Prognostic value of electroencephalography pattern in prediction of survival and early myoclonus after cardiac arrest

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Received 19 January 2020
Revised 16 February 2020
Accepted 01 March 2020
Published 10 August 2020

Journal of Current Medical Research and Practice
2020, 5:316–321

Background
Evolution of the electroencephalography (EEG) background pattern is a robust contributor to the prediction of poor or good outcome of comatose patients after cardiac arrest (CA).

Aim
The aim of the study was to use EEG as a prognostic tool for the prediction of survival after CA and the incidence of early postanoxic myoclonus.

Patients and methods
We enrolled 40 patients, post-CA. A 30-min EEG was performed on all patients, as soon as possible after the patients had arrived in the ICU using a portable EEG.

Results
Out of the 40 patients studied, 29 (72.5%) were alive while 11 (27.5%) patients were dead: Regarding patterns of EEG, 86.2% of alive patients had a benign pattern, while 63.6% of dead patients had a highly malignant pattern. Regarding the cerebral performance category (CPC), 79.3% of alive patients had cerebral performance grade 1 (CPC 1) while 54.5% of dead patients had CPC 4. Frequency of seizures after resuscitation was significantly higher in dead patients (45.5%) versus 17.2% in alive patients ($P = 0.03$).

Conclusion
Benign EEG patterns and CPC 1 and CPC 2 were correlated to good outcome in patients post-CA in comparison to malignant EEG pattern and CPC 3 and CPC 4, respectively. Presence of early posthypoxic myoclonus had been invariably related to poor outcome.

Keywords:
cardiac arrest, electroencephalography, hypoxic ischemic injury, myoclonus

J Curr Med Res Pract 5:316–321

2357-0121

Introduction

Cardiac arrest (CA) is a clinical emergency. If it is treated immediately, survival is possible. Administering cardiopulmonary resuscitation, treating with a defibrillator, or even just compressions to the chest until the emergency personnel arrive are important [1].

Anoxic brain damage after CA is one of the most common causes of coma worldwide, of all comatose patients after CA surviving hospital admission, 40–66% never regained consciousness as a result of severe postanoxic encephalopathy, with current conventional measures only 10–20% of patients with a poor outcome can be detected reliably [2].

The survivors of the CA may additionally expand neurological complications, including posthypoxic myoclonus (PHM) or Lance–Adams syndrome [3]. Clinical significance of early PHM may indicate devastating irreversible brain damage [4].

Electroencephalography (EEG) is sensitive to the detection of hypoxia-induced cerebral damage. In the context of prognostication, EEG is very informative because several EEG features correlate with the degree of neuronal injury [5,6].

Aim

The aim was to use EEG as a prognostic tool for prediction of survival after CA and the occurrence of early postanoxic myoclonus.

Patients and methods

Forty post-CA patients were included and met the following inclusion criteria: all patients were adults with IHCA of presumed cardiac origin admitted to the Cardiology Department of Assiut University Hospital from October 1, 2016 to May 31, 2017.

Any patient, who met the criteria mentioned below was excluded from the start: (a) patients with out of hospital CA, (b) patients with CA of noncardiac origin; as the presence of severe neurological injury or presence of severe extraneurological pathology (hepatic or renal impairment).

Each patient will be subjected to the following:
(1) Full history and neurological examination (including corneal and pupillary reflexes, any myoclonus, and motor reaction).
(2) Postarrest EEG trace for 30 min.
(3) Functional outcome at 6 months according to a semistructured phone interview using cerebral performance categories (CPC: 1–2 good, 3–5: poor) [7].

Electroencephalography recordings

Standard 30-min EEG recordings were initiated as soon as possible after the patients arrived in the ICU using a portable digital machine (Nihon Kohden EEG-1200; Nihon, Tokyo, Japan); electrodes were placed according to the International 10–20 System. EEG recording is done by two specialized paramedical and an EEG technician.

Electroencephalography interpretation

All EEGs were analyzed, interpreted, and reported by two EEG experts (neurology staff members at Assiut University Hospital) in two separate sessions.

