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Use of the bispectral index during the early postresuscitative phase after out-of-hospital cardiac arrest

Shigehiro Shibata[1], Tsuyoshi Imota[2], Souhaku Shigeomi[3], Wakana Sato[3], and Keiji Enzan[3]

[1]Department of Critical Care Medicine, Iwate Medical University, 19-1 Uchimaru, Morioka 020-8505, Japan
[2]Department of Neurology, Akita City Hospital, Akita, Japan
[3]Department of Anesthesiology, Akita City Hospital, Akita, Japan

Abstract
Non-invasive and real-time measures of neurological status after cardiac arrest are needed to be able to make an early determination of the postresuscitative outcome. We investigated whether the bispectral index (BIS) predicts the postresuscitative outcome in 10 patients with out-of-hospital cardiac arrest. We measured the BIS after return of spontaneous circulation (ROSC) in the emergency room and on admission to the intensive care unit (ICU). We determined the Glasgow Coma Scale (GCS) on admission to the emergency room and the ICU and the Glasgow Outcome Scale (GOS) on discharge from the ICU. The BIS increased after about 30 min of ROSC or reached a plateau in patients rated as achieving a good recovery or moderate disability, but it did not increase to >80 in patients rated as being in a permanent vegetative state/dead. The GCS on admission to the ICU was the same as that on admission to the emergency room. The BIS values were significantly lower in the nonsurviving group than in the surviving group. There was a positive correlation between the BIS on admission to the ICU and the GOS on discharge from the ICU. The BIS can thus be used to predict the postresuscitative outcome of patients with out-of-hospital cardiac arrest.

Key words Bispectral index · Out-of–hospital · Glasgow Outcome Scale · Glasgow Coma Scale

Introduction

The mortality rate after cardiopulmonary resuscitation with return of spontaneous circulation (ROSC) is high with out-of-hospital cardiac arrest [1–3], and it is not possible to predict the neurological prognosis at this stage. If we could determine the neurological prognosis at an early stage after ROSC, we might be able to tailor treatments relative to the prognosis of the ROSC patients. A recent study reported that the brain-derived proteins S-100 and NSE and electroencephalography (EEG) results predict the long-term outcome after cardiac arrest [4]. Although these measures are useful clinically, we wanted to find simpler, noninvasive, reproducible, and quantifiable monitoring methods for therapeutic strategies.

The bispectral index (BIS) is a novel EEG-derived parameter that is based on a combination of time domain, frequency domain, and second-order spectral subparameters. The BIS ranges from 100 (awake) to 0 (isometric EEG) and has been shown to correlate well with the level of hypnosis or depth of sedation produced by volatile agents, propofol, midazolam, and opioids [5]. Because BIS is a noninvasive tool and a real-time indicator, it may be more useful than other measures (e.g., EEG or the S-100 or NSE assay) as a clinical monitoring tool for predicting the prognosis of postcardiac arrest outcomes from brain damage caused by cardiac arrest. In addition, because the relation between BIS and outcome is not well studied, we investigated whether BIS could be used as an early predictive tool for the neurological prognosis of postresuscitation in out-of-hospital cardiac arrest patients.

Methods

After obtaining approval for the trial from the hospital's ethics committee, we measured the BIS after ROSC in the emergency room and on admission to the intensive care unit (ICU). We determined the Glasgow Coma Scale (GCS) on admission to the emergency room and ICU and the Glasgow Outcome Scale (GOS) on discharge from the ICU.

We enrolled 10 postresuscitative patients with out-of–hospital cardiac arrest between December 2000 and January 2002. There were seven men and three women aged 51–87 years (70.7 ± 13.2 years, mean ± SD). Patient

Address correspondence to: S. Shibata
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diagnoses were categorized as follows: five cardiogenic, two suffocation, two respiratory, one trauma. Patients with brain injury such as acute cerebral hemorrhage or infarction, metabolic disease, or psychiatric disease were excluded. The resuscitation procedures were performed in accordance with the 2000 American Heart Association guidelines.

