful stimuli, absence of pupillary reflexes and posturing motor response, were independent predictors of $N20_{ABS}$. When available, the highest NSE was also an independent predictor of $N20_{ABS}$.

Conclusions: Clinical and EEG findings predicting patients with $N20_{ABS}$, confirm that $N20_{ABS}$ reflects a severe and permanent cerebral damage after CA.

Keywords: SSEP, Cortical evoked potential, Prognosis, Cardiac arrest, Prediction

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Introduction

Poor neurological outcome remains common among survivors from cardiac arrest (CA), principally because of extensive brain injury.[1] Neurological prognostication of these patients remains a major clinical challenge. Besides clinical factors that are known to account for poor outcome after CA, such as duration of cardiopulmonary resuscitation (CPR), bystander CPR and no-flow time, the most accurate tool to evaluate the severity of the post-anoxic insult is neurological examination.[2] However, because of the wide spread of target temperature management (TTM) as a neuroprotective strategy to reduce the extent of brain damage in this setting, the accuracy of neurological examination is altered by the use of sedative and analgesic agents during TTM in the first days after injury,[3,4] and additional tools have been implemented to help clinicians to improve the outcome prediction of CA patients.

Somato-sensory evoked potentials (SSEPs) have been widely studied both in patients with and without TTM.[5] In particular, bilateral absence of cortical responses ($N20_{ABS}$) to the stimulation of the median nerve, in the presence of a high-quality examination, was consistently associated with irreversible brain damage and poor prognosis.[6,7] Some authors have reported few cases of neurological recovery after CA despite of $N20_{ABS}$ after TTM;[8] poor quality of SSEPs recordings or the presence of peripheral neuropathy might have explained these findings and $N20_{ABS}$ is still recommended as a strong indicator of poor neurological outcome in this setting.[5]

As $N20_{ABS}$ was associated with a large cortical cerebral necrosis in autopsy studies,[9,10] we hypothesized that $N20_{ABS}$ would be associated with other predictors of poor outcome, including clinical signs (i.e. myoclonus, or absent brainstem reflexes), malignant electroencephalography (EEG) patterns, or high levels of biomarkers of brain injury.[5,11,12] Moreover, as many hospitals are still unable to perform SSEPs,[13] such association might help to potentially identify patients with $N20_{ABS}$ using alternative prognostic tools.

Thus, the aim of this study was to characterize patients with $N20_{ABS}$ in comparison with those with present N20 (either bilaterally or unilaterally, $N20^{+}$) in CA patients undergoing multimodal approach for neurological prognostication.

Methods

Study population

We retrospectively analyzed the institutional databases (2008–2015) of three academic intensive care units (ICUs) (i.e. Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium; Department of Perioperative Medicine, Intensive Care and Emergency, Ospedali Riuniti, Trieste, Italy; Department of Intensive Care Medicine, CHUV, Lausanne, Switzerland) including all adult comatose CA patients treated with TTM who underwent multimodal assessment including SSEPs (at 48–72 h after CA) as part of standard care. The local Ethical Committees approved the study, but waived the need for informed consent because of its retrospective nature.

Post-resuscitation care

All comatose patients were treated with TTM (target temperature: 33 °C; range: 32–34 °C) for 24 h, according to standardized locals protocols. For in-hospital CA, cooling was started immediately after return of spontaneous circulation (ROSC), while for out-of-hospital cardiac arrest (OHCA), TTM was initiated after hospital admission. Hypothermia was induced with a cold fluid bolus (20–30 ml/kg over 30 min of either NaCl 0.9% or Ringer lactate solution) and maintained for up to 24 h using a water-circulating blanket device. Body temperature was mostly measured using bladder or rectal temperature probes. All patients undergoing TTM received sedation (i.e. midazolam, as a continuous infusion of 0.03–0.1 mg/kg/h, or propofol 1–2 mg/kg/h) and analgesia (i.e. morphine or, in case of renal failure, remifentanil at an equipotent dose of 0.1–0.3 mg/kg h). For shivering control, neuromuscular blocking agents (NMBAs) were administered in the induction phase (i.e. cisatracurium as a bolus of 0.15 mg/kg) and, if needed, as a continuous infusion thereafter (1–3 mcg/kg/min). Rewarming was obtained passively after interruption of cooling, with a target rate of 0.5 °C/h; sedation, analgesia and NMBAs were discontinued when normothermia (>37 °C) was achieved. All patients were kept in a semi-recumbent position (0-30°); mechanical ventilation was set to target a $PaCO_2$ between 35 and 45 mmHg and a SpO_2 of 94–98%. Blood glucose levels were kept between 110 and 150 mg/dL using a continuous intravenous insulin administration. Control of hemodynamic was achieved using volume resuscitation, dobutamine and/or norepinephrine, whenever needed, targeting a mean arterial pressure at least of 65–70 mmHg. Enteral nutrition was initiated as soon as possible after target temperature achievement.

