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Multimodal Prediction of Favorable Outcome After Cardiac Arrest: A Cohort Study

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Introduction

- Hypoxic-ischemic brain injury after cardiac arrest (CA) is related to considerable morbidity and mortality
- Existing guidelines focus on prediction of unfavorable outcome
- Leaving many patients in an intermediate prognosis.
- A crucial need to reliably identify patients with good recovery chances, not only to reduce prognostication uncertainty, but also to reassure families and direct resources from caregivers.

Introduction

- Several indicators of good outcome have already been identified:

1. continuous, reactive EEG without epileptiform features
2. absence of diffusion-weighted changes on brain MRI
3. Glasgow Coma Scale (GCS) motor score greater than or equal to 3
4. Normal values of serum neuron-specific enolase (NSE)

- Variables have been mostly described separately.

Introduction

- Favorable outcome is not always efficiently achieved by simply inverting sensitivity and specificity of poor outcome predictors

- Some predictors are continuous or ordinal variables and require a threshold identification

- The aim of this study was to identify and combine predictors of favorable outcome into a multimodal prognostication model

MATERIAL AND METHODS

- Retrospective analysis of prospectively collected data (January 2016 to June 2021)
- Patients dying within 24 hours of admission are not included in the registry.
- Targeted temperature management (TTM) at 36°C for 24 hours with external cooling devices.
- Propofol (2–3 mg/kg/hr) or midazolam (0.1 mg/kg/hr) were given for 24–36 hours;
- fentanyl was administered as needed

MATERIAL AND METHODS

- Patients with myoclonus or EEG seizures were treated with levetiracetam and valproate.
- Patients underwent repetitive routine (20 min) or continuous video-EEGs.
- A first EEG (EEG1) was performed during TTM (12–36 hr)
- A second EEG (EEG2) in normothermic conditions off-sedation (36–72 hr)
- EEGs were interpreted at the same recording day by clinical neurophysiologists

MATERIAL AND METHODS

- The presence of sedative and antiseizure medication during EEG was recorded.

- EEGs were categorized on the recording day into:

1. Highly malignant (suppression or burst-suppression, with or without periodic discharges)
2. Malignant (periodic or rhythmic patterns, abnormal or nonreactive background)
3. benign (absence of all malignant features)

MATERIAL AND METHODS

- Between 60 and 84 hours, when normothermic and off sedation, patients were repetitively examined by certified neurologists:

- Full Outline of UnResponsiveness (FOUR score)
- Presence of early (within 72 hr) myoclonus.
- Somatosensory-evoked potentials (SSEPs) after 24 hours
- Serum NSE at 24 and 48 hr

MATERIAL AND METHODS

- Demographic and clinical parameters were collected

- CA etiology: cardiac versus noncardiac
- Initial cardiac rhythm: shockable versus nonshockable.

- Time to return of spontaneous circulation (ROSC) was estimated upon admission.

- The best neurologic outcome at 3 months was assessed, using Cerebral Performance Categories (CPCs).
- CPC 1–2 was considered as favorable outcome

MATERIAL AND METHODS

External Validation:

- This was performed on a registry of comatose adults treated following CA at the Brigham and Women’s Hospital (BWH), Boston.

- January 2015 to December 2020

Statistics

- ontingency tables were assessed by chi-square or two-sided Fisher exact tests, and normally distributed variables by two-sample Student t tests
- Thresholds identified through receiver operating characteristic (ROC) curve analyses
- STATA software, Version 17

RESULTS

- 499 patients were included
- 191 (38.3%) reached functional independence (CPC 1–2) at 3 months,
- 63 (12.1%) survived with CPC 3
- 3 (0.6%) were in a vegetative state (CPC 4)
- 242 died (48.5%) (CPC 5)

RESULTS

Patients with a favorable outcome:

- shorter time to ROSC,
- more likely to have cardiac etiology
- initial shockable rhythm;
- more often had preserved brainstem reflexes
- FOUR score greater than or equal to 5
- motor GCS greater than or equal to 3
- absence of myoclonus
- presence of SSEPs
- benign EEG features (reactive, continuous, and nonirritative)
- higher quantitative-PLR values and lower NSE

RESULTS

The following variables were most informative (sensitivity ≥ 90%, specificity ≥ 50%):

- Not highly malignant EEG1
- EEG1 background reactivity
- EEG2 background reactivity and continuity
- presence of all brainstem reflexes
- FOUR score greater than or equal to 5
- NSE less than or equal to 41 µg/L.

