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Is bispectral index (BIS) monitoring in the emergency department helpful for prognostication during resuscitation of cardiac arrest patients?

Chin Siah Lim[1], Joshua Yu Le Koh[2], Wai Yee Ng[3], Nur Shahidah[1] and Marcus Eng Hock Ong[1,4]

Abstract

Objective: It has been suggested that bispectral index (BIS) can be indicative of cerebral perfusion during advanced cardiac life support (ACLS) resuscitation of cardiac arrest patients. Our aim was to determine whether BIS monitoring during resuscitation in the emergency department (ED) can predict survival or neurological outcomes of patients with cardiac arrest.
Methods: This was a prospective, single-centre, observational cohort study in the ED of a tertiary hospital, where we included 100 patients whom received resuscitation in the ED between December 2010 and March 2014. We recorded BIS values, suppression ratio, electromyography and signal quality index; throughout the resuscitation. A research coordinator set up the monitoring apparatus at the earliest time possible.
Results: Out of the 100 patients recruited, 22 had a sustained return of spontaneous circulation (ROSC) and were admitted to the intensive care unit (ICU). Of these, 19 patients subsequently died in the ICU, two were discharged with good neurological recovery (cerebral performance category (CPC) 1) and one was discharged with poor neurological recovery (CPC4). By comparing the groups of patients who died in the ICU and were discharged, we found there was no significant difference in the initial BIS score ($p = 0.64$), the score upon ROSC ($p = 0.36$), the average BIS score 10 minutes post-ROSC ($p = 0.35$), nor the BIS score upon admission to the ICU ($p = 0.22$).
Conclusions: Very early monitoring of BIS before admission to the ICU predicts neither survival nor neurological recovery in patients with cardiac arrest. Very low BIS scores in the ED may not indicate a poor prognosis, especially in patients undergoing therapeutic hypothermia.

Keywords

Bispectral index, cardiac arrest, cerebral performance, emergency department, hypothermia, neurological recovery, prognosis, resuscitation, return of spontaneous circulation

Introduction

Out-of-hospital cardiac arrest (OHCA) is a major health problem, because it results in high mortality and disability. Cardiac arrest affects 700,000 individuals in Europe and more than 400,000 in the US, annually.[1] It is estimated that 400,000–460,000 people die every year from OHCA,[2] representing one-third of all cardiovascular deaths.[3] In the local context, the incidence of OHCA in a 1-year period was estimated to be 1500, of which only 3% survived to discharge.[4]

Spontaneous circulation may return in some patients; however, most victims end up with multiple organ failure and death, despite aggressive management. Even if they survive,

[1]Department of Emergency Medicine, Singapore General Hospital, Singapore
[2]Yong Loo Lin School of Medicine, National University Health System, Singapore
[3]Division of Research, Singapore General Hospital, Singapore
[4]Health Services and Systems Research, Duke-NUS Medical School, Singapore

Corresponding author:
Chin Siah Lim, Department of Emergency Medicine, Singapore General Hospital, 1 Hospital Drive, Singapore 169608, Singapore.
Email: lim.chin.siah@singhealth.com.sg

Table 1. Definition of BIS readings.

BIS value	A value that derives from processing raw EEG data and is calculated into a number between 0–100, indicating a patient's level of consciousness.
SQI	Measures the signal quality of the EEG channel source and is derived from calculating impedance data, artefact and other variables.
SR	The calculated percentage over the last 63-second period, where the signal is considered to be in an isoelectric (flatline) state.
EMG indicator	Displays the power in decibels in the frequency range between 70 –110 Hz. This frequency range contains power from muscle activity, as well as power from other high-frequency artefacts. EMG activity is low when the indicator is low.

BIS: bispectral index; EEG: electroencephalogram; EMG: electromyography indicator; Hz: Hertz; SQI: signal quality indicator; SR: suppression ratio.

they suffer from severe neurological disability. Hence, preserving neurologic function after resuscitation is a critical issue, which includes the ability to predict potential long-term outcomes at an early stage of resuscitation.