Prognostication and withdrawal of care

At normothermia, repeated neurologic examination was performed daily. Also, standard or continuous EEG recording was initiated since ICU admission and repeated or maintained until the 48–72 h after CA. SSEPs were performed at normothermia, in general at 48–72 h after the CA. Certified neurophysiologists on site performed the interpretation of EEG and SSEPs records. Blood samples were collected for neuron specific enolase (NSE; Cobas e601, Roche Diagnostics GmbH, Mannheim, Germany) at least once at 24 and 48–72 h after CA.

Withdrawal of life-sustaining therapies was based on an interdisciplinary approach, which considered the bilateral absence of the N20 cortical responses to SSEPs, persisting coma with absent motor response or extension posturing, presence of status myoclonus, malignant EEG patterns, or bilaterally absent pupillary reflexes.

Data collection

Demographics, co-morbidities, data on CPR (first rhythm, bystander CPR, time to ROSC) were prospectively collected as part of the registries. Clinical examinations including pupillary reflexes and GCS motor response were collected from the patient data monitoring system from clinical charts. EEG results were collected from local databases as reported by the neurophysiologist; no attempt to reanalyze SSEP and EEG recordings was made. Prognostic data indicating unfavorable neurological outcome (UO) included clinical examination (i.e. bilateral absence of pupillary reflexes, absent or posturing motor response and myoclonus on day 2–3) or EEG findings (i.e. absence of reactivity to painful stimuli; presence of a "highly malignant" patterns,[11] such as burst-suppression or suppressed background, with or without superimposed repetitive epileptiform transients, seizures or status epilepticus); the worst clinical and EEG finding over the first 72 h was considered for the

analysis. The highest (i.e. "peak") NSE levels over the first 72 h from CA was also collected; according to previously published data, high NSE values were defined as a peak of NSE > 75 ng/mL.[14]

Neurological evaluation at 3 months was assessed using the cerebral performance category score (CPC; 1 = no neurological disability, 2 = mild neurological disability, 3 = severe neurological impairment, 4 = vegetative state, 5 = death). A favorable outcome was defined as a CPC of 1 or 2, while UO as a CPC 3–5.

Statistical analysis

Calculations were performed using IBM SPSS Statistics 21 for Windows and GraphPad Prism software. Descriptive statistics were computed for all study variables and normal distribution was assessed using the Kolmogorov–Smirnov test. Data are presented as count (percentage) or median [25th–75th percentiles]. Differences between groups were assessed using a Fisher's exact test for categorical variables and a Wilcoxon rank test for continuous variables and one-way ANOVA for groups' comparison. In order to identify the variables independently associated with $N20_{ABS}$, a multivariable logistic regression analysis with $N20_{ABS}$ as the dependent variable was performed in all patients, and then only in those with the peak NSE available; co-linearity between variables was excluded prior to modelling and only variables associated with $N20_{ABS}$ on a univariate basis (i.e. $p < 0.1$) were introduced in the multivariate models. Odds ratios (OR) with 95% confidence intervals (CIs) were computed. After the multivariable analysis, the discriminative ability of the peak NSE values, as well as the one sampled at 24 h and 48–72 h after the arrest, to predict $N20_{ABS}$ was evaluated using receiver operating characteristic (ROC) curves with the corresponding area under the curve (AUC) and related sensitivity and specificity. Youden's index was computed to identify the NSE value with the best sensitivity and specificity to predict $N20_{ABS}$. Finally, each potential prognosticator of UO and different combinations were also assessed using the area under the ROC curve, applying nonparametric comparisons. A p value <0.05 was considered statistically significant.

Results

On a total of 547 patients being comatose on day 3 after arrest, SSEPs were not available in 15 patients (unreadable tracings, n = 12; device availability, n = 3). As such, 532 patients (Brussels, n = 126; Trieste, n = 95 and Lausanne, n = 302) were included in the final analysis over the study period (Table 1). Median time from arrest to return of spontaneous circulation was 20 [13–29] min; most of patients had in-hospital CA and a shockable initial rhythm. An UO was observed in 334 (63%) of patients.

