

The Predictive Role of QEEG in the Post-Operative Delirium and Prognosis of Cardiac Surgery Patients

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Research

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The predictive role of qEEG in the post-operative delirium and prognosis of cardiac surgery patients

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Abstract

Objective

To determine whether qEEG has the capable of predicting the onset of post-operative delirium (POD) and prognosis of cardiac surgery patients.

Methods

We prospectively studied a cohort of cardiac surgery patients undergoing EEG for evaluation of altered mental status. Patients were assessed for delirium with the CAM-ICU or CAM. EEG were interpreted clinically by clinician, and reports were reviewed to identify features such as aEEG, alpha, beta, theta or delta relative band energy, alpha variability and spectral entropy. Generalized linear models were used to quantify associations among EEG findings, delirium, and clinical outcomes, including length of stay and mortality.

Results

60 patients were evaluated and 29 (48.33%) met delirium criteria. The EEG finding most strongly associated with delirium presence was aEEG, whether the peak value or valley value less than lower quartile or greater than upper quartile.

Conclusions

The peak or valley value of aEEG in F3-P3/F4-P4 derivation is a good predictor of post-operative delirium in cardiac surgery patients.

Trial registration: Clinical Trials.gov Identifier, NCT03351985. Registered 1 December 2017

Key words: delirium; qEEG; cardiac surgery; peak or valley value

Take home message

In this prospective cohort study, 60 cardiac surgery patients were evaluated by qEEG for evaluation of altered mental status, and nearly half patients (48.3%) had post-operative delirium (POD). We found that the peak value or valley value less than lower quartile or greater than upper quartile of F3-P3/F4-P4 derivation was most strongly associated with delirium presence. The qEEG is a good predictor of POD in cardiac surgery patients with a high sensitivity, a high specificity, and an overall good accuracy.

Introduction

Delirium characterized as a fluctuating disturbance of attention and awareness that develops over a short time period occurs in 20-56% of patients after cardiac surgery, which resulted in many poor outcomes including cognitive decline, longer hospital stays, as well as increased costs, morbidity and mortality [1-2]. However, proper interventions for post-operative delirium (POD) are extremely limited, which is ascribed to the difficulty in detecting the impending onset of delirium timely enough to enable development or implementation of preventative therapies.

There are mountain of evidences showed that the longer patients suffering from delirium, the greater its severity, and will be hard to treat [3]. It will increase 10-fold in cognitive impairment and 3-fold in mortality, which results in the financial burden to families and society [4]. An ideal physiological method should be able to provide objective and accurate measurement, erase the consideration related to interrater reliability, and forewarn the evolving of delirium before behavioral changes. Then, we will get rid of dilemma of lacking the ability to distinguish delirium[5].

There are many theories, most of them are complementary rather than competing, attempted to explain the pathogenesis of delirium [6]. These theories likely demonstrated the processes which lead to the biochemical derangement, such as reduced cholinergic function, excess released of dopamine, glutamate and norepinephrine, and changes in γ -aminobutyric acid (GABA) and serotonergic activity may underlie delirium [7]. The above changing ultimately induced the electro-encephalographic (EEG) pattern changes which followed by behavioral symptoms and clinical presentations.

As we all know, the levels of neurotransmitters in the brain will change when we confronted the

physiological stress. Once these changes surpassed the brain's ability to compensate, behavioral signs start to appear, meaning delirium is well established prior to detection [8]. Therefore, delirium was taken as an end product of various neurotransmitters pathways which leads to the brain failure [7].

It is critical to establish an early, objective and accurate assessment tool to distinguish delirium as its complication severity will increase over time. Although more than 40 clinical assessment tools were developed over the past decades, delirium remains largely undetected. Despite these instruments have high reliability and validity in the research environment, their performance were unsatisfied when translation into the clinical setting [9].

Recently, EEG has been proved to be an accurate and reliable method for detecting delirium [8, 10], which further confirmed delirium is an encephalopathy with malfunction of neural networks [11]. EEG-based monitor and quantification have tremendous scientific potential for the prediction and detection of delirium in daily routine practice as it is much more objective, physiological, capable of early detection and applicable for all patients even those with sedation, language or sensory barriers [12-13]. However, traditional EEG usually uses 16 to 32 metal leads, which required a skilled clinician to setup machine and locate the appropriate lead sites. As a result, traditional EEG is a time-consuming and unpractical task for standard delirium monitoring.

