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Clinical paper

Preliminary experience with point-of-care EEG in post-cardiac arrest patients[☆]



Jon C. Rittenberger^{a,*}, Alexandra Weissman^a, Maria Baldwin^b, Kathryn Flickinger^a, Melissa J. Repine^a, Francis X. Guyette^a, Ankur A. Doshi^a, Cameron Dezfulian^c, Clifton W. Callaway^a, Jonathan Elmer^{a,c}, The Pittsburgh Post Cardiac Arrest Service¹

^a Department of Emergency Medicine, University of Pittsburgh, United States

^b Department of Neurology, University of Pittsburgh, United States

^c Department of Critical Care Medicine, University of Pittsburgh, United States

Abstract

Objective: Abnormal electroencephalography (EEG) patterns are common after resuscitation from cardiac arrest and have clinical and prognostic importance. Bedside continuous EEGs are not available in many institutions. We tested the feasibility of using a point-of-care system for EEG acquisition.

Methods: We prospectively enrolled a convenience sample of post-cardiac arrest patients between 9/2015–1/2017. Upon hospital arrival, a limited EEG montage was applied. We tested both continuous EEG (cEEG) and this point-of-care EEG (eEEG). A board-certified epileptologist and a board-certified neurointensivist jointly reviewed all EEGs. Cohen's kappa coefficient evaluated agreement between eEEG and cEEG and Fisher's exact test evaluated their associations with survival to hospital discharge and proximate cause of death.

Results: We studied 95 comatose post-cardiac arrest patients. Mean age was 59 (SD17) years. Most (61%) were male, few (N=22; 23%) demonstrated shockable rhythms, and PCAC IV illness severity was present in 58 (61%). eEEG was interpretable in 57 (60%) subjects. The most common eEEG interpretations were: continuous (21%), generalized suppression (14%), burst-suppression (12%) and burst-suppression with identical bursts (10%). Seizures were detected in 2 eEEG subjects (2%). No patient with seizure or burst-suppression with identical bursts survived. cEEG demonstrated generalized suppression (31%), burst-suppression with identical bursts (27%), continuous (18%) and seizure (4%). The eEEG and cEEG demonstrated fair agreement (kappa=0.27). Neither eEEG nor cEEG was associated with survival ($p=0.19$; $p=0.11$) or proximate cause of death ($p=0.14$; $p=0.8$)

Conclusions: eEEG is feasible, although artifact often precludes interpretation. eEEG is fairly associated with cEEG and may facilitate post-cardiac arrest care.

Keywords: Resuscitation, Cardiac arrest, EEG, Prognostication, Outcomes

Introduction

After resuscitation from cardiac arrest, most patients are comatose.¹ Similar to other comatose patient populations, abnormal

electroencephalography (EEG) patterns, including non-convulsive status epilepticus, are common.^{2–4}

Although data evaluating the efficacy of rapid administration of anti-epileptic medications are limited in the post-arrest population, time to initiation of anti-epileptic medication is considered a powerful

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* Corresponding author at: 3600 Forbes Avenue, Suite 400A Pittsburgh, PA 15213, USA.

E-mail address: rittjc@upmc.edu (J.C. Rittenberger).

¹ For Pittsburgh Post Cardiac Arrest Service investigators see Appendix A.

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predictor of whether seizure control is ultimately successful in the general critical care population.³ Moreover, other EEG patterns on the ictal-interictal spectrum may contribute to secondary brain injury and are often treated with anti-epileptic medications.²

EEG findings also have prognostic significance after cardiac arrest. Several epileptiform patterns and seizures are associated with poor neurologic outcome, while reactivity and the presence of a continuous background suggest the potential for good neurological recovery.^{5–7} Developing a rapidly deployable system would enable rapid delivery of time-sensitive interventions such as appropriate anti-epileptic treatment. It would also refine initial estimations of patient illness severity, which could help decisions about inter-facility transfers and involvement of subspecialty services.

Continuous EEG (cEEG) monitoring can identify these patterns, but is resource-intensive and not immediately available in most hospitals.⁸ Systems that use fewer EEG leads, such as amplitude-integrated EEG, require fewer resources but amplitude-integrated EEG does not permit evaluation of the raw EEG recording.⁹ A system using a few EEG leads while permitting evaluation of the raw EEG signal could expand its application. Thus, we tested the application of an early point-of-care EEG (eEEG) system on post-cardiac arrest patients.