Electroencephalography classification

All EEGs had been classified according to the American Clinical Neurophysiology Society [3,8,9]:
(1) Highly malignant: suppressed background with or without continuous periodic discharges; burst suppression.
(2) Malignant: abundant periodic discharges, or rhythmic epileptiform transients, electrographic seizure, discontinuous or low-voltage background, reversed anterior–posterior gradient, unreactive EEG to stimuli.
(3) Benign EEG (absence of all malignant features stated above).

Ethical aspects

The study was approved by the ethics committee in the Faculty of Medicine, Assiut University (Approval Number 17100925). Patient's relatives were informed about the nature and steps of the study and consent was obtained from each patient's relative.

Statistical analysis

Data were collected and analyzed using Statistical Package for the Social Sciences (version 20; IBM, Armonk, New York, USA). Continuous data were expressed in the form of mean ± SD or median (range), while nominal data were expressed in the form of frequency (percentage).

χ^2 test was used to compare the nominal data of different groups in the study while Student's *t* test was used to compare the mean of two different groups. Predictors of poor outcome in post-CA patients were determined by multivariate regression analysis while diagnostic performance of EEG was assessed by receiver operating characteristic curve analysis.

The level of confidence was kept at 95%; hence, a *P* value less than 0.05 indicated a significant association.

Results

Forty patients were included in our study. Table 1 shows the demographic data of all patients including the comorbidities (heart diseases, diabetes mellitus, others).

Outcome of the study

Out of the 40 patients studied, 29 (72.5%) patients were alive while 11 (27.5%) patients were dead. Tables 2 and 3 show the characteristics of the studied patients based on the outcome.

It was noticed that the following variables were predictors of a poor outcome in the studied patients

The pattern of EEG had 86.3% sensitivity and 100% specificity in the prediction of poor outcome in post-CA patients with an area under curve of 0.94 and *P* value less than 0.001 (Table 4 and Fig. 1).

Of those without post-CA seizures, 66.7% had CPC 1 while only 30% of those with seizures had CPC 1. It was noticed that both groups of patients (patients with and without seizures) had insignificant differences as regards CPC and pattern of EEG as shown in Table 5.

Table 1 Demographic data of the studied patients

Variables	*n*=40
Age (years) (mean±SD)	49.60±13.77
Range (years)	20-80
Sex	
Male	25 (62.5)
Female	15 (37.5)
Comorbidities	
Ischemic/rheumatic heart diseases	33 (82.5)
Diabetes mellitus	17 (42.5)
Hypertension	16 (40)
Neurological diseases	1 (2.5)

Data were expressed in the form of mean±SD and *n* (%).

Table 2 Characteristics of the studied patients based on the outcome

Variables	Dead (*n*=11)	Alive (*n*=29)	*P*
Age (years)	47.64±17.32	50.34±12.45	0.58
Sex			**0.04**
Female	7 (63.6)	8 (27.6)	
Male	4 (36.4)	21 (72.4)	
Comorbidities			
Ischemic heart disease	6 (54.5)	27 (93.1)	**0.01**
Hypertension	3 (27.3)	14 (48.3)	0.20
Diabetes mellitus	3 (27.3)	13 (44.8)	0.44
Neurological disease	1 (9.1)	0	0.27
Seizure before cardiac arrest	1 (9.1)	2 (6.9)	0.63
Seizures after resuscitation	5 (45.5)	5 (17.2)	**0.03**
Shockable 1st rhythm	2 (18.2)	24 (82.8)	**<0.001**
Time to return to spontaneous circulation	22±5.72	5.95±2.5	**<0.001**
Glasgow coma scale at the time of EEG	4.7±2.64	12.6±2.16	**<0.001**
Pattern of EEG			**<0.001**
Benign	0	25 (86.2)	
Malignant	4 (36.4)	4 (13.8)	
Highly malignant	7 (63.6)	0	
Cerebral performance scale			**<0.001**
1	0	23 (79.3)	
2	0	3 (10.3)	
3	2 (18.2)	3 (10.3)	
4	6 (54.5)	0	
5	3 (27.3)	0	