With the development of technology, several medical device companies have developed proprietary algorithms and monitors capable of processing EEG waveform over the past few decades. These monitoring devices needs minimal technical setup, such as qEEG, which based on a limited number of electrodes and EEG waveform data are automatic processed by proprietary algorithms and converted into a score which displayed on the monitor made it more practical [14]. However, it is not yet clear whether the qEEG with limited number of electrodes can predict the onset of delirium and the prognosis in cardiac surgery patients.

In this prospective study, we have performed qEEG monitoring in patients suffering from cardiac surgery from the ICU admission to post-operative 24 h, which is the most common period of delirium, to test the hypothesis whether qEEG has the capable of predicting the onset of post-operative delirium and prognosis of cardiac surgery patients.

Methods

Study Design and patients

In this single-center observational study, qEEGs were recorded in included patients underwent cardiac surgery who were admitted to the ICU of the Zhongda Hospital, Southeast University. The study protocol (number 2017ZDSYLL054-P01) is approved by the institutional review, and written informed consent is collected from preoperative outpatients or hospital admission prior to surgery. Patients aged ≥ 18 year-old were eligible for this study if they were to undergo cardiac surgery. We excluded those patients with a history of any neurologic or psychiatry diseases, neurological and cognitive dysfunction, and stroke history within the last 3 year that may develop a fault of the diagnosis of delirium or the qEEG. Postoperative sedation was achieved with propofol and dexmedetomidine infusion until tracheal extubation criteria were met. Both groups received opioid analgesics (morphine or remifentanyl) for postoperative pain management.

Delirium Diagnosis and Data Collection

A well-trained researcher (both theoretically and practically) visited the included patients before surgery, and on the first day after surgery to perform eye closed qEEG recording (using electrode derivation F3-P3 and F4-P4) . Daily mental status assessment, including delirium screening, was carried out by nurses and physicians using Richmond Agitation and Sedation Scale (RASS) and CAM-ICU or CAM during the first 7 postoperative days. If the surgery was complicated, delirium will be evaluated twice a day during the first 3 postoperative days and once a day during the following 4 postoperative days when RASS > -3 .

qEEG monitoring were recorded according to the international 10/20 system, aEEG monitoring was regarded as the primary EEG measure, and six secondary EEG variables, including alpha relative band energy, beta relative band energy, theta relative band energy, delta relative band energy, alpha variability and spectral entropy, were calculated as secondary measure. We selected 20 min of artifact-free data with patients' eyes closed for quantitative analysis. Blood samples of patients were harvested by nurses within the first 1 hour when patients were admitted to ICU. NSE, IL-6, Hs-CRP, SaO₂, ScvO₂, Lac, TNI, and NT-ProBNP were studied as chemical markers in blood. Several characteristic of patients were registered as follows: age, sex, Acute Physiology and Chronic Health Evaluation (APACHE) II score, MAP, surgery type, and CPB time.

Sample size calculation

Based on the differences, the sample-size were calculated in aEEG analysis. However, almost no studies reported the aEEG data in a similar group of cardiac surgery population. Therefore, we

used the data from a preliminary experiment. The mean of peak values of aEEG in derivation F3-P3 were 23 μ V and 14 μ V for the non-delirious and delirious groups respectively. Meanwhile, the statistical power was assumed to be 0.8 and the significance level was regarded as 0.05. A total of 27 subjects per group were needed at least.

Statistical analysis

Patient baseline features were tested for normality by the Kolmogorov-Smirnow test. Continuous, normally distributed variables were presented by using the mean \pm SD and the comparison was used ANOVA test. Continuously, not normally distributed variables were described with median and interquartile range (IQR) and compared using a Man-Whitney U test. Categorical variables were analyzed by chi-squared test or Fisher exact test. Statistical analysis was calculated performed on SPSS 20.0 version (SPSS Inc., Chicago, IL, USA) . All data were analyzed by a person who was not familiar with the results of CAM-ICU testing.

Results

Sixty-four cardiac surgery patients were initially included, and one patient was excluded for the history of neurologic disease, two patients were excluded for the neurologic event during the study period and one patient was excluded due to technical problems (Figure 1). Finally, data from sixty patients were analyzed, and of whom 29 (48.3%) patients were delirious and 31 patients (51.7%) were non-delirious.