RESULTS

- Several other items showed a high sensitivity in identifying good outcomes, but with specificities less than 50%:

- Quantitative pupillometry,
- Non-epileptiform EEG 1 and 2,
- Not highly malignant EEG2,
- Absence of myoclonus, and cortical SSEP presence.

RESULTS

- After multivariable logistic regression, six variables:

1. not highly malignant EEG1
2. EEG1 background reactivity
3. EEG2 background reactivity
4. EEG2 background continuity
5. NSE less than or equal to 41 µg/L
6. FOUR score greater than or equal to 5

TABLE 1. - Multimodal Score (Full Outline of UnResponsiveness Score ≥ 5 at 72 hr) to Predict Favorable Outcome in Comatose Patients After Cardiac Arrest

Eponym	Clinical Variable	Score
No	EEG 12–36 hr not "highly malignant"	1 point
2R	EEG 12–36 hr with reactive background	1 point
	EEG 36–72 hr with reactive background	1 point
Co	EEG 36–72 hr with continuous background	1 point
N	Peak neuron-specific enolase within 48 hr ≤ 41 µg/L	1 point
4	Full Outline of UnResponsiveness score within 72 hr ≥ 5/16	1 point

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RESULTS

- There were more favorable outcomes in the subgroup of patients in whom one or more score items were missing, compared with the subgroup of 346 with a full score (46.4% vs 34.7%; $p = 0.013$).

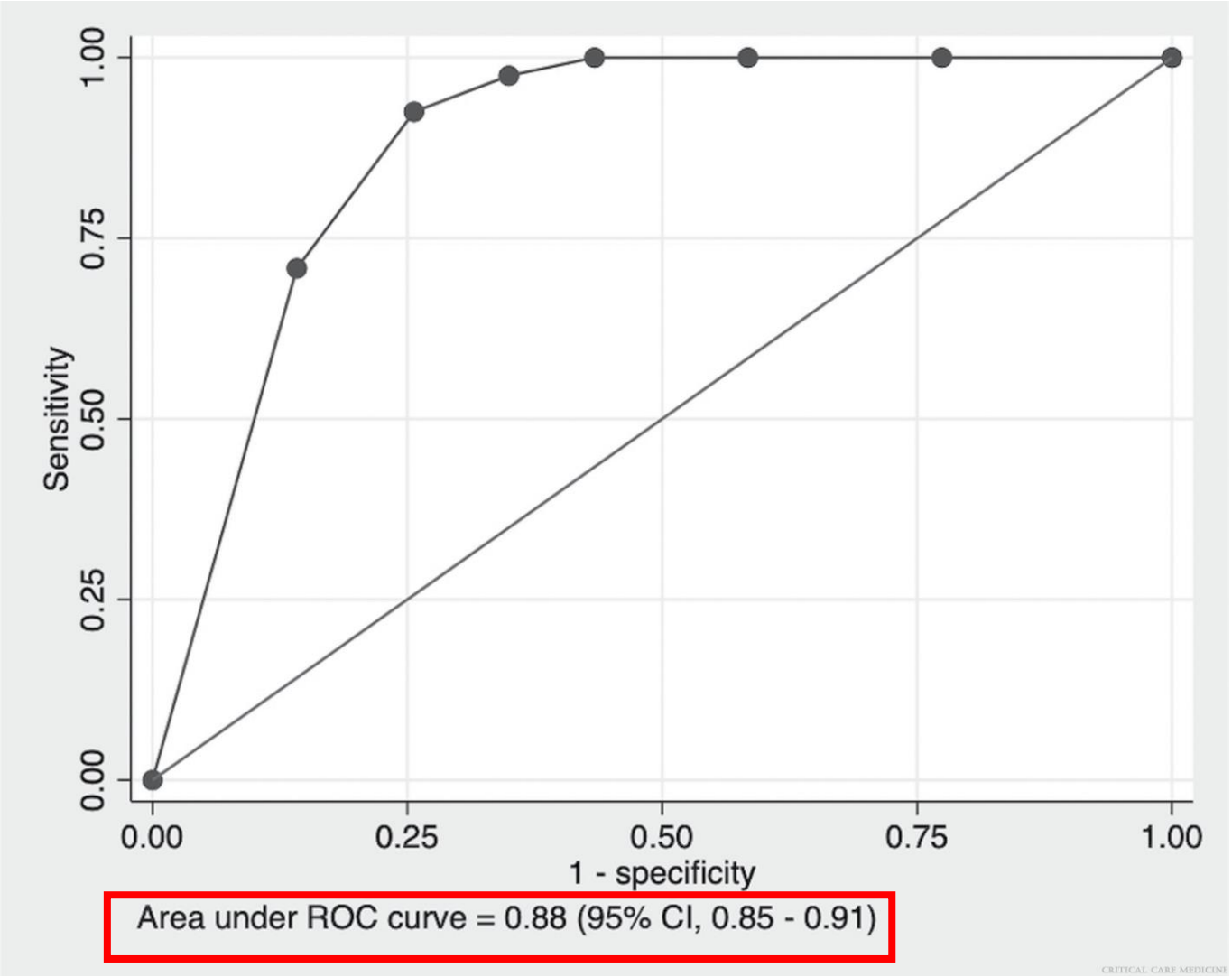
- At cutoff greater than or equal to 4, the score showed a sensitivity of 97.5% (95% CI, 92.9–99.5%) and specificity of 65.0% (95% CI, 58.4–71.3%) for CPC 1–2.
- The LASSO function showed similar results for the seven items (lambda 0.0015, R^2 0.383, Bayes information criterion [BIC], 328.31) and the six items (lambda 0.0115, R^2 0.380, Bayesian information criterion–BIC 326.79) score obtained after omitting brainstem reflexes.