Data were expressed in the form of mean±SD) and *n* (%). EEG, electroencephalography. *P* value was significant if less than 0.05. Bold values represent significant *P* value (significant if less than 0.05)

Table 3 Multivariate regression analysis for the prediction of poor outcome

Variables	Odds ratio	95% CI	*P*
Female sex	3.20	1.45-4.90	0.22
IHD	1.52	0.99-1.76	0.39
GCS (≤3)	**7.79**	**3.98-11.1**	**0.01**
Time to spontaneous circulation	4.60	2.58-3.78	0.23
Shockable 1st rhythm	1.45	1.56-3.98	0.85
Pattern of EEG	**24.74**	**19.34-69.1**	**0.03**
CPC	**18.44**	**14.3-36.9**	**0.04**

CI, confidence interval; CPC, cerebral performance grades; EEG, electroencephalography; GCS, Glasgow coma scale; IHD, ischemic heart disease. *P* value was significant if less than 0.05. Bold values GCS is significant in prediction poor outcome according to odds ratio and *P* value

Table 4 Diagnostic performance of electroencephalography in the prediction of poor outcome

Indices	Pattern of electroencephalography (%)
Sensitivity	86.3
Specificity	100
Positive predictive value	100
Negative predictive value	73.3
Area under the curve	0.94
P	<0.001

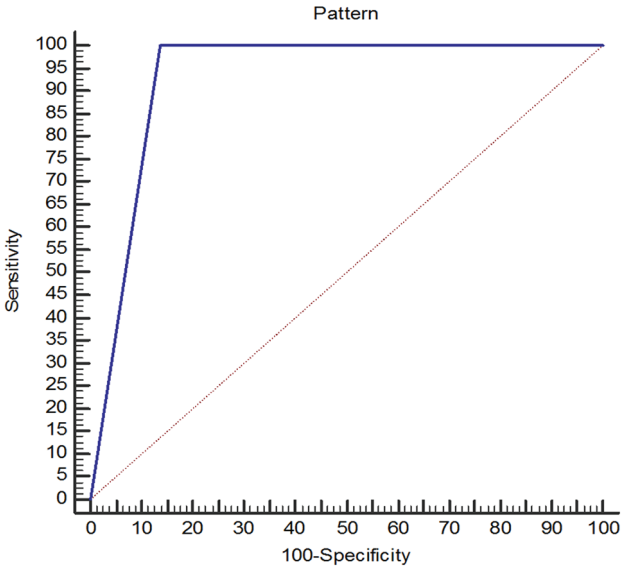
P value was significant if less than 0.05.

Table 5 Cerebral performance category grades and pattern of electroencephalography based on postcardiac arrest seizures

	Postarrest seizures (*n*=10)	No postarrest seizures (*n*=30)	*P*
Pattern of EEG			0.23
Benign	4 (40)	21 (70)	
Malignant	3 (30)	5 (16.7)	
Highly malignant	3 (30)	4 (13.3)	
CPC			0.33
1	3 (30)	20 (66.7)	
2	1 (10)	2 (6.7)	
3	2 (20)	3 (10)	
4	3 (30)	3 (10)	
5	1 (10)	2 (6.7)	

CPC, cerebral performance grades; EEG, electroencephalography. *P* value was significant if less than 0.05.

Figure 1



Diagnostic performance of EEG in the prediction of poor outcome. EEG, electroencephalography.

Discussion

The current study revealed that the mean age was 49.60 ± 13.77 years (range, 20–80 years) and male-to-female ratio was 25: 15 (62.5%: 37.5%). These findings are in agreement with those of Spalletti *et al*. [10], who studied the single EEG as a predictor of outcome after CA among 211 patients and reported that the mean age was 57.1 ± 18.8 years (16–90 years) and male-to-female ratio was 133: 78 (63.0%: 37.0%). While these findings are not consistent with Beuchat *et al*. [11] who studied standardized EEG interpretation in patients after CA among 202 patients and reported that the mean of age was 64.99 ± 14.5 and male-to-female ratio was 143: 59 (70.9%: 29.1%). The age range in this study is mostly attributed to rheumatic heart diseases which are more common in our locality and affect the younger age groups.