The BIS was measured twice using a BIS monitor (model A1050, version 3.4; Aspect Medical Systems, Newton, MA, USA): after ROSC in the emergency room and on admission to the ICU. The tracheas of all patients were intubated in the emergency room and vecuronium 0.1 mg · kg^{-1} was administered intravenously in the ICU to eliminate electromyographic (EMG) activity. To prevent contamination, the signal quality index and EMG activity in the BIS monitor were confirmed before BIS measurements. Patients were not given any sedation before the BIS measurements. We used a standard BIS strip (BIS Sensor; Aspect Medical Systems) with three gel electrodes: two active and one ground. The two active electrodes were applied to the forehead, with the proximal lead at the center of the forehead and the distal lead on the temple. The ground electrode was placed between the two active electrodes. Electrode impedance was maintained at <5 kΩ. Spectral edge frequency (SEF), the frequency below which 95% of the total EEG power resides, and the median frequency (MF), the frequency below which 50% of the total EEG power resides, were measured as other EEG parameters.

All clinical measurements were assessed by the neurologist. The coma level was assessed using the GCS, which is calculated as the sum of eye opening, motor response, and verbal response subscores and is scored from 3 (worst) to 15 (best). The GCS was determined on admission to the emergency room and ICU. The postresuscitative outcome was determined on discharge from the ICU using the GOS and included good recovery (G), moderate disability (MD), severe disability (SD), and permanent vegetative state/death (D).

The data were given as means ± SD. All statistical analyses were performed with StatView J4.5 (Abacus Concepts, Berkeley, CA, USA), using the Spearman rank correlation. $P < 0.05$ was considered statistically significant.

Results

Clinical characteristics for the patients are presented in Table 1. As shown in Fig. 1, the BIS increased abruptly after about 30 min of ROSC or reached a plateau of >80 in patients who achieved a good recovery (patients 4, 7, and 10 in Table 1) and moderate disability (patient 6); it did not increase in patients ranked as being in a permanent vegetative state/dead (patients 1, 5, 9). In addition, there was a slight, gradual increase in SEF and MF in patients who achieved a good recovery and moderate disability but little change in the permanent vegetative state/death group (data not shown). However, we could not analyze the recordings within 30 min of ROSC in three patients (nos. 2, 3, 8) because of EMG contamination.

Table 1. Clinical characteristics for each patient ($n = 10$)

Patient	Age (years)	Sex	Diagnostic category	GOS
1	80	F	Cardiogenic	D
2	59	M	Respiratory	D
3	51	F	Cardiogenic	SD
4	81	M	Suffocation	G
5	79	F	Cardiogenic	D
6	63	M	Trauma	MD
7	52	M	Cardiogenic	G
8	87	M	Suffocation	SD
9	74	M	Respiratory	D
10	81	M	Cardiogenic	G

GOS, Glasgow Outcome Scale; G, good recovery; MD, moderate disability; SD, severe disability; D, permanent vegetative state/death

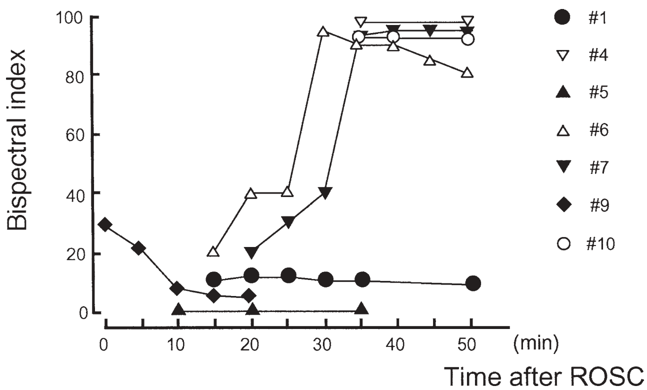

Fig. 1. Time courses of the bispectral index (BIS) in patients during cardiopulmonary resuscitation. On the *right* are the patient numbers from Table 1. *ROSC*, return of spontaneous circulation; *G*, good recovery; *MD*, moderate disability; *SD*, severe disability; *D*, permanent vegetative state/death

Figure 2A shows a comparison of BIS in the surviving and nonsurviving groups on admission to the ICU. The BIS values were significantly lower ($P < 0.01$) in the nonsurviving group than in the surviving group (9.7% ± 16.0% for the nonsurviving group vs. 81.3% ± 16.9% for the surviving group). There was a strong positive relation between the BIS on admission to the ICU and the GOS on discharge from the ICU (mean 8 days), as shown in Fig. 2B ($P = 0.004$, $r = 0.956$). The GCS on admission to the ICU was 3 in all patients, equivalent to that seen on admission to the emergency room. Even