The clinical characteristics of the patients are presented in Table 1a. Significant differences were identified in delirious versus non-delirious participants in age (63.3 \pm 10.5 versus 54 \pm 13.1 years old, P = 0.03), APACHE II scores (average value:15 versus 10, P = 0.004) , lactate (average value: 2.1 versus 1.2 mmol/L, P = 0.03), and hospital days (average value: 13 versus 11 days, P = 0.048). Concerning the type of surgery, obviously more patients with the diagnosis 'delirium' had aortic dissection surgery as compared to non-delirious patients (17.2 % versus 0%), and this difference reached the significance level (P=0.01). In addition, it was noticeable that the CPB time was longer in delirium group compared with non-delirium group (151.6 \pm 56.8 versus 108.3 \pm 44.4 min), which revealed that hypoperfusion time could be an important influence factor in the occurring of delirium. No difference is detected in the mortality between the two groups, although the mortality in delirium group (n=5, 17.2%) is higher than that in non-delirium group (n=1, 3.2%), however, this difference failed to reach the significance level (P=0.07). At the same time, there

was no statistical differences in the hemodynamic and blood data between the groups (for example, MAP, NSE, IL-6, TNI, SaO₂ et., al). Concerning preoperative risk factors (diabetes mellitus, hypertension, peripheral occlusive vascular disease, et al), no significant differences between delirious and non-delirious patients were observed (date not shown). Finally, there was no statistical difference in the proportion of using analgesic and sedative drugs between the two groups, for example, the proportion of patients using morphine for analgesia in two groups were 57.2% vs. 54.8% ($p=0.98$).

In present study, bipolar longitudinal electrodes (F3-P3 and F4-P4) were set according to the international 10/20 system, and qEEG monitoring was commenced within an hour after the admission to ICU and continued for 24 hours or to turn out of ICU. Twenty minutes of artifact-free data with patients' eyes closed were selected for quantitative analysis. aEEG monitoring was regarded as the primary EEG measure, and alpha/beta/theta/delta relative band energy, alpha variability and spectral entropy were calculated as secondary measures. EEG monitoring was technically successful except one patient.

The qEEG characteristics for F3-P3/F4-P4 derivation of study population are shown in [Table 1b.](#) and [Figure 2](#). In delirious patients, peak or valley value of aEEG for F3-P3/F4-P4 derivation measurements [median (interquartile range IQR, 25th-75th percentiles)] were lower than that in non-delirious patients [for example, 19.06 (13.38-38.60) μV vs. 20.68 (17.43-25.62) μV of peak value and 11.84 (8.56-24.09) μV vs. 13.08 (10.84-15.15) μV of valley value for F3-P3 derivation], although there was no significant difference ($p=0.83$ and $p=0.77$ respectively). The relative alpha power significant decrease determined after power spectral analysis of raw EEG data was paralleled by increase in theta power in delirious patients as compared to non-delirious patients (for example, for F3-P3 derivation, relative alpha power: 8.22 vs.12.34 percents, $p=0.066$; and relative theta power: 71.14 vs. 65.63 percents, $p=0.177$). Therefore, the theta/alpha ratio was significantly higher in delirious patients. Our data also showed that the alpha variability and spectral entropy were lower in delirious patients as compared to non-delirious patients.

To determine the predictors of post-operative delirium, an univariate regression analysis was used. Initial covariates included in the model were: age; sex; hospital and ICU stay; APACHE II score; MAP; surgery type; CPB time; qEEG (including aEEG; relative band energy; alpha variability and spectral entropy); NSE; IL-6; Hs-CRP; SaO₂; ScvO₂; Lactate; TNI; NT-BNP. We

find that the first or fourth interquartile of peak value or valley value of F3-P3/F4-P4 derivation [for example, Q1 of peak value for F3-P3 derivation: OR 8.0, 95% CI 1.52-42.04, $p=0.014$; Q1 of peak value for F4-P4 derivation: OR 5.5, 95% CI 1.15-26.41, $p=0.033$] (table 2a), age (OR 1.1, 95% CI 1.02-1.13, $p=0.007$), APACHE II score (OR 1.2, 95% CI 1.04-1.27, $p=0.007$) and lactate (OR 1.6, 95% CI 1.01-2.69, $p=0.045$) (table 2b) had a higher incidence of post-operative delirium.