SSEPs were performed at 72 [48–72] h after CA; $N20_{ABS}$ was observed in 143 (27%) of patients (Fig. 1). Unfavorable outcome was, as expected, observed in all of these patients. Also, the absence of

Table 1 – Characteristics of study population, according to the presence or absence ($N20_{ABS}$) of cortical response to somato-sensory evoked potentials.

	All patients (n = 532)	$N20_{ABS}$ (n = 143)	Others (n = 389)	*p value*
Demographics				
Age, years	62 [52–72]	61 [51–71]	62 [52–62]	0.38
Male gender, n (%)	390 (73)	101 (71)	289 (74)	0.56
Time to ROSC, min	20 [13–29]	25 [18–30]	19 [10–25]	<0.001
Cardiac origin of CA, n (%)	377 (71)	77 (54)	300 (78)	<0.001
VF/VT, n (%)	318 (60)	55 (38)	263 (68)	<0.001
OHCA, n (%)	186 (35)	48 (34)	138 (35)	0.65
Prognostic evaluation				
Myoclonus at any time, n (%)	86 (16)	55 (38)	31 (8)	<0.001
Pupillary reflex absent, n (%)	122 (23)	83 (58)	39 (10)	<0.001
Motor response	1 [1–4]	1 [1–2]	3 [1–5]	<0.001
Motor response bad day 3, n (%)	281 (53)	135 (94)	146 (37)	<0.001
Seizures/SE, n (%)	102 (19)	49 (34)	53 (14)	<0.001
Unreactive EEG, n (%)	253 (48)	129 (90)	124 (32)	<0.001
Burst suppression, n (%)	122 (23)	56 (39)	66 (17)	<0.001
Suppressed background, n (%)	45 (8)	25 (18)	20 (5)	<0.001
NSE day 1, ng/mL	23.8 [15.5–39.5] (n = 298)	55.0 [27.7–112.0] (n = 64)	20.1 [14.7–31.3] (n = 234)	<0.001
NSE day 3, ng/mL	21.0 [14.0–54.0] (n = 120)	78.0 [48.0–186.0] (n = 25)	17.0 14.0–29.0] (n = 95)	<0.001
Highest NSE, ng/mL	25.2 [16.1–50.7] (n = 303)	77.2 [37.5–120.9] (n = 66)	20.9 [14.9–32.6] (n = 237)	<0.001
Time of SSEP, day	72 [48–72]	72 [48–72]	72 [48–72]	0.46
Outcomes				
Hospital mortality, n (%)	277 (52)	135 (94)	142 (36)	<0.001
Favorable neurological outcome, n (%)	198 (37)	0 (0)	198 (37)	<0.001

CA = cardiac arrest; ROSC = return of spontaneous circulation; VF/VT = ventricular fibrillation/ventricular tachycardia; OHCA = out-of-hospital cardiac arrest; EEG = electroencephalogram; NSE = Neuron specific enolase; SSEP = somatosensory evoked potentials; SE = status epilepticus.

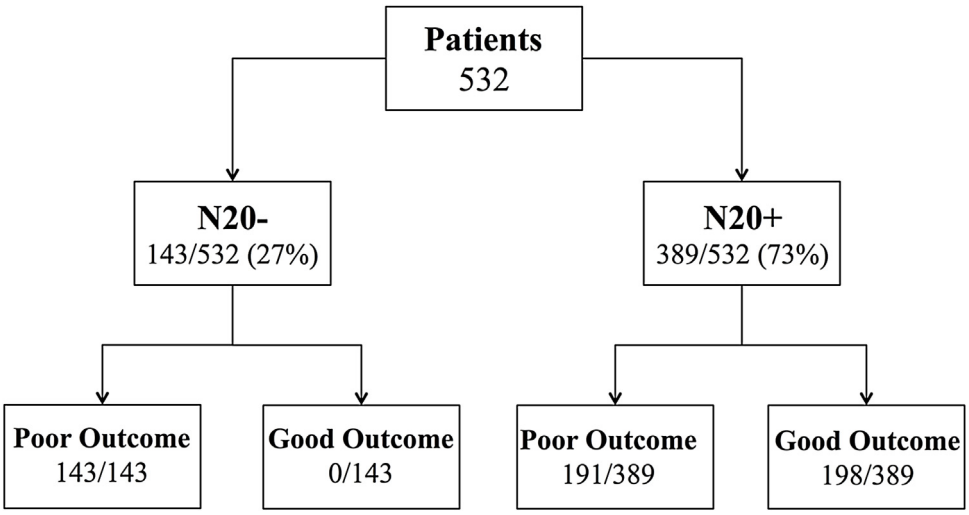

Fig. 1 – Outcome of the patients with N20 present or absent.