Methods

The University of Pittsburgh Human Research Protection Office (formerly IRB) approved this study with a waiver of informed consent. We enrolled a convenience sample of comatose post-arrest patients from September 2015 to January 2017.

Patients were recruited from a tertiary care cardiac arrest facility with a volume of 328 cardiac arrest patients in 2017. This facility has a dedicated post-cardiac arrest service directing the care provided to this patient population from the prehospital, emergency department, intensive care unit, floor and rehabilitation units. This facility has 24/

7 cardiac catheterization, emergency electroencephalography along with neurophysiology monitoring.

We included post-cardiac arrest patients who presented to or were transferred to our facility. The majority are referred from outlying hospitals for post-cardiac arrest care and the minority are transported directly from the field. Patients were evaluated as soon as possible after arrival in the emergency department. In the case of inter-facility transport with admission directly to the intensive care unit (ICU), patients were evaluated as soon as possible after ICU arrival.

We applied 6 disposable adhesive disc electrodes (Cadwell Ambulatory Monitor, Kennewick, WA) in the following 10–20 electrode positions: Fp1, F7, Fp2, F8, A1 and A2 [Supplemental Figure]. These locations were selected as they are largely on the frontal scalp and thus readily accessible in the comatose, intubated patient. We selected these electrodes rather than a cup electrode to facilitate ease of placement by providers without any special training. The local skin was scrubbed using an alcohol pad, the lead was placed by one of the authors who also confirmed the presence of an initial biologic waveform prior to placing the device in ambulatory mode (no waveform available for direct clinician interpretation). We taped the electrodes in position to minimize the potential for movement during recording. We continued eEEG recording until cEEG monitoring was initiated in the ICU. The eEEG leads were removed when the cEEG was applied. These cEEG recordings used a full 22 gold cup electrodes montage in the standard 10–20 system of electrode placement. For clinical purposes, the results of the cEEG recording were interpreted by an epileptologist and available to the treating team for clinical care. The eEEG results were not used clinically. For this study, both eEEG and the first 30 min of cEEG were jointly reviewed by a board certified epileptologist and a board certified neurointensivist, who resolved all discrepancies by consensus. This was classified as the research interpretation. The research interpretation, rather than the clinical interpretation, of both the eEEG and cEEG was used for all analyses.

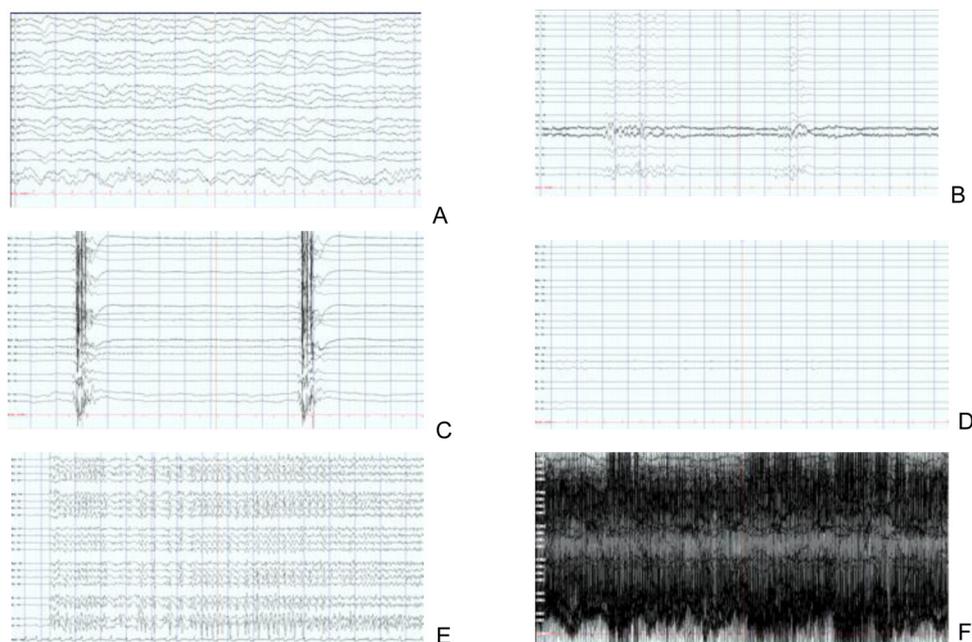


Fig. 1 – Examples of EEG patterns. (A) Continuous; (B) burst suppression; (C) burst suppression with identical bursts; (D) suppressed; (E) status epilepticus; (F) uninterpretable.