To further identify the risk factors for post-operative delirium, multivariate regression analysis was used based on the results of the univariate regression analysis above. Age, APACHE II score, lactate, and peak value and valley value of F3-P3/F4-P4 derivation were included in the model. The results showed that Q1 and Q4 of peak or valley value of F3-P3/F4-P4 derivation (for example, Q1 of peak value for F3-P3 derivation: OR 12.4, 95% CI 1.72-89.76, $p=0.012$), and age (OR 1.1, 95% CI 1.00-1.14, $p=0.039$) (Table 3 and data not shown) had higher relationships with the incidence of post-operative delirium. On the other hand, no significant relationship was obtained between post-operative delirium and APACHE II score ($p=0.119$) nor lactate ($p=0.090$).

The present data indicated that aEEG (peak value and valley value of F3-P3/F4-P4 derivation) had significant correlation in relation to the incidence of post-operative delirium. In order to further assess the accuracy of the peak or valley value of F3-P3/F4-P4 derivation as post-operative delirium prediction index, Receiver operating characteristic (ROC) analysis was used to evaluate the AUC area under ROC curve. ROC analysis showed an area under the curve for peak value of F3-P3 of 0.81, for valley value of F3-P3 0.82, 0.77 and 0.77 for peak value and valley value of F4-P4 respectively. In general, the aEEG could predict POD with a high sensitivity, a high specificity, and an overall good accuracy. For example, the peak value of F3-P3 derivation as a predictor of POD showed a 90% sensitivity and 72% specificity with a cutoff value of 16.4 ($p < 0.001$) (Figure 3).

Discussion

Patients in ICU are monitored for various of physiologic alterations, whereas no alteration can predict the occurring of delirium pretty well. This research represents an innovative approach to predict the postoperative delirium. We found that with only four electrodes and 20 min of qEEG recording in the 1 hour after admission to ICU and the lower or higher aEEG significantly increased the probability of developing delirium after cardiac surgery. For all we know, our study

is the first investigate what are the best EEG characteristics to predict delirium. In our study, we also found out age, APACHE II, and lactate are associated with delirium, these suggest us the elder, severe and tissue hypoperfusion can increase the incidence of delirium. It has shown that beta wave are closely tied to the active thinking or active concentration [15], we first found that beta band energy have the potential to predict the onset of delirium in the research.

Recently studies [16] investigated whether aEEG monitoring can be regarded as a potential predictor of outcome in hypothermia-treated comatose survivors of cardiac arrest. They found that a continuous aEEG at the time of normothermia correlated to regaining consciousness. A flat, suppression-burst or status epilepticus aEEG pattern was a strong predictor of a poor outcome, and all such patients died in hospital without regaining consciousness. Thus, we came up with a hypothesis that if there are pathological brain changes taking place and resulting in delirium, then perhaps aEEG could identify abnormalities before the onset of symptoms and allow preventive strategies to be implemented. Although we did not found there are significant difference between the delirium and non-delirium group in aEEG, we found that either high voltage or low voltage aEEG are more likely to develop delirium. These results declare that we should pay more attention to these patients who performed the above aEEG pattern and to identify the risk factors, and ultimately to intervene and prevent delirium from occurring.

A large body of evidences verified that delirium is associated with slowing of EEG background activity, specifically an increased relative delta power [8, 17]. As a result, EEG-based monitoring could have plenty of potential to predict and detect delirium in routine daily practice as it is an objective and applicable in all patients despite of language or sensory barriers [12-13]. Contrary to the results of previous published studies, we found that there are no significant different between two groups although delta relative power increased in delirium group. We considered that the difference of subjects, detected time and derivate could explain the contrary points. Hence, the further studies should be carried into execution to test the predictive and detective roles of delta relative power for delirium in different kinds of patients.

As we all know, surgery can contribute to the development of a systemic inflammatory response that can cause multi-organ dysfunction. Post-surgical neuro-inflammation is associated with synaptic plasticity impairments and neuronal dysfunction which may illustrate the occurring of post-operative delirium [18-20]. Certain studies indicated that Hs-CRP and IL-6 may have the

potential to predict the onset of delirium [21, 22], whereas we did not find the correlation ship between Hs-CRP or IL-6 with delirium. In addition, our results did not show the significant different of NSE, a specific biomarker of neurons impairments [23], between the two groups. So, the predictive roles of these biomarkers in occurring of delirium need to be future studied.

Limitation

There were several limitations in this study. Firstly, we did not use a validated test to diagnose POD. Nevertheless, the incidence of delirium in our study was quit similar to other trials [2, 12]. Secondly, the sample size was relative small and not good enough to study all meaningful outcomes and association. Thirdly, our blood draw, which was 1 hour after enrollment, may lead to the no sense of biomarkers.

Conclusion

The peak value or valley value of aEEG in F3-P3/F4-P4 derivation is a good predictor of post-operative delirium in cardiac surgery patients.

Acknowledgements

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Ethics approval and consent to participate

Approval was obtained from the ethics committee of Clinical Research of Zhongda Hospital, Southeast University, Jiangsu province of China. The study protocol (number 2017ZDSYLL054-P01; the trial registration number: NCT03351985) is approved by the institutional review, and written informed consent is collected from preoperative outpatients or hospital admission prior to surgery

Consent for publication

Not applicable

Availability of data and materials

After publication, data will be made available to other investigators on reasonable requests to the corresponding author. A proposal with a detailed description of study objectives and statistical analysis plan will be needed for evaluation of the reasonability of requests. Additional materials might also be required during the process of evaluation. Deidentified participant data will be provided after approval from the corresponding author

Competing interests

We declare no competing interests

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Authors' contributions

YC and YY had the idea and designed, supervised the study; All authors contributed to acquisition, analysis, or interpretation of data. GZ and LW wrote the manuscript. All authors revised the report and approved the final version before submission.

Figures and tables:

Figure 1 Flowchart of patient inclusion

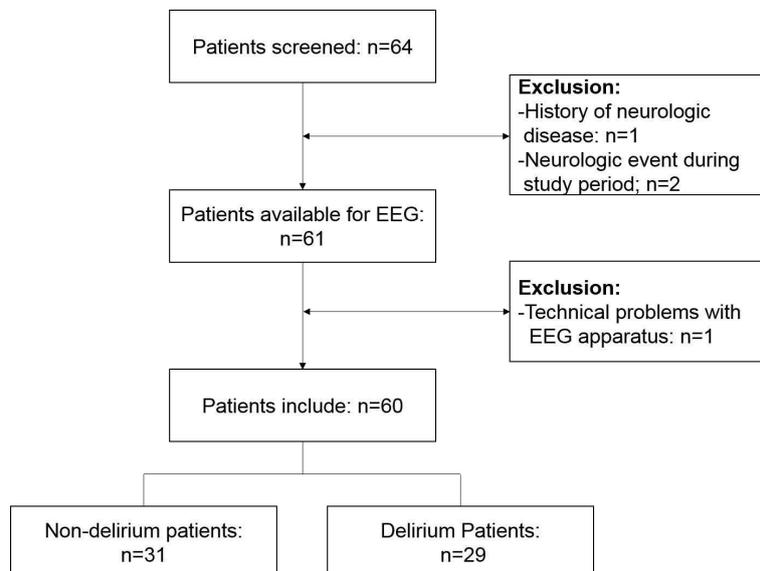


Table 1(a) Baseline characteristics and surgical and hemodynamic characteristics of study population

	Delirious (n = 29)	Nondelirious (n = 31)	Level of significance (<i>p</i>)
Age (years)	63.3±10.5	54±13.1	0.03
Male sex	19 (65.5%)	20(64.5%)	0.93
Hospital mortality	5 (17.2%)	1 (3.2%)	0.07
Hospital stay (days)	13 (10, 22)	11 (9, 13)	0.048
ICU stay (hours)	24.9 (21.4, 105.6)	24.9 (20.8, 25.8)	0.12
APACHE II score	15 (11, 21)	10 (8, 14)	0.004
MAP (mm Hg)	82.3±10.0	79.4±10.9	0.29
Type of surgery			
CABG	15 (51.7%)	14 (45.2%)	0.61
Valve	8 (27.6%)	12 (38.7%)	0.36
Aortic dissection	5 (17.2%)	0	0.01

Others	1 (3.5%)	5 (16.1%)	0.10
Surgery with CPB	16 (55.2%)	22 (70.9%)	0.20
CPB time (min)	151.6±56.8	108.3±44.4	0.12
Drugs for analgesia and sedation			
Morphine	16(57.2%)	17(54.8%)	0.98
Remifentanyl	13 (44.8%)	14(45.2%)	0.98
Propofol	24 (82.7%)	20(64.5%)	0.11
Dexmedetomidine	6 (20.6%)	9(29.0%)	0.45
NSE (ng ml ⁻¹)	31.9 (18.7, 38.2)	25.1 (16.8, 30.5)	0.64
IL-6 (pg ml ⁻¹)	434.7 (157.4, 874)	215.4 (114.9, 498.8)	0.11
Hs-CRP (mg ml ⁻¹)	4.54 (1.0, 20.6)	6.59 (0.8, 42.1)	0.51
Lactate (mmol l ⁻¹)	2.1 (1.2, 3.1)	1.6 (1.0, 2.2)	0.03
TNI (ng ml ⁻¹)	1.5 (0.3, 3.25)	1.1 (0.5, 2.3)	0.73
NT-BNP (pg ml ⁻¹)	595 (232, 1330)	338 (67, 915)	0.22
SaO ₂ (mm Hg)	99.1 (97.8, 99.9)	99.6 (98.8, 99.9)	0.30
ScvO ₂ (mm Hg)	70.8 (62.7, 77.8)	76 (63.9, 80.9)	0.58

APACHE Acute Physiology and Chronic Health Evaluation; *CABG* coronary artery bypass graft; *CPB* cardiopulmonary bypass; *ICU* intensive care unit; *IQR* interquartile range; *NSE* neuronspecific enolase; *SD* standard deviation. Normally distributed variables were presented as mean ± SD and the comparison was used ANOVA test. Continuously, not normally distributed variables were described as median (IQR) and compared using a Man-Whitney U test. Categorical variables were reported as percentages and compared using 2 test or Fisher exact test.

Table 1(b) The qEEG characteristics for F3-P3/F4-P4 derivation of study population

		Delirious (n = 29)	Nondelirious (n = 31)	Level of significance (p)
Peak value of aEEG	F3-P3	19.06 (13.38, 38.60)	20.68 (17.43, 25.62)	0.830
	F4-P4	20.14 (12.83, 35.89)	21.79 (16.61, 28.57)	0.947
Valley value of aEEG	F3-P3	11.84 (8.56, 24.09)	13.08 (10.84, 15.15)	0.773
	F4-P4	12.57 (8.16, 22.25)	13.24 (10.42, 16.97)	0.887
Relative alpha power	F3-P3	8.22(3.85, 16.73)	12.34 (7.79, 19.11)	0.066
	F4-P4	8.76 (4.56, 14.46)	11.01 (7.77, 20.60)	0.064
Relative beta power	F3-P3	2.88 (1.52, 5.42)	3.78 (2.02, 7.92)	0.093
	F4-P4	2.82 (1.57, 4.83)	3.62 (1.97, 8.41)	0.126
Relative theta power	F3-P3	13.09 (9.71, 16.48)	12.21 (8.81, 20.09)	0.970
	F4-P4	12.82 (9.55, 15.97))	12.58 (9.41, 18.05)	0.853
Relative delta power	F3-P3	71.14 ± 15.35	65.63 ± 15.79	0.177
	F4-P4	72.21 ± 14.24	66.99 ± 16.27	0.193
Alpha variability	F3-P3	28.00 ± 13.44	33.12 ± 14.94	0.169
	F4-P4	26.62 ± 12.92	31.40 ± 15.11	0.194
Spectral entropy		66.97 ± 6.52	70.14 ± 6.00	0.056

Figure 2. The relationship between incidence of delirium and qEEG characteristics of the F3-P3/F4-P4 derivation