The primary end-point of advanced cardiac life support (ACLS) is cerebral resuscitation. Currently, there are no objective means to measure the effectiveness of advanced life support on cerebral resuscitation. Non-invasive and real-time measures of neurological status after cardiac arrest are needed, to make an accurate and early determination of post-resuscitative outcome. Bispectral (BIS) index monitoring during ACLS might provide an objective indication of cerebral resuscitation.[5–7]

Currently, there are no universally accepted objective means to measure the efficiency of resuscitation, to determine and prognosticate post-resuscitative outcome. Our study intends to explore the utilisation of a BIS monitoring device in the emergency department, during ACLS resuscitation. BIS measures the level of consciousness by processing the patient's electroencephalogram (EEG) information, and calculates a number between 0 and 100.[8] A BIS score of 0 indicates an absence of brain activity and a score of 100 indicates that the patient is fully conscious. It is currently extensively used by anaesthetists, to gauge the depth of anaesthesia during surgery. There are a series of case reports that suggest that BIS could be a useful method for monitoring cerebral function, and prognosticate survival and neurological outcome after cardiac arrest[5,6,9–12]; however, there have been few studies conducted that utilise BIS monitoring in the emergency department (ED).

BIS monitoring can potentially be used to predict resuscitative outcomes for cardiac arrest, and possibly assist the emergency physician to make the difficult decision to terminate or continue resuscitation with better confidence. It can also be a guide to initiate more aggressive resuscitation, using therapeutic hypothermia (TH) following cardiac arrest, or even extra-corporeal membrane oxygenation (ECMO), for example.

Methods

We conducted a prospective, single-centre, observational cohort pilot study of 100 patients whom presented with cardiac arrest to the ED of the Singapore General Hospital, between December 2010 and March 2013. As this was a pilot study, convenience sampling was used to determine the sample size of 100 patients. Cardiac arrest was defined as absence of spontaneous ventilation and absence of palpable carotid pulse. Any cardiac arrest patient with > 18 years of age was eligible for the study. Exclusion criteria were: Patients younger than 18 years of age and trauma-based arrest. The study was approved by the SingHealth Centralized Institutional Review Board. As these patients were unconscious and critically ill, a waiver of informed consent for this study was granted. Our primary objective was to establish whether the trend of BIS values during and after resuscitation in the ED would predict a return of spontaneous circulation (ROSC), survival or neurological recovery.

These patients received resuscitation as per ACLS protocols, regardless of their arrest location (in-hospital or out-of-hospital cardiac arrest). When a patient with cardiac arrest arrives in the ED, the medical team in the resuscitation room will immediately attend to the patient and resuscitate the patient, as per ACLS protocols. BIS Quatro sensor electrodes (Covidien Ltd, Minnesota, US) would then be applied on the patient's forehead, before connecting it to the BIS VISTA monitor (Covidien Ltd, Minnesota, US). This was done at the earliest time practicable, during on-going cardiopulmonary resuscitation (CPR). The data collected include: BIS values, suppression ratios (SRs), electromyographic (EMG) activity and the signal quality index (SQI). The definition of these readings are presented in Table 1. The readings were recorded throughout the patient management in the ED, until the patient was either admitted to the intensive care unit (ICU) or expired in the ED. The application and monitoring of the BIS apparatus did not interfere with the standard procedures for cardiac arrest and post-cardiac arrest management. The BIS monitor was covered with a cardboard flap, so as to blind the resuscitation team members to the BIS readings during resuscitation. Therapeutic hypothermia and emergency percutaneous coronary intervention (PCI), if indicated, were initiated after the patient had a ROSC, according to the departments' guidelines.

Outcome measures

Patient demographic and clinical data were collected by reviewing ambulance records from the Singapore Civil Defence Force, as well as in-hospital electronic medical records. Data collected included: Age, gender, medical history, arrest location and downtime, whether the arrest was witnessed, the presence of bystander CPR, the initial rhythm of the arrest, and continuous measurement of the BIS values. The BIS values were taken into account only when the SQI was above 50%.