pupillary reflexes (58% vs. 10%; $p < 0.001$), posturing or absent motor response (94% vs. 37%; $p < 0.001$) or myoclonus (38% vs. 8%; $p < 0.001$) on day 2–3 was observed more frequently in $N20_{ABS}$ patients than in others (Table 1). Patients with $N20_{ABS}$ had also more frequently seizures or status epilepticus, unreactive EEG or highly malignant patterns on EEG (Table 1). Finally, peak NSE levels were significantly higher in $N20_{ABS}$ patients.

The occurrence of $N20_{ABS}$ with regard of the combination of clinical and EEG findings of UO is reported in Table 2. No patient with absent PLR and myoclonus during the ICU stay had N20 present; similar results were observed with the combination of absent PLR, myoclonus and any EEG pattern (i.e. unreactive or highly malignant). Similar results were observed in the subgroup of patients where NSE was available (Supplemental Table 1). Only 4 out of 210 patients (2%) with no clinical or EEG findings suggesting an UO had also $N20_{ABS}$.

Compared to those with favorable outcome, UO patients with $N20_{ABS}$ had a longer resuscitation, and had less frequently a shockable initial rhythm; also, UO patients with $N20_{ABS}$ had more frequently poor clinical signs and EEG malignant patterns than others, as well as higher NSE levels (Supplemental Table 2). Similar results were found when patients with FO and UO without $N20_{ABS}$ or UO patients with and without $N20_{ABS}$ were compared.

Predictors of absent N20

In a multivariate logistic regression analysis, non-cardiac etiology of arrest, unreactive EEG to painful stimuli, absence of pupillary reflexes, and extension or no motor response were independent predictors of $N20_{ABS}$ (Table 3). The AUC of the multivariate logistic model was 0.901 (95% CIs = 0.884–0.934, $p < 0.001$). If the multivariable analysis was conducted only including those patients with available peak NSE (n = 303 — Supplemental Table 3), non-cardiac etiology of arrest, unreactive EEG to painful stimuli, absence of pupillary reflexes, extension or no motor response and peak NSE levels were independent predictors of $N20_{ABS}$ (Table 3). The AUC of the multivariate logistic model was 0.920 (0.883–0.958, $p < 0.001$). In particular, the AUCs of NSE concentration on day 1 and day 3 was 0.81 (0.75-0.87; $p < 0.001$) and 0.91 (0.86–0.97; $p < 0.001$), respectively. The optimum cut-off of NSE to predict $N20_{ABS}$ was 31 ng/mL (sensitivity 74%; specificity 73%) and 39 ng/mL (sensitivity 85%; specificity 88%), on day 1 and day 3, respectively.

Predictors of unfavorable neurological outcome

The model with the highest prognostic accuracy for UO included at least one clinical sign, one EEG finding, peak NSE and SSEP.

Table 2 – Frequency of the absence of N20 in relationship with clinical signs and electroencephalographic patterns. Data are presented with 95% confidence intervals (CIs).

	N20 absent (n = 143)	N20 present (n = 389)	Sensitivity	Specificity	PPV	NPV
Absent PLR	83	39	58 [50–65]	90 [87–92]	68 [59–76]	86 [82–88]
Absent PLR + Myoclonus	29	0	20 [14–28]	100 [99–100]	100 [88–100]	77 [73–81]
Absent PLR + HM EEG	78	17	55 [43–62]	96 [93–97]	82 [73–88]	85 [81–88]
Absent PLR + uEEG	77	24	54 [46–61]	94 [91–96]	76 [67–83]	85 [81–88]
Absent PLR + Myoclonus + HM EEG	28	0	20 [13–26]	100 [99–100]	100 [88–100]	77 [73–81]
Absent PLR + Myoclonus + uEEG	27	0	19 [13–26]	100 [99–100]	100 [88–100]	77 [73–80]

EEG = electroencephalogram; PLR = pupillary reflex; HM = highly malignant; uEEG = unreactive EEG; PPV = positive predictive value; NPV = negative predictive value.