This study reported that 25 (62.5%) patients had benign EEG pattern, eight (20%) patients had malignant EEG pattern, and seven (17.5%) patients had highly malignant pattern (n = 40). The pattern of EEG in multivariate regression analysis concluded that malignant pattern of EEG was correlated to poor prognosis [odds ratio = 24.74, 95% confidence interval (CI)=19.34; P = 0.03]. The pattern of EEG in those who lived (n = 29) was benign [25 (86.2%) patients] or malignant [four (13.8%) patients], while in the dead patients (n = 11) it was malignant [four (36.4%) patients] or highly malignant [seven (63.6%) patients]. When the pattern of EEG is used as a predictor of outcome, it shows a sensitivity of 86.3%, specificity of 100% (95% CI = 19.34–69.1), and positive predictive value of 100%.

These findings are consistent with Rossetti *et al.* [8] who studied EEG as a predictor of poor and good outcomes after CA among 97 patients at Mayo Clinic and reported that benign EEG was found in 54 (55.7%) patients and malignant EEG in 19 (19.6%) patients (n = 97). The benign EEG record showed a sensitivity of 76.1%, positive predictive value of 86.2%, and 95% CI = 69.2.

The findings of the current study are consistent with Scarpino *et al.* [12], who studied neurophysiological and neuroradiological multimodal approach for early poor outcome prediction after CA among 183 patients and reported that benign EEG was found in 130 (71%) patients (70 patients with poor prognosis and 60 patients with good prognosis), while malignant EEG was found in 53 (28.9%) patients, all with poor prognosis (n = 183).

While these findings are not consistent with that of Beuchat *et al.* [11] who found that 63 (31.1%) patients had benign EEG pattern, and 127 (62.8%) patients (n = 202) had nonbenign EEG pattern (malignant and highly malignant). Discrepancies across studies may be accounted for by patient heterogeneity, timing of EEG, and different EEG criteria.

These findings are not consistent with Westhall *et al.* [13], who found that 14 (14%) patients had benign EEG record, while 89 (86%) patients had nonbenign EEG record (n = 103). This is mostly accounted for by patient heterogeneity, timing of EEG, and different EEG criteria.

The current study found that 23 (57.5%) patients had CPC 1, three (7.5%) patients had CPC 2, five (12.5%) patients had CPC 3, six (15%) patients had CPC 4, and three (7.5%) patients had CPC 5 (n = 40).

In this study, cerebral performance grading scales 1 and 2 [26 (65%) patients] predict good outcome, while cerebral performance 4 and 5 [nine (22.5%) patients] predict poor outcome (odds ratio = 18.44, 95% CI = 14.3–36.9; P = 0.04), CPC 3 is heterogeneous; depending on the time of assessment and the possible improvement of the patient, it may be related to a favorable outcome. The alive patients (n = 29) in the current study had either CPC 1 [23 (79.3%) patients], CPC 2 [three (10.3%) patients], or CPC 3 [three (10.3%) patients], while the dead patients (n = 11) had either CPC 3 [two (18.2%) patients], CPC 4 [six (54.5%) patients], or CPC 5 [three (27.3%) patients].

These findings are consistent with Hsu *et al.* [14], who studied CPC at hospital discharge predicting long-term survival after CA among 582 patients, who successfully resuscitated and reported that CPC 1 and CPC 2: 70%. Hsu *et al.* [14] found a significant correlation between good CPC scores and survival (good outcome) at 6 months and at 1-year follow-up as 95% CI of the patients with CPC 1 = 0.933, CPC 2 = 0.763, CPC 3 = 0.577, and CPC 4 = 0.438. The hazard ratio was more conclusive, as worse CPC scores had a larger hazard ratio than good CPC scores (P < 0.001): hazard ratio in CPC 1 = 1, CPC 2 = 3.24, CPC 3 = 5.12, and CPC 4 = 18.56.

Scarpino *et al.* [12] studied the CPC at 6-month follow-up post-CA among 183 patients and found CPC 1 in five (2.7%) patients, CPC 2 in 12 (6.5%) patients, CPC 3 in 33 (18%) patients, CPC 4 in 72 (39.3%) patients, and CPC 5 in 61 (33.2%) patients (n = 183). These findings were not consistent with the findings of the current study.

This could be explained by the Glasgow coma scale (GCS) and CPC evaluation at the early post-CA state, as in the current study the mean of GCS was 10 ± 4, which indicate that patients with good CPC state (1, 2, and 3) are more than patients with poor CPC (4 and 5), while in Scarpino *et al.*'s [12] study the majority of patients included had a mean of GCS of 6 ± 4, which indicate that patients with poor CPC state are more than patients with good CPC.

The current study found that 10 (25%) patients (n = 40) had post-CA early myoclonus; of those five (50%) patients lived and five (50%) patients died, but the frequency of seizures after resuscitation were significantly higher in dead patients 45.5% (n = 11) versus 17.2% in alive patients (n = 29; P = 0.03).

It was noticed that the majority of patients with post-CA seizures (40%) and those without seizures (70%) had benign EEG pattern, while 30% of those with seizures had a highly malignant pattern and only 13.3% of those

without seizure had such pattern; Also 66.7% of those without postarrest seizures had CPC 1 while 30% of those with seizures had CPC 1.These findings indicate that the presence of early PHM following CA were invariably related to poor outcome, but do no longer exclude that patients with early PHM may live with good neurological function.

These findings are less than that of Ribeiro *et al*. [15] who studied the clinical outcome of generalized periodic epileptiform discharges (malignant feature) on first EEG in patients with hypoxic encephalopathy post-CA among 36 patients and reported that 17 (47.2%) patients had PHM; this is mostly due to that all patients in Ribeiro *et al*.'s [15] study had malignant EEG pattern. Also, Ribeiro *et al*. [15] proved that PHM does not appear to affect outcomes in those with these EEG findings (generalized periodic epileptiform discharges) and outcomes are equally poor if they are present; from those 36 patients 10 survivors from whom three had PHM trend toward improved outcomes; in those with reactive EEG, only two patients of survivors in the entire cohort had CPC more than or equal to 3.

In the study of Bisschops *et al*. [16] the predictors of poor neurologic outcome in patients after CA treated for hypothermia among 103 patients reported that 40 (38.8%) had PHM and from those 103 patients, 36 patients with good outcome; from those four (11%) patients had PHM, while from 67 patients with bad outcome 36 (53%) patients had PHM. Bisschops' findings support the findings of this study.

The findings in the current study are consistent with Rossetti *et al*. [17], who studied prognostication after CA and hypothermia among 111 patients and reported that 37 (33.3%) patients with early PHM, 25 patients (n = 111) had CPC 1–2 and from whom only one (4%) patient had early PHM; while the rest 84 patients had CPC 3–5 and from whom 35 (42%) patients had early PHM ($P < 0.001$).

The findings in this study are also consistent with Amorim *et al*. [18] who studied the prognostic value of postanoxic myoclonus and malignant EEG pattern in comatosed CA survivors among 289 patients and reported that 97 (33.5%) patients had PHM, from those, 69 had malignant EEG patterns, 12 of whom survived, and five had good outcomes (malignant EEG predicted in-hospital mortality), while the rest of patients had PHM (28 patients) without malignant EEG patterns; there is no increase in mortality or poor outcome.

Limitations of the study

(1) The number of patients is small, limiting the multivariate analysis, although in our analysis, there were no clear differences between the groups in terms of other prognostically important data.
(2) The far distance may affect the timing of EEG.
(3) The quality of the portable EEG device may affect the EEG records.

Conclusion

(1) Malignant EEG patterns were correlated to poor outcome, while benign pattern was associated with a favorable outcome.
(2) Cerebral performance grading scales 1 and 2 predict good outcome while 4 and 5 predict poor outcome.
(3) Presence of early PHM was associated with poor outcome; however, it does not exclude survival with good neurological function.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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