We recorded baseline demographic information, including initial illness severity as measured by the Pittsburgh Cardiac Arrest Category (PCAC). PCAC is a validated scale that predicts survival and neurologic outcome.¹ We classified proximate cause of death as unstable (re-arrest or death due to multisystem organ failure or intractable shock), brain death, withdrawal of life-sustaining therapy for perceived poor neurologic prognosis, or withdrawal of life-sustaining therapy because of other medical considerations (e.g. pre-arrest medical comorbidities such as dementia or preexisting advanced directives).^{1,10}

We reviewed both eEEG and cEEG for prognostically important features and classified them as: continuous background without epileptiform activity; burst-suppression; burst suppression with identical bursts; suppressed; status epilepticus; or uninterpretable.^{2,5} (Fig. 1) We separated burst-suppression from a burst-suppression with identical bursts as the latter is more firmly associated with poor outcome.^{5,7} This classification system has been used by our group previously and is associated with outcome.^{2,5}

We used descriptive statistics to summarize population characteristics and outcomes, and present means with standard deviation and raw numbers with corresponding percentages. We used Cohen's kappa coefficient to compare eEEG and cEEG interpretations. Fisher's exact test was used to test associations between cEEG and eEEG interpretation of outcome along with associations with proximate cause of death. We used Stata v.14.1 (College Station, TX) for analysis of data.

Results

Five of the 100 patients rapidly awoke and did not have either eEEG or cEEG testing completed. Mean age was 59 (SD 17) years and the majority (N=57; 61%) were male. Few patients (N=22; 23%) experienced a shockable rhythm. The majority of patients experienced cardiac arrest in the out-of-hospital setting (N=89; 95%). PCAC IV illness severity was most common (N=58; 61%). Withdrawal due to poor neurologic prognosis was the most common cause of death (N=21; 48%) (Table 1).

Table 1 – Demographic characteristics of the study population (N = 95).

Age, years (SD)	59 (17)
Male	57 (61%)
Out of hospital cardiac arrest	89 (95%)
Rhythm	
VF/VT	22 (23%)
PEA	29 (31%)
Asystole	29 (31%)
Unknown	14 (15%)
Pittsburgh Cardiac Arrest Category	
II	21 (22%)
III	8 (8%)
IV	58 (61%)
Unknown	8 (8%)
Survival	20 (22%)
Good Outcome	10 (11%)
Etiology of death	
Unstable	12 (28%)
Brain death	8 (19%)
Withdrawal due to poor neurologic prognosis	20 (46%)
Withdrawal due to other comorbidities	3 (7%)

Because of signal artifact from electrical interference, we could not obtain EEG interpretations on 38 (40%) eEEG studies and 9 (13%) cEEG studies. The most common interpretations for the eEEG studies were continuous (21%) or generalized suppression in 12 (14%). A burst-suppression pattern was found in 11 (12%) while a burst-suppression with identical bursts was found in 10 (10%). Seizures were detected in two eEEG subjects (2%). Mean time from arrival to start of eEEG monitoring was 96 (SD 85) min. Mean duration of eEEG monitoring was 354 (SD 250) min. Agreement between interpretable eEEG and cEEG patterns was fair (kappa 0.27) (Table 2). There was no association between interpretable eEEG patterns and survival to hospital discharge ($p = 0.19$). Interpretable eEEG was not associated with proximate cause of death ($p = 0.14$). Of the patients found in burst-suppression with identical bursts on eEEG, none survived.

Of the 67 subjects who received cEEG, 58 (87%) were interpretable. The most common patterns were generalized suppression (N=21; 31%) followed by burst-suppression with identical bursts (N=18; 27%), continuous (N=12; 18%) and seizure (N=3; 4%). Interpretable cEEG recordings were neither associated with survival nor etiology of death ($p = 0.11$ and $p = 0.8$).

Discussion

We describe our preliminary experience with point-of-care EEG. Among eEEG included in the analysis, the initial pattern was associated with later cEEG pattern, but not associated with survival or proximate cause of death. If validated in future studies, these data suggest that eEEG could aid in the care of post arrest patient.

Guidelines recommend either continuous or intermittent EEG monitoring for the comatose post-arrest patient.⁸ However, the optimal duration and timing of this monitoring is not known. Early trajectories of EEG evolution are associated with outcome.^{11–13} Determining trajectories over time requires continuous or frequent intermittent monitoring. A portable eEEG monitor deployed to sites that do not have 24-h EEG monitoring capabilities could guide clinicians regarding which patient requires transfer for cEEG monitoring. Using telemedicine, an expert reviewer could comment on the presence of reactivity, background rhythm and malignant patterns. This has been employed in acute stroke care, dermatology and certain neurophysiology studies, which include electroencephalography. Importantly, no patient with an eEEG finding of burst-suppression with identical bursts survived to discharge. This pattern demonstrated a high correlation with subsequent cEEG, likely because the characteristic high-amplitude polyspike bursts could be detected despite concomitant electrical artifact. Importantly, this is a pattern that has been previously described in the literature as incompatible with neurological recovery.^{5,7} A test of proportions on the cohort with burst-suppression with identical bursts to determine the statistical potential of survival yields a 95% CI of 0.15–0.34. Larger, prospective cohorts are needed to confirm these findings. If validated, such information may allow providers to stratify a non-viable cohort early after resuscitation and may prevent futile referral to dedicated post cardiac arrest centers.

Beyond the post-arrest population, prior literature has also demonstrated that a significant proportion of ICU patients experience EEG abnormalities, including status epilepticus.^{3,4} Response to antiepileptic medications in the setting of status epilepticus decreases over time, thus rapid diagnosis and treatment is required.⁴ These data are from the general ICU population and may not apply to the post-cardiac arrest patient. We eagerly await the results of the TELSTAR trial which has been designed to rigorously evaluate the efficacy of

Table 2 – Association between eEEG and subsequent cEEG.

cEEG	eEEG					
	Continuous	Suppressed	Burst suppression	Burst suppression-identical	Uninterpretable	Seizure
Continuous	5	1	2	0	4	0
Suppressed	3	8	3	0	7	0
Burst suppression	2	0	1	1	0	0
Burst suppression-identical	3	1	2	3	8	1
Uninterpretable	0	2	2	1	4	0
Seizure	1	0	1	1	0	0

anti-epileptic medication administration to the post-cardiac arrest population.¹⁴ Deploying point-of-care EEG in the emergency department may allow for rapid treatment and referral of these patients as well. Even after apparently successful treatment of convulsive status epilepticus, non-convulsive status epilepticus remains in up to half of patients.¹⁵ Deployable eEEG monitors could permit rapid diagnosis and treatment in both the emergency department and ICU settings.

Our study has several limitations. First, a number of eEEG studies were not interpretable because of artifact, yielding a smaller than anticipated sample size. Confounders include movement related to placement of central venous and arterial lines, transport to and from radiographic imaging, and transport to the ICU or cardiac catheterization suite. The study design focused on rapid deployment, resulting in limited skin preparation. The cEEG preparation requires skin preparation, placement of gold-plated cups with collodion gel adhesive along with detailed analysis of each channel signal before initiation of recording. Rapid techniques to minimize electrical interference and maintain good electrode contact are needed. Second, clinicians did not have access to the eEEG data in real-time. Thus, the presence of malignant EEG patterns was unknown until the clinical cEEG was placed. Third, the number of patients demonstrating each individual eEEG pattern is small. This is one potential reason for a lack of association between EEG pattern and outcome. Finally, our data represent a single center's with a dedicated post-cardiac arrest service's experience. The volume and outcomes reported at this facility differ from other local institutions and may not be generalizable.¹⁰

Conclusions

Point-of-care eEEG is presently limited by electrical interference in many patients. eEEG patterns are fairly associated with cEEG interpretation. Reliable identification of specific patterns such as status epilepticus or burst suppression with identical bursts might assist patient triage and disposition.

Conflicts of interest

The authors declare they have no conflicts of interest.

Author contributions

JCR, MB, CWC, and JE conceived the study and designed the trial. JCR obtained research funding. JCR, AW, KF, MR, FXG, AAD, CD, CWC, and JE undertook recruitment of subjects and directed the conduct of the trial. JCR, CWC, and JE conducted the statistical analyses. JCR drafted the manuscript and all authors contributed substantially to its revision. JCR takes responsibility for the paper as a whole.

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Appendix A

The Pittsburgh Post Cardiac Arrest Service investigators are:

Clifton W. Callaway, MD, PhD
Cameron Dezfulian, MD
Ankur A. Doshi, MD
Jonathan Elmer, MD, MS
Francis X. Guyette, MD, MS
Masashi Okubo, MD, MS
Jon C. Rittenberger, MD, MS
Alexandra Weissman, MD, MS

Appendix B. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.resuscitation.2018.12.022>.

REFERENCES

- Rittenberger JC, Holm MB, Guyette FX, Tisherman SA, Callaway CW. An early, novel illness severity score to predict outcome after cardiac arrest. *Resuscitation* 2011;82:1399–404.
- Rittenberger JC, Popescu A, Guyette FX, Callaway CW. Frequency and timing of nonconvulsive status epilepticus in comatose post-cardiac arrest subjects treated with hypothermia. *Neurocrit Care* 2012;16:114–22.
- Claassen J, Goldstein JN. Emergency neurological life support: status epilepticus. *Neurocrit Care* 2017;27:152–8.
- Young GB, Jordan KG, Doig GS. Assessment of nonconvulsive seizures in the intensive care unit using continuous EEG monitoring: and investigation of variables associated with mortality. *Neurology* 1996;47:83–9.
- Elmer J, Rittenberger JC, Faro J, Molyneaux B, Popescu A, Callaway CW. Clinically distinct electroencephalographic phenotypes of early myoclonus after cardiac arrest. *Ann Neurol* 2016;80:175–84.
- Admiraal MM, Van Rootselaar A-F, Horn J. Electroencephalographic reactivity testing in unconscious patients: a systematic review of methods and definitions. *Eur J Neurol* 2017;24:245–54.
- Hofmeijer J, Tjepkema-Cloostermans MC, van Putten MJAM. Burst-suppression with identical bursts: a distinct EEG pattern with poor outcome in postanoxic coma. *Clin Neurophysiol* 2014;125:947–54.

8. Soar J, Callaway CW, Aibiki M, et al. Part 4: advanced life support 2015 international consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations. *Resuscitation* 2015;95:e71–120.
9. Oh SH, Park KN, Shon YM, et al. Continuous amplitude-integrated electroencephalographic monitoring is a useful prognostic tool for hypothermia-treated cardiac arrest patients. *Circulation* 2015;132:1094–103.
10. Elmer JE, Rittenberger JC, Coppler PA, Guyette FX, Doshi AA, Callaway CW. Long-term survival benefit from treatment at a specialty center after cardiac arrest. *Resuscitation* 2016;108:48–53.
11. Elmer J, Gianakas JJ, Rittenberger JC, et al. Group-based trajectory modeling of suppression ratio after cardiac arrest. *Neurocrit Care* 2016;25:415–23.
12. Cloostermans MC, van Meulen FB, Eertman CJ, Horn HW, van Putten MJAM. Continuous electroencephalography monitoring for early prediction of neurological outcome in postanoxic patients after cardiac arrest: a prospective cohort study. *Crit Care Med* 2012;40:2867–75.
13. Hofmeijer J, Beernink TM, Bosch FH, et al. Early EEG contributes to multimodal outcome prediction of postanoxic coma. *Neurology* 2015;85:137–43.
14. Ruijter BJ, van Putten MJ, Horn J, et al. Treatment of electroencephalographic status epilepticus after cardiopulmonary resuscitation (TELSTAR): study protocol for a randomized controlled trial. *Trials* 2014;548:433.
15. DeLorenzo RJ, Waterhouse EJ, Towne AR, et al. Persistent nonconvulsive status epilepticus after the control of convulsive status epilepticus. *Epilepsia* 1998;39:833–40.