Table 3 – Logistic regression analysis on predictors of absent somatosensory evoked potentials in all patients (n = 532), and in patients for whom at least one neuron specific enolase (NSE) was available (n = 303).

Variable	OR	95% Confidence Intervals	P value
All patients			
Non-cardiac etiology of CA	1.970	1.173–3.307	0.010
Unreactive EEG	9.181	4.671–18.045	<0.001
Pupillary reflex absent	3.559	2.033–6.232	<0.001
Motor response absent	13.079	5.560–30.768	<0.001
Patients with at least one NSE measurement			
Non-cardiac etiology of CA	2.560	1.207–5.433	0.014
Unreactive EEG	5.252	2.107–13.091	<0.001
Pupillary reflex absent	3.283	1.408–7.657	0.006
Motor response absent	10.103	2.682–38.058	0.001
Peak NSE, ng/mL	1.011	1.001–1.020	0.024

OR = odds ratio; CA = cardiac arrest; EEG = electroencephalogram; NSE = Neuron specific enolase.

However, the addition of SSEP only slightly and non-significantly improved the accuracy of the model (Table 4).

Discussion

In this study, we have observed that 27% of patients undergoing a multimodal prognostic approach including SSEPs had $N20_{ABS}$. Patients with $N20_{ABS}$ presented more frequently with other clinical, EEG or biological predictors of unfavorable neurological outcome than others. No patients with absent PLR and myoclonus had N20 present. A non-cardiac etiology of arrest, unreactive EEG to painful stimuli, absence of pupillary reflexes, and posturing motor response were independent predictors of $N20_{ABS}$. The additional role of SSEPs to predict UO was limited when compared to a multimodal approach including clinical signs, EEG findings and NSE.

The bilateral absence of N20 when SSEPs are performed at normothermia is a strong predictor of UO after CA, with a false positive below 1%.[5] In the recent TTM-study, 313 patients underwent a multimodal prognostication assessment; $N20_{ABS}$ was present only in 1 patient with good neurological recovery.[15] False predictions of poor outcome by $N20_{ABS}$ at SSEP have been already reported,[8] but artifacts which may have caused this single false positive, are a recognized cause of error.[3] Nevertheless, as SSEPs results are available for clinicians, it is difficult to understand whether some "self-fulfilling prophecy" could influence its accuracy to identify UO in this setting.[16] On the other hand, the concordance between SSEPs findings and results from EEG and NSE measurements are reassuring for the accuracy of such test to identify patients with extensive brain damage after cardiac arrest. Moreover, SSEPs are not available in all centers, are time-consuming and require a specific expertise for interpretation. Also, SSEPs sensitivity rarely exceeds 50%, which results in many patients with UO after CA despite recordable N20 waves.[5] In our study, 74% of patients with bilateral N20 waves had poor outcome. However, reduced N20 amplitudes $\leq 0.62\ \mu V$ could have a better specificity to predict UO in this setting.[17] Unfortunately, this analysis was not available in our cohort.

Considering that $N20_{ABS}$ is associated with >99% specificity to predict poor outcome in comatose CA patients,[5] we aimed to identify predictors of $N20_{ABS}$ as potential substitutes for SSEPs, in settings where SSEPs are not available or could not be adequately performed (i.e. interference, artifacts, unavailable technician during the week-end, peripheral neuropathy). We identified non-cardiac etiology of arrest, unreactive EEG to painful stimuli, absence of pupillary reflexes, and unfavorable motor response as predictors of $N20_{ABS}$. Interestingly, the bilateral absence of PLR and myoclonus was highly specific to predict $N20_{ABS}$, although sensitivity was very low. In a previous study including 66 patients, Daubin et al. identified a score based on factors that were independently associated with an $N20_{ABS}$, including absence of corneal reflex, myoclonus, and extensor or absent motor response.[18] The ROC curves for this score were 0.885 and 0.919 at day 1 and 3, respectively. We also

Table 4 – Areas under the receiving operator characteristic curves of several models combining different tools to predict unfavourable neurological outcome (UO).