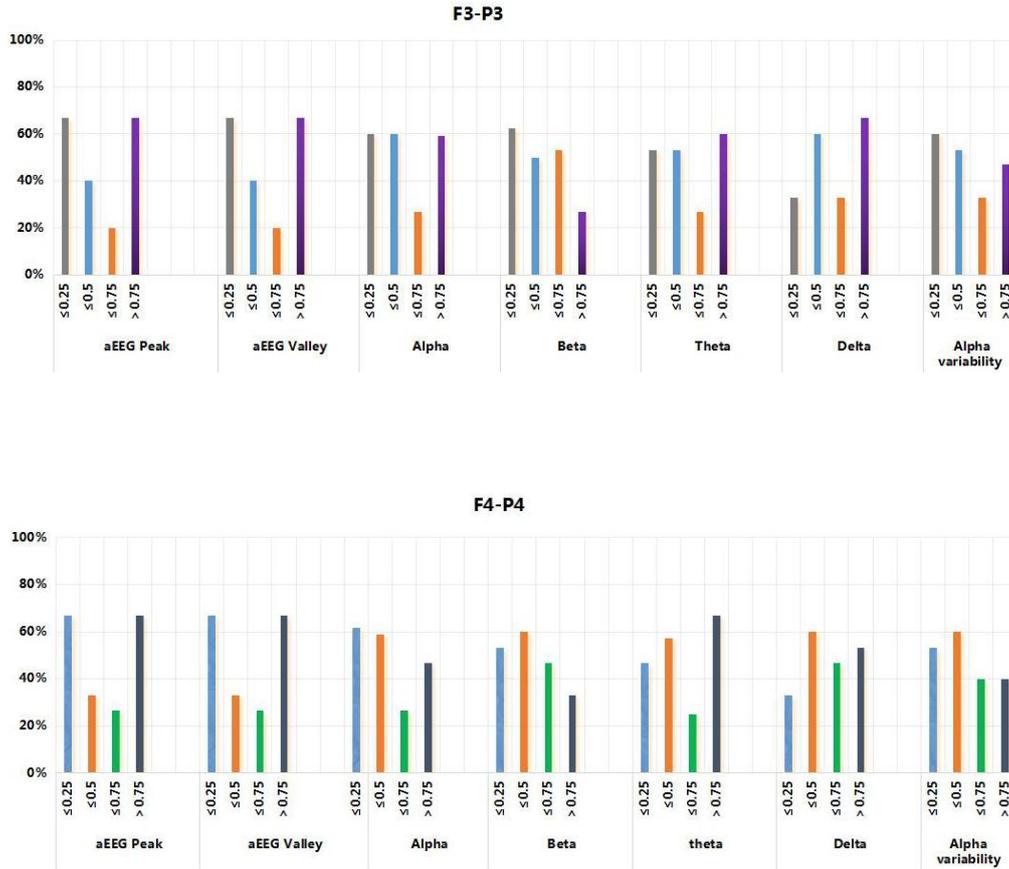


Figure 2. The incidence of delirium is higher when the peak value or valley value less than lower quartile or greater than upper quartile.

Table 2(a) Predictors of postoperative delirium in univariate regression analysis

Variable	Q1			Q2			Q3			Q4			
	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P	
F3-P3	Peak value	8.0	1.52, 42.04	0.014	2.7	0.52, 13.65	0.239	ref		8.0	1.52, 42.04	0.014	
	Valley value	8.0	1.52, 42.04	0.014	2.7	0.52, 13.65	0.239	ref		8.0	1.52, 42.04	0.014	
	Alpha	4.1	0.88, 19.27	0.072	4.1	0.88, 19.27	0.072	ref		2.4	0.52, 11.10	0.260	
	Beta	4.1	0.88, 19.27	0.072	3.1	0.68, 14.50	0.142	3.1	0.68, 14.50	0.142	ref		
	Theta	3.1	0.68, 14.50	0.142	3.1	0.68, 14.50	0.142	ref		4.1	0.88, 19.27	0.072	
	Delta		ref		0.2	0.06, 1.14	0.074	0.75	0.17, 3.33	0.705	0.2	0.06, 1.14	0.074
	Alpha variability	3.0	0.68, 13.31	0.148	2.3	0.52, 10.01	0.273	ref		1.7	0.40, 7.66	0.458	
F4-P4	Peak value	5.5	1.15, 26.41	0.033	1.4	0.29, 6.60	0.691	ref		5.5	1.15, 26.41	0.033	
	Valley value	5.5	1.15, 26.41	0.033	1.4	0.29, 6.60	0.691	ref		5.5	1.15, 26.41	0.033	
	Alpha	4.4	0.89, 21.78	0.069	3.9	0.88, 17.56	0.073	ref		2.4	0.52, 11.10	0.260	
	Beta	2.8	0.61, 13.34	0.182	4.2	0.89, 19.43	0.069	2.2	0.45, 10.21	0.319	ref		
	Theta	0.6	0.13, 2.50	0.458	1.7	0.40, 7.29	0.466	ref		1.3	0.31, 5.48	0.715	
	Delta		ref		3.0	0.67, 13.31	0.148	1.7	0.40, 7.66	0.458	2.3	0.52, 10.01	0.273
	Alpha variability	1.7	0.40, 7.29	0.466	2.3	0.52, 9.70	0.277	ref		1.0	0.23, 4.31	1.000	
Spectral Entropy	1.0	0.16, 5.98	1.000		ref		1.5	0.22, 10.08	0.677	0.5	0.07, 3.43	0.481	

Table 2(a) shows the F3-P3/F4-P4 derivation and EEG characteristics for qEEG. The incidence of delirium is higher when the peak value or valley value less than the first quartile or greater than

the third quartile. However, the occurring of delirium was not presented an association with relative band energy, alpha variability and spectral entropy. The relationships between delirium and aEEG, relative band energy (alpha; beta; theta; delta) , alpha variability and spectral entropy were calculated with linear regression using univariate models. Abbreviations: CI=confidence interval; OR=odds ratio; ref=reference.