We analysed the data by comparing three main groups (ROSC versus no ROSC, sustained ROSC until admission versus non-sustained ROSC and discharge alive versus deceased in the ICU). Then BIS data was analysed at specific time points and the intervals that could potentially be important in the process of resuscitation. The four potentially significant values are: The initial BIS score upon presentation, the BIS score on ROSC, the average BIS score for 10 minutes after ROSC and the average BIS score for the 10 minutes before admission to the ICU.

The judgement of functional neurological outcome was established using the cerebral performance category score (CPC) upon discharge. The neurological examinations of the study patients were performed by physicians whom were not involved in the ED management of the patients and whom were not informed about the results of the BIS monitoring.

Statistical analysis

Study data were entered using Microsoft EXCEL 2010 and analysed using SPSS version 22 (SPSS, Chicago, IL, USA). Descriptive statistics like the mean and standard deviation (SD), and frequencies, were used to describe the subjects' demographic and clinical characteristics. We used the Chi-square test to compare the difference between ROSC and non-ROSC groups. The distribution of the BIS values were skewed; therefore, a non-parametric test like the Wilcoxon rank sum test was used to compare the initial BIS, BIS upon ROSC and the 10-min post-ROSC between the three main groups. Receiver operator characteristic curves were constructed, to determine the area under the curve (AUC), and the optimal cut-off values to predict ROSC and survival. An alpha of < 0.05 was considered statistically significant.

Results

The demographic characteristics of the study's recruited patients are shown in Table 2. Out of the 100 patients recruited, 43 patients obtained ROSC, of which 22 had sustained ROSC and were admitted to the ICU. Of these patients whom were admitted to the ICU, three were discharged alive, with two of them discharged with good neurological recovery (Figure 1). Patients with ROSC had similar characteristics with the patients who had no ROSC, except for the initial rhythm of arrest, with a *p*-value of 0.02 (Table 3).

There was no significant difference in the initial BIS values, when comparing between the patients who had ROSC and those who did not have ROSC ($p = 0.55$). When comparing the groups of patients that had non-sustained ROSC versus sustained ROSC (Figure 2), there was no significant difference in the initial BIS score ($p = 0.52$), the BIS upon ROSC ($p = 0.69$) and the average BIS score 10 minutes after ROSC ($p = 0.71$).

For the patients whom had sustained ROSC and were admitted to the ICU, we compared the groups of patients whom had died in the ICU versus those whom were discharged alive: There was no significant difference in their initial BIS score ($p = 0.64$), their BIS upon ROSC ($p = 0.36$), their average BIS score 10 minutes after ROSC ($p = 0.35$) and their average BIS score 10 minutes before admission ($p = 0.22$); as is represented in Figure 3.

Table 2. Characteristics of study patients.

Characteristics	*n* = 100
Age, mean (SD)	64.7 (15.2)
Gender, male	76
Race	
Chinese	74
Malay	11
Indian	7
Other	8
Initial arrest rhythm	
Asystole	52
PEA	27
VF/VT	21
Witnessed arrest	66
Bystander CPR	26
Any ROSC	43
Therapeutic hypothermia initiated	10
PCI initiated	6
Outcome	
Died in ED	78
Survived to admission	22
Survived to discharge or remains alive at day 30 post-arrest	3
CPC 1 – 2	2

CPC: Cerebral performance category; CPR: cardiopulmonary resuscitation; ED: emergency department; PCI: percutaneous coronary intervention; PEA: pulseless electrical activity; ROSC: return of spontaneous circulation; VF/VT: ventricular fibrillation/ventricular tachycardia

In one patient who survived with good neurological recovery, the initial BIS values were very low, while undergoing therapeutic hypothermia. The areas of curve were < 0.7 and the *p*-values were insignificant, for all BIS values; therefore, they were not useful in predicting ROSC and survival, due to the small sample size.

Discussion

We believe that this is the first study that utilised the BIS monitor exclusively in the ED, during the early phase of on-going resuscitation, for patients presenting with cardiac arrest. Our results showed that BIS values during and after resuscitation in the ED predict neither ROSC nor survival. Two studies that used the BIS monitor during on-going resuscitation have conflicting findings. Chollet-Xemard et al.[13] reveal similar findings: That there was no relationship between the patient BIS values and their survival. Though their patient cohort was very similar, they applied the BIS monitor only after all the ACