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·Original Article·

Correlation of continuous electroencephalogram with clinical assessment scores in acute stroke patients

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Abstract: Objective To compare electroencephalogram (EEG) symmetry values between stroke patients with different 28-day outcomes, and to assess correlations between clinical characteristics and 28-day outcomes. **Methods** Twenty-two patients presenting with acute ischemic stroke and persistent neurological deficits at EEG recording were incrementally included. At 28 days after admission, the modified Rankin scale (mRS) was used to evaluate the outcomes, based on which the patients were divided into two *a posteriori* groups, mRS = 6 and mRS <6. Student's *t*-test was used to compare these two groups in terms of brain symmetry index (BSI), National Institutes of Health stroke scale (NIHSS), Glasgow coma scale (GCS) and acute physiology and chronic health evaluation II (APACHE II) assessed at admission. Then EEG parameters, NIHSS, GCS and APACHE II were correlated with the mRS. **Results** There were significant differences in BSI, NIHSS, GCS, and APACHE II between the two groups. Survivors had lower BSI, NIHSS and APACHE II, and higher GCS values, compared with patients who died within 28 days after admission. Besides, BSI at admission had a positive correlation with mRS at 28 days ($r = 0.441$, $P = 0.040$). NIHSS and APACHE II were also correlated with mRS ($r = 0.736$, $P < 0.000\,1$; $r = 0.667$, $P = 0.001$, respectively). GCS at admission had a negative correlation with mRS ($r = -0.656$, $P = 0.001$). **Conclusion** A higher BSI predicts a poorer short-term prognosis for stroke patients. Acute EEG monitoring may be of prognostic value for 28-day outcomes. The early prediction of functional outcomes after stroke may enhance clinical management and minimize short-term mortality.

Keywords: electroencephalography; brain symmetry index; stroke; prognosis

1 Introduction

Stroke is a major cause of adult death and disability worldwide. Early and accurate assessment of the prognosis may improve stroke management. There are many tools to evaluate prognosis, such as the National Institutes of Health stroke scale (NIHSS), the Glasgow coma scale (GCS) and acute physiology and chronic health evaluation II (APACHE II). The NIHSS is a stroke-specific quantitative scale which shows excellent clinimetric properties in terms of reliability and validity[1,2]; it is known to be effective in predicting the likelihood of recovery. The GCS is widely used to describe the consciousness level of head-injured patients and has been validated for its inter-observer reliability[3,4]. The APACHE II score consists of three components: age, acute physiologic score, and chronic health. The total APACHE II score ranges from 0 to 71; higher scores imply more severe disease and a less favorable prognosis[5]. Previous studies have described a relationship between APACHE II and 30-day survival in patients who receive transjugular

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intrahepatic portosystemic shunts[6] and those with acute tubular necrosis[7]. However, NIHSS, GCS and APACHE II all evaluate patient conditions through external signs, which occur after the internal changes. In severe stroke patients who are unconscious, general clinical examinations may be insufficient and fail to constantly monitor their condition. Early detection of changes and effective intervention are essential for the clinical management of stroke. The continuous electroencephalogram (CEEG) is the most sensitive neurodiagnostic tool for detecting acute cerebral ischemia[8]. Studies of intraoperative EEG monitoring and animal models have shown that EEG changes occur within 5 min of acute cerebral ischemia[9]. Among the EEG parameters, the brain symmetry index (BSI) is one of the most frequently used and has been demonstrated to be useful. Previous studies have shown a positive correlation between BSI and the NIHSS, and that CEEG monitoring using the BSI is technically feasible and provides real-time information on the effect of thrombolysis in acute hemispheric stroke patients[10]. However, further studies are needed to demonstrate the utility of CEEG in stroke prognosis. In the present study, we extracted symmetry values from the EEG and compared them between patients with different 28-day outcomes. Correlations between clinical characteristics (BSI, NIHSS, GCS and APACHE II) and the modified Rankin scale (mRS) for outcome assessment were also explored.

2 Subjects and methods

2.1 Study population Twenty-two stroke patients (15 males and 7 females) admitted to the Department of Neurology, Beijing Dongzhimen Hospital affiliated with Beijing University of Chinese Medicine, from the beginning of 2007 to the beginning of 2008, participated in this study. A computed tomography scan or magnetic resonance imaging was performed on all patients to rule out hemorrhagic stroke. Patients were treated according to the Guideline for Preventing and Treating Cerebrovascular Diseases in China[11]. All patients or family members (of those with disturbed consciousness) gave informed oral consent. This study was approved by the Ethics Committee of Dongzhimen Hospital.

Patients with primary diseases of the liver, kidney, cardiovascular and hematopoietic systems, fever, seizures, significant sequelae of stroke, EEG abnormalities consistent with encephalitis, or the use of benzodiazepines, tricyclic antidepressants and neuroleptic medications were excluded. In addition, NIHSS, GCS and APACHE II were quantitatively assessed at admission, and the mRS was administered in survivors on the 28th day post-stroke. EEGs were recorded within 48 h of admission and typically continued for 12–24 h. In addition, EEGs were acquired from seven healthy participants who reported no history of seizures, neurological diseases, or psychiatric disorders. The control participants were generally awake during EEG acquisition and resting quietly with eyes closed for 13 min.

2.2 EEG recording and analysis

2.2.1 EEG recording EEGs were recorded according to the international 10–20 system. Collodion was used to attach individual electrodes to improve long-term recording stability and reduce movement artifacts[12]. With reference to the linked earlobes, we used a 16-channel EEG system (Fp1-A1, Fp2-A2, F3-A1, F4-A2, F7-A1, F8-A2, C3-A1, C4-A2, T3-A1, T4-A2, P3-A1, P4-A2, O1-A1, O2-A2, T5-A1 and T6-A2). Initial recordings were performed using a Brain Lab EEG system (Cadwell 32-channel EEG amplifier Easy II) with a 12-bit A/D converter at 100 Hz and a bandpass frequency of 0.53 to 50 Hz. Impedance was kept below 5 kΩ to reduce polarization effects.

2.2.2 EEG data processing Data containing artifacts due to eye blinks, significant muscle activity, and electrode movement were removed offline during visual screening by an experienced EEG physician. Savitzky-Golay filtering was used to eliminate noise in wide-range signals from the original dataset (the set of all the observed data). The total record from each patient was broken into segments, and samples in constant duration were chosen to represent the global dataset. Ten-second artifact-free EEG recordings involving 100 sample points per second (as experts read the EEG signal in the apparatus with approximately 10 seconds on each entire screen) were selected from each segment for every subject. The spectral density was transformed by fast Fourier transform and BSI was computed as the mean value of the whole recording.

The BSI is an improved marker of ischemic damage in patients with acute ischemic stroke. It is defined as the mean of the absolute value of the difference between the mean hemispheric amplitude spectra and has a value between 0 and 1[13]. As a measure of symmetry, we considered the spectral densities of the right and left hemispheres in the frequency range from 1 to 20 Hz, and the frequency bands over all channels are delta (1–3 Hz), theta (4–7 Hz), alpha (8–13 Hz) and beta (14–20 Hz)[14]. Therefore, for the amplitude of a signal obtained from a particular hemispheric channel pair i (i =1, 2, …N) at frequency j (or the Fourier coefficient, with index j = 1, 2, . . . , M), we write $R_{ij}(t)$ and $L_{ij}(t)$ for the right and left hemispheres. The BSI is then defined as:

$$\mathrm{BSI}(t) = \left\| \frac{1}{N}\frac{1}{M}\sum_{i=1}^{N}\sum_{j=1}^{M}\frac{R_{ij}(t)-L_{ij}(t)}{R_{ij}(t)+L_{ij}(t)} \right\| \qquad (1)$$

where N is the number of channel pairs, M is the number of Fourier coefficients, and t is the time variable indicating the time point of sample. All procedures were written and implemented in Matlab 7.0.

2.3 Statistical analysis Data analyses were performed using the Statistical Product and Service Solution (SPSS, version 13.0) software package for Windows. The BSI, NIHSS, GCS and APACHE II scores were considered continuous variables, and the outcome parameter mRS was dichotomized for analysis. Comparisons between groups were made using Student's t-test. The Pearson correlation coefficient and Spearman's correlation coefficient were used to assess the relationships between clinical characteristics and outcomes. P <0.05 was considered statistically significant.

3 Results

3.1 Clinical characteristics of patients EEGs were recorded in 22 stroke patients, 10 who experienced posterior circulation strokes and 12 with anterior circulation infarctions (8 left hemisphere and 4 right hemisphere). On day 28 after admission, mRSs were evaluated as patient outcomes. Sixteen patients had mRS <6, and six had mRS = 6. They were thus assigned into the corresponding groups according to the mRS score. There were no significant differences between the two groups in demographics, consciousness or history of disease (Tables 1 and 2).

Table 1. Characteristics of patients

	mRS28d <6 (n = 16)	mRS28d = 6 (n = 6)	P value
Demographics			
Age (years)	73.06 ± 4.06	65.5 ± 14.90	0.069
Range (years)	67–81	50–84	
Gender	Male 11 (69%) Female 5 (31%)	Male 4 (67%) Female 2 (33%)	0.926
Consciousness			
Disturbances	8 (50%)	3 (50%)	1
Conscious	8 (50%)	3 (50%)	
History of stroke			
Yes	7 (44%)	2 (33%)	0.658
No	9 (56%)	4 (67%)	
History of hypertension			
Yes	12 (75%)	5 (83%)	0.678
No	4 (25%)	1 (17%)	
History of heart disease			
Yes	6 (38%)	2 (33%)	0.856
No	10 (62%)	4 (67%)	
History of diabetes			
Yes	5 (31%)	2 (33%)	0.926
No	11 (69%)	4 (67%)	

mRS28d: modified Rankin scale score on day 28 after admission. No significant differences were found between patients with different outcomes (mRS28d < 6 and mRS28d = 6) in demographics, consciousness and history of disease.

3.2 Comparison of BSI between stroke patients and healthy participants EEG data from the seven control participants were analyzed and compared with those from the stroke patients. The median BSI in the controls (0.060, interquartile range 0.007) and that in the stroke patients (0.066, interquartile range 0.005) were significantly different ($Z = -3.771$, P <0.001; nonparametric test).

Table 2. BSI, GCS, NIHSS, APACHE II and mRS28d scores of each patient

Patient number	BSI	GCS	NIHSS	APACHE II	mRS28d
1	0.066	9	16	16	4
2	0.065	10	15	11	3
3	0.066	6	19	21	5
4	0.065	10	17	16	4
5	0.067	7	18	13	5
6	0.067	14	10	9	4
7	0.068	9	17	12	5
8	0.062	14	10	7	3
9	0.064	10	17	13	5
10	0.070	13	9	7	3
11	0.064	5	23	22	5
12	0.066	11	14	9	5
13	0.063	5	22	19	5
14	0.067	14	5	7	4
15	0.063	11	11	9	2
16	0.061	9	15	16	5
17	0.070	5	23	20	6
18	0.073	10	18	19	6
19	0.065	5	26	20	6
20	0.066	10	18	14	6
21	0.075	5	24	16	6
22	0.069	5	20	16	6
Mean ± SD	0.067 ± 0.003	8.955 ± 3.184	16.682 ± 5.349	14.182 ± 4.837	4.682 ± 1.171

APACHE II, acute physiology and chronic health evaluation II; BSI, brain symmetry index; GCS, Glasgow coma scale; mRS28d, modified Rankin scale on day 28 after admission; NIHSS, National Institutes of Health stroke scale (0–42 points).

3.3 Comparisons of BSI, NIHSS, GCS and APACHE II between patients with different outcomes The *t*-test was used to compare the BSI, NIHSS, GCS and APACHE II scores at admission between the mRS = 6 (n = 6) and the mRS <6 (n = 16) groups (Table 3). There were significant differences between the groups in all four measures; the survivors had higher GCS, lower NIHSS, lower APACHE II, and lower BSI scores than those with mRS = 6 at 28 days after admission.

3.4 Correlation analysis of clinical parameters with mRS

3.4.1 Correlations between BSI, NIHSS, GCS and APACHE II NIHSS at admission was correlated with GCS (r = −0.920, P <0.000 1), which remained significant after controlling for APACHE II (r = −0.732, P <0.000 1). NIHSS was also correlated with APACHE II (r = 0.868, P < 0.000 1), but this was not significant after controlling for GCS (r = 0.400, P = 0.072). APACHE II was negatively correlated with GCS (r = −0.842, P <0.000 1), which remained significant after controlling for NIHSS (r = −0.237, P = 0.030). No correlations were found between BSI and the other parameters (Tables 4 and 5).

Table 3. Differences between patients with different outcomes [mRS28d = 6 (*n* =6) and mRS28d <6 (*n* =16)] in BSI, NIHSS, GCS and APACHE II scores

	Group	*n*	Mean ± SD	*P* value	95%CI	
					Lower	Upper
BSI	Died	6	0.070 ± 0.004	0.003	0.002	0.007
	Survived	16	0.065 ± 0.002			
NIHSS	Died	6	21.500 ± 3.331	0.006	2.108	11.142
	Survived	16	14.875 ± 4.856			
GCS	Died	6	6.667 ± 2.582	0.035	−6.055	−0.236
	Survived	16	9.813 ± 3.016			
APACHE II	Died	6	17.500 ± 2.510	0.046	0.094	9.031
	Survived	16	12.938 ± 4.959			

“Survived” equals the mRS28d <6 group; "Died" equals the mRS28d = 6 group. APACHE II, acute physiology and chronic health evaluation II; BSI, brain symmetry index; GCS, Glasgow coma scale; mRS28d, modified Rankin scale on day 28 after admission; NIHSS, National Institutes of Health stroke scale (0–42 points).

Table 4. Correlation coefficients between BSI, GCS , NIHSS and APACHE II

	BSI	GCS	NIHSS	APACHE II
BSI	1.000	−0.075	0.158	−0.002
GCS	−0.075	1.000	−0.920**	−0.842**
NIHSS	0.158	−0.920**	1.000	0.868**
APACHE II	−0.002	−0.842**	0.868**	1.000

$^{**}P$ <0.01, Spearman's correlation (2-tailed). APACHE II, acute physiology and chronic health evaluation II; BSI, brain symmetry index; GCS, Glasgow coma scale; mRS28d, modified Rankin scale on day 28 after admission; NIHSS, National Institutes of Health stroke scale (0–42 points).

Table 5. Correlation coefficients between NIHSS, GCS and APACHE II after controlling for other variables

	NIHSS	GCS	APACHE II
NIHSS	1.000	−0.732**	0.400
GCS	−0.732**	1.000	−0.237*
APACHE II	0.400	−0.237*	1.000

$^{*}P$ <0.05 and $^{**}P$ <0.01, Spearman's correlation (2-tailed). APACHE II, acute physiology and chronic health evaluation II; BSI, brain symmetry index; GCS, Glasgow coma scale; mRS28d, modified Rankin scale on day 28 after admission; NIHSS, National Institutes of Health stroke scale (0–42 points).

Table 6. Correlation coefficients between clinical parameters and mRS

Correlation coefficients	mRS
BSI	0.441*
GCS	–0.656**
NIHSS	0.736**
APACHE II	0.667**

$^{*}P$ <0.05 and $^{**}P$ <0.01, Pearson correlation (2-tailed). APACHE II, acute physiology and chronic health evaluation II; BSI, brain symmetry index; GCS, Glasgow coma scale; mRS28d, modified Rankin scale on day 28 after admission; NIHSS, National Institutes of Health stroke scale (0–42 points).

3.4.2 Correlations between clinical parameters (BSI, GCS, NIHSS and APACHE II) and mRS BSI, along with NIHSS and APACHE II at admission were positively correlated with mRS, whereas GCS at admission was negatively correlated with mRS (Table 6).

4 Discussion

BSI captures a particular asymmetry in spectral power between the two cerebral hemispheres and has been implemented as an additional criterion for determining the need for shunts in carotid endarterectomy[13]. BSI can serve as a valid and readily observable indicator of stroke prognosis when combined with other clinical indicators, and can also help doctors to evaluate the condition of patients[10,15-18]. The lower bound value for the BSI is zero (perfect symmetry for all channels), and the upper value is 1 (maximal asymmetry)[10]. In healthy controls, the BSI is 0.042 ± 0.005[17]. The median BSI in our study was 0.006, which is higher than that reported in a previous study[17], but there was also a significant difference in BSI between stroke patients and healthy controls.

In addition, we compared the BSIs of stroke patients with different outcomes and explored the correlation between BSI and mRS. The BSI was significantly higher in patients with mRS = 6 (0.070 ± 0.004) than in those with mRS <6 (0.065 ± 0.002), implying that higher BSI scores predict a poorer short-term prognosis. In addition, a statistically significant Pearson correlation ($r = 0.441$, $P = 0.040$) was found between BSI and mRS.

To the best of our knowledge, this study is the first to explore the correlations between BSI, GCS and APACHE II. However, no correlation was found between the BSI and other evaluated parameters. Unlike the previous studies, we did not find a correlation between the BSI and NIHSS, which may be for the following reasons. First, the patient conditions differed from those in previous studies. In our study, half of the patients experienced disturbances of consciousness and presented with higher mean scores on the NIHSS than the subjects in the previous study. Second, our study included 10 patients with posterior circulation strokes. As a symmetry index, the BSI is used mainly in patients with a unilateral stroke in the anterior circulation, and previous studies focused primarily on unilateral stroke in the territory of the middle cerebral artery. Third, The BSI value varies considerably even in patients with similar conditions and prognoses. This may be due to the varying degrees of stroke, different monitoring instruments, or even dissimilar reference electrodes. Studies have shown that different references may result in different BSIs, and the linked-ear reference reduces BSI values[19,20].

In our study, we took the asymmetry as a total value for all pairs of electrodes and frequency bands and ignored differences among bands, brain areas and whether the unilateral stroke was on the left or right. This may be another reason for the reduced BSI values compared with the previous study, and the significance of BSI as a total value for all pairs of electrodes and frequency bands raises is a new question. Nevertheless, the results revealed differences in BSI between patients and healthy people and between patients with different outcomes.

However, our study had several limitations because it was a preliminary exploratory study involving posterior circulation stroke using BSI. In addition, compared with previous work, the condition of the patients was relatively poor, as indicated by the mean NIHSS of 17. Because only one surviving patient had an mRS <2 and a Barthel index >60, we did not perform receiver operating characteristic curve regression analysis, which can accurately illustrate the prediction of hospital mortality risk for critically ill, hospitalized stroke patients.

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