Variable	AUC	95% Confidence Interval	P
Motor response	0.77	0.72–0.81	<0.001
Clinical signs	0.82	0.79–0.85	<0.001
Clinical signs + SSEP	0.84	0.81–0.87	<0.001
Clinical signs + EEG	0.87	0.84–0.90	<0.001
Clinical signs + NSE[a]	0.89	0.83–0.95	<0.001
Clinical signs + EEG + SSEP	0.88	0.85–0.91	<0.001
Clinical signs + EEG + NSE[a]	0.91	0.87–0.97	<0.001
Clinical signs + EEG + NSE[a] + SSEP	0.92	0.86–0.97	<0.001

AUC = area under the curve; CA = cardiac arrest; SSEP = somatosensory evoked potentials; EEG = electroencephalogram; NSE = Neuron specific enolase.
[a] 303 patients.

observed a very good accuracy for our model to predict $N20_{ABS}$ at day 3, in particular when NSE was available. In clinical practice, these factors could allow early identification of a subgroup of patients with extensive brain injury and in whom aggressive intensive care could be considered as futile. We observed that most of patients with $N20_{ABS}$ concomitantly showed other signs of severe brain damage, such as the absence of pupillary reflexes, posturing or myoclonus or severe EEG abnormalities and high NSE levels. Whether these predictors could be used as substitutes for SSEPs, particularly when considering early withdrawal of intensive treatment, should be tested in larger studies.

Outcome prognostication following CA is a challenging situation for ICU physicians; combining multiple tests, such as clinical findings, SSEP, EEG, biochemical markers or neuro-imaging, has been proposed into the Guidelines to reduce the risk of early withdrawal of life-sustaining therapies but it is not easy to apply. First, when multiple tests show "discordant" results (i.e. $N20_{ABS}$ with the absence of highly malignant EEG patterns and NSE of 25 ng/mL), one may argue that additional tests would be needed to further characterize the severity of post-anoxic brain injury and/or question the reliability and quality of the different tools. In our cohort, only very few patients showed an isolated $N20_{ABS}$ without other predictors of UO; in clinical practice, repetition of SSEPs would have been logical to avoid misclassification or check for very low N20 amplitude or interferences. Second, the best combination of multiple tests to provide the highest accuracy for outcome prediction remains unknown. It has been recently showed that clinical examination, EEG findings and NSE provided the highest predictive value of UO in a cohort of 134 patients, whereas somatosensory-evoked potentials did not provide any complementary information.[14] In another study, De Santis et al. showed that the addition of SSEPs to clinical examination and EEG did not improve the sensitivity to predict UO.[19] However, in a recent study including 323 patients, the AUC for outcome prediction significantly increased from 0.85 to 0.93 when SSEPs were included.[20] All these studies suggest that the combination of predictors of UO is more accurate than a single prognostic tool. How the combination of such tools may help to identify patients with late awakening (i.e. after 5 days) after CA or those with favourable neurological outcome, it remains to be further studied.

This study has some limitations. First, as all centers have experienced neurophysiologists, the generalizability of our findings could be limited in other settings, although the internal validity should be strengthened. Second, we did not develop a predictive model for "present N20"; however, as this finding has a poor specificity and sensitivity to prognosticate favourable neurological outcome, this analysis would not be relevant for clinical practice. Third, only a subgroup of patients had available NSE measurements, which limited the number of cases available for the multivariable models. Fourth, EEG could be recorded either continuously or intermittently; it remains difficult to determine whether this might have biased our observations, but recent data argue against a massive impact on outcome using both approachs.[21–23] Fifth, we did not consider brain imaging in this study, as both CT-scan and brain magnetic resonance imaging (MRI) were not part of the standard prognostic approach in the three centers and were considered only in selected cases. However, several studies have shown that brain imaging could contribute to both early and late prediction of UO in CA patients.[24,25] Sixth, we could not really make an hypothesis of the predictive role of non-cardiac origin for $N20_{ABS}$. Finally, as $N20_{ABS}$ was used to limit life-sustaining therapies, we could not specifically assess its intrinsic prognostic value because of some extent of self-fulfilling prophecy

Conclusions

This study showed that non-cardiac etiology of arrest, unreactive EEG to painful stimuli, absence of pupillary reflexes and posturing motor response could predict the bilateral absence of N20. Only 2% of patients with no clinical or EEG findings suggesting UO had $N20_{ABS}$. However, SSEPs provided only additional predictive value to a multimodal approach including clinical signs, EEG findings and NSE.

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Conflict of interests

None to declare.

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