Table 2(b) Predictors of postoperative delirium in univariate regression analysis

Variable	OR	95% CI	P
Age	1.1	1.02, 1.13	0.007
APACHE II	1.2	1.04, 1.27	0.007
Lactate	1.6	1.01, 2.69	0.045

Table 2(b) The relationships between delirium and age, APACHE II and lactate were calculated with linear regression using univariate models. Abbreviations: APACHE=Acute Physiology and Chronic Health Evaluation; CI=confidence interval; OR=odds ratio.

Table 3 Predictors of postoperative delirium in multivariate regression analysis

Variable	OR	95% CI	P
F3-P3 Peak			
Q1	12.4	1.72 89.76	0.012
Q2	2.9	0.46 18.50	0.257
Q3	ref		
Q4	15.8	1.97 127.58	0.009
Age	1.1	1.00 1.14	0.039
APACHE II	1.1	0.97 1.26	0.119
Lactate			0.090

Table 3 The relationships between delirium and aEEG, beta relative band energy, alpha variability and spectral entropy, age, APACHE II and Lactate were calculated with linear regression using multivariate models. Abbreviations: APACHE=Acute Physiology and Chronic Health Evaluation; CI=confidence interval; OR=odds ratio;

Figure 3 aEEG as a predictor of POD in ROC analysis

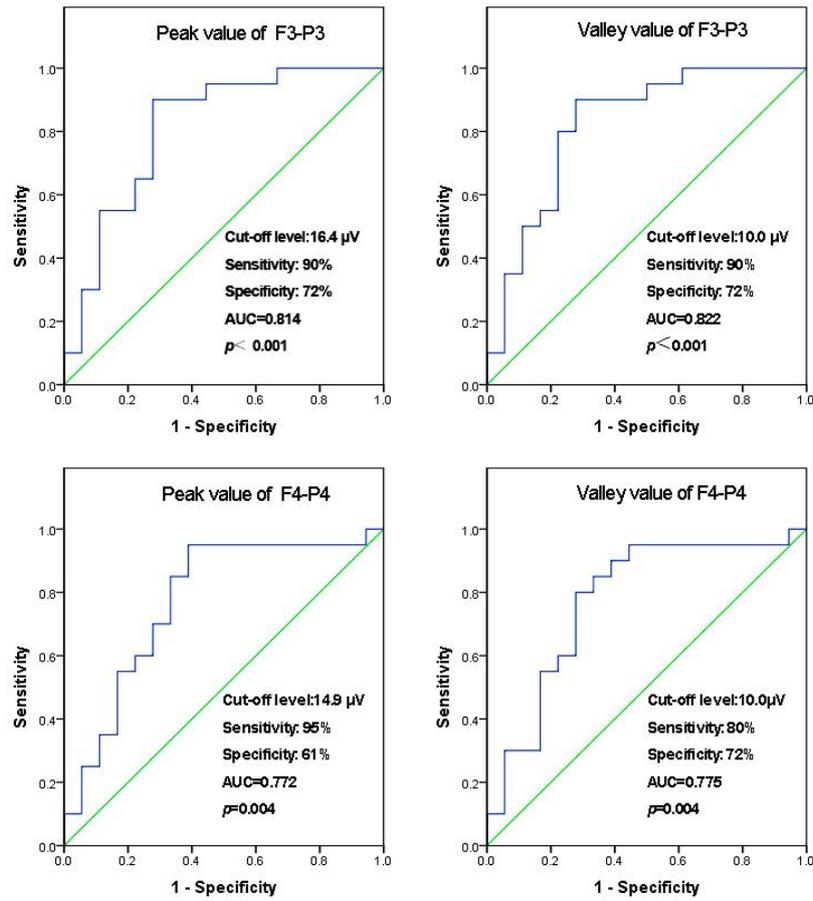


Figure3. ROC analyses showed that aEEG as a predictor of POD had high sensitivity and specificity

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