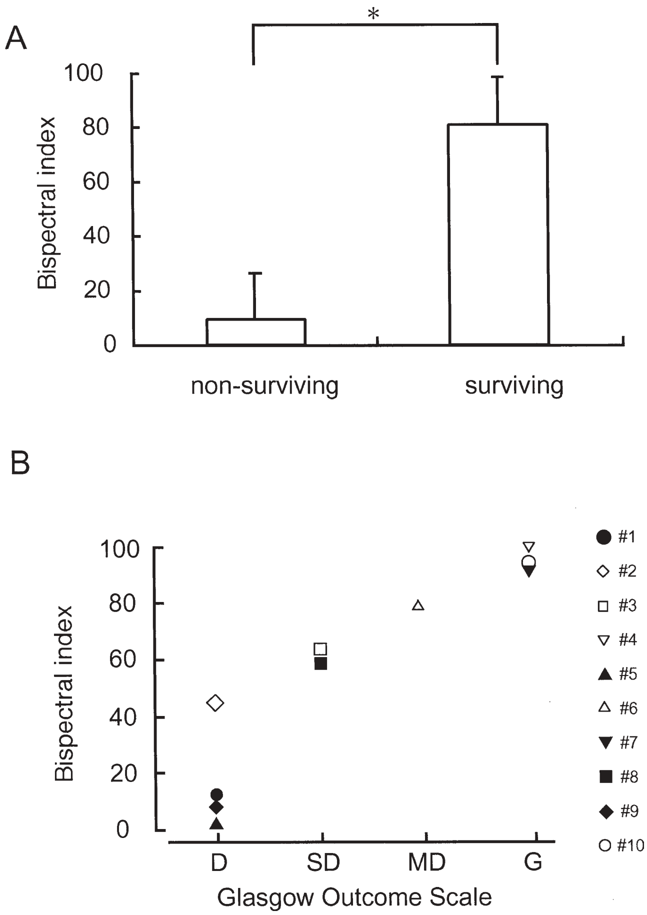

Fig. 2. A Comparison of the BIS in surviving and nonsurviving groups on admission to the intensive care unit (ICU). The Glasgow Outcome Scale (GCS) of each patient was 3. $^*P < 0.01$. **B** Relation between the BIS on admission to the ICU and the GOS on discharge from the ICU. There is a good relation between the BIS and GOS ($P = 0.004$, $r = 0.956$). On the *right* are patient numbers from Table 1

though the BIS increased to >80 before admission to the ICU (patients 4, 7, 10), the GCS on admission to the ICU did not increase.

Discussion

This study showed that the BIS, which is a novel EEG-derived parameter, might predict the postresuscitative outcome after out-of-hospital cardiac arrest because there was a positive relation between the BIS on admission to the ICU and the GOS on discharge from the ICU (Fig. 2). Similarly, Gilbert et al. reported that there is a significant correlation between BIS and neurological scores (GCS) in unsedated, critically ill patients [6]. Some other research has shown that EEG results are useful for predicting long-term outcomes after anoxic or traumatic brain injury [7,8].

It has been reported that the closest correlation between prognosis and good outcomes was achieved with EEG results at 48h [9]. In our study, the BIS increased after about 30min of ROSC in patients with good or moderate recovery but not in patients with severe symptoms or death. Thus, the BIS may be used as an early-stage clinical tool to predict postresuscitative outcomes.

Although the BIS reached >80 after about 30min of ROSC in patients with good or moderate recovery, the patient's levels of awareness had not improved at that point (GCS 3). In general, patients receiving anesthesia lose consciousness at a BIS of 65 [5] and are awake at a BIS of 80 [5,10]. This discrepancy may indicate that the neuroelectrophysiological mechanism of awakening following brain damage caused by cardiac arrest is different from that for awakening following general anesthesia or sedation.

Electromyographic activity interference may be considered one of the most important limitations. During cardiopulmonary resuscitation (CPR) in the emergency room, the BIS recordings within 30min of ROSC could not be analyzed in three patients because of BIS contamination by EMG activity. To eliminate EMG activity, vecuronium was administered intravenously in the ICU before the BIS was measured. Recently, overestimation of the BIS in ICU patients without a muscle relaxant has been reported [11,12]. However, identification of contamination by EMG activity may be difficult during CPR. Tools that could discriminate such artifacts as EMG activity are needed.

Conclusions

The BIS may allow assessment of the patient's neurological status and postresuscitative outcome after cardiac arrest because it can be used to predict the postresuscitative outcome of patients with out-of-hospital cardiac arrest. In the future, the BIS may become an important tool for determining therapeutic strategies in out-of-hospital cardiac arrest patients.

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