RESULTS

- The area under the curve (AUC) was 0.88 (95% CI, 0.85–0.91)

At the same cutoff:

- for midazolam-only sedated subjects (83 patients) score sensitivity and accuracy were 95.7% (95% CI, 78.1–99.9%), and 73.5% (95% CI, 62.7–82.6%),
- for propofol-only sedation (137 patients) they were 98.0% (95% CI, 89.6–100.0%), and 74.5% (95% CI, 66.3–81.5%)



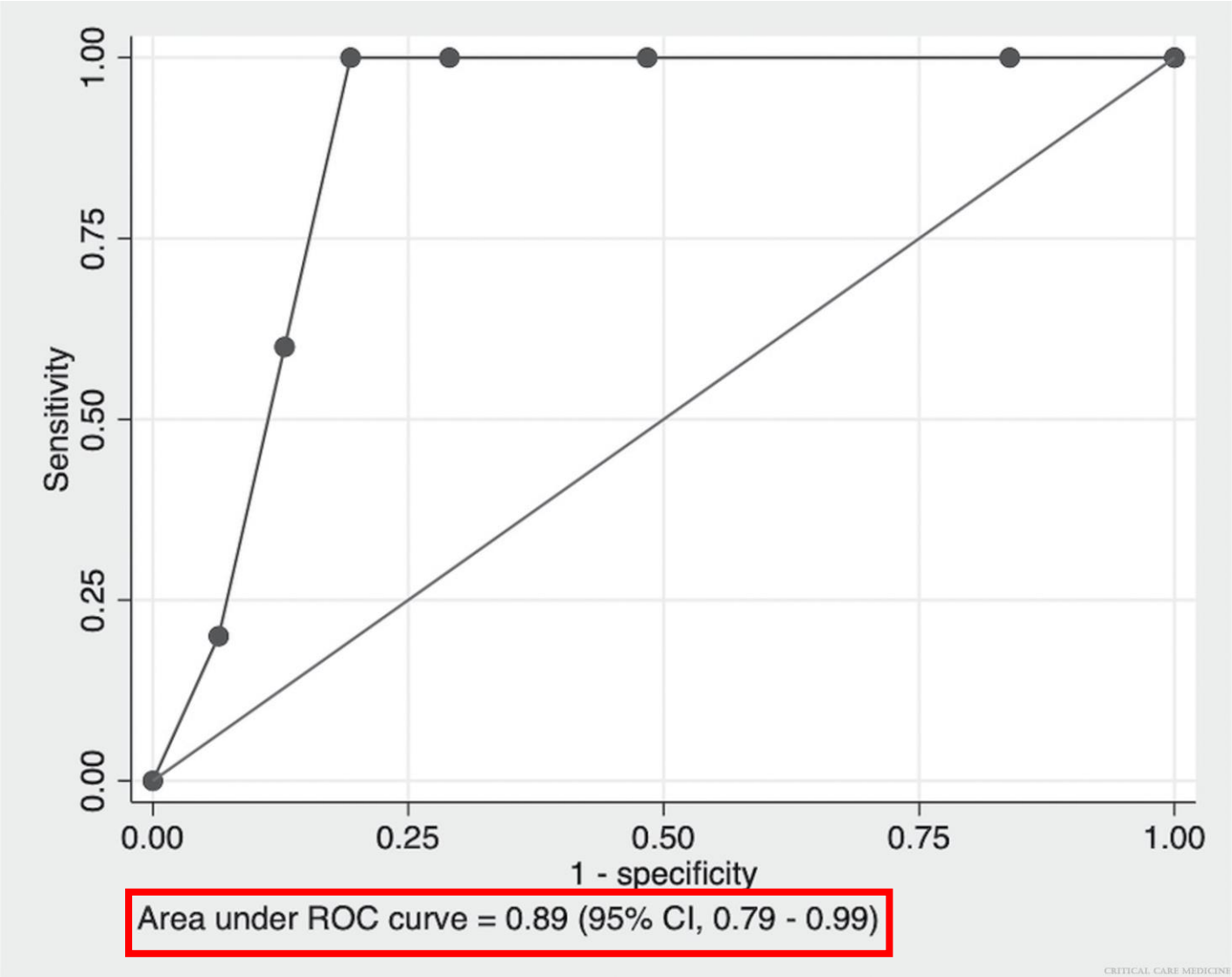
Prognostic performance of the multimodal score in the **Centre Hospitalier Universitaire Vaudois cohort** to predict good neurologic outcome (Cerebral Performance Categories 1–2) at 3 mo, assessed using receiver operating characteristic (ROC) curve analysis.

RESULTS

External Validation:

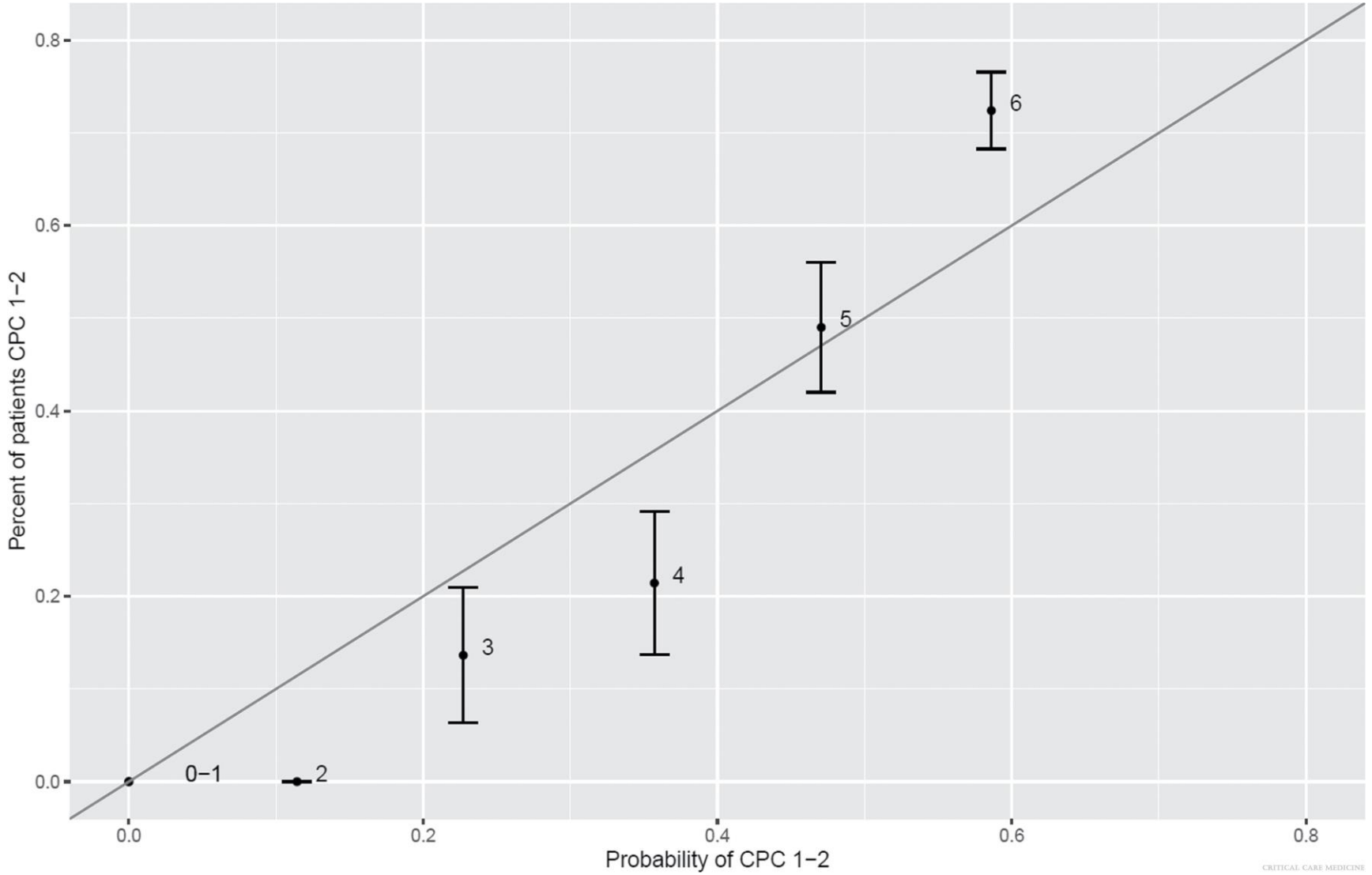
- age distribution (mean 58.5 vs 62.3 yr; p = 0.0944) was similar

- On the ROC curve at a cutoff of greater than or equal to 4, the score showed a sensitivity of 100.0% (95% CI, 47.8–100.0%) and a specificity of 80.7% (95% CI, 62.5–92.6%)



Prognostic performance of the multimodal score in the **Brigham and Women's Hospital cohort** (external validation) to predict good neurologic outcome (Cerebral Performance Categories 1–2) at 3 mo, assessed using receiver operating characteristic (ROC) curve analysis.

Centre Hospitalier Universitaire Vaudois	Good Outcome CPC 1–2		
Score	**Sensitivity (95% CI)**	**Specificity (95% CI)**	**Accuracy (95% CI)**
≥ 1/6	100.00 (96.97–100.00)	22.57 (17.29–28.58)	52.21 (46.80–57.58)
≥ 2/6	100.00 (96.97–100.00)	41.59 (35.09–48.32)	63.95 (58.64–69.02)
≥ 3/6	100.00 (96.97–100.00)	56.64 (49.90–63.19)	73.24 (68.24–77.83)
≥ 4/6	**97.50 (92.87–99.48)**	**65.04 (58.44–71.25)**	**77.47 (72.70–81.76)**
≥ 5/6	92.50 (86.24–96.51)	74.34 (68.12–79.90)	81.29 (76.77–85.26)
6/6	70.83 (61.84–78.77)	85.84 (80.60–90.11)	80.10 (75.49–84.17)
Brigham and Women's Hospital	**Good Outcome CPC 1–2**		
Score	**Sensitivity (95% CI)**	**Specificity (95% CI)**	**Accuracy (95% CI)**
≥ 1/6	100.00 (47.82–100)	16.13 (5.45–33.73)	24.52 (11.77–41.68)
≥ 2/6	100.00 (47.82–100.00)	51.61 (33.06–69.85)	56.45 (38.95–72.85)
≥ 3/6	100.00 (47.82–100.00)	70.97 (51.96–85.78)	73.87 (56.58–87.04)
≥ 4/6	**100.00 (47.82–100.00)**	**80.65 (62.53–92.55)**	**82.58 (66.31–93.14)**
≥ 5/6	60. 00 (14.66–94.73)	87.10 (70.17–96.37)	84.39 (68.43–94.29)
6/6	20.00 (0.51–71.64)	93.55 (78.58–99.21)	86.19 (70.60–95.38)



Performance of the Multimodal Score to Predict Favorable Neurologic Outcome (Cerebral Performance Categories 1–2) at 3 Months (Centre Hospitalier Universitaire Vaudois Cohort [n = 346] and Brigham and Women's Hospital Cohort [n = 36])

Strengths/Limitations
CONCLUSIONS

- Multimodal prognostic score with high performance for good outcome after CA, whose combination (six items, available within 72 hr) identifies patients at different cutoffs reaching good outcome (CPC 1–2) or survival (CPC 1–3) after 3 months, with high sensitivities and accuracies above 70%.
- Internal calibration and external validation showed highly comparable results.
- The main strengths of the present study are the large size of the derivation cohort, strict WLST criteria, and early application to patients still comatose at 72 hours. Furthermore, the prognostic score uses six readily available items
- WLST can bias outcome
- The score is multimodal but strongly relies on EEG (4/6 items). Even though we confirm that EEG is an excellent tool for good outcome forecast


با تشکر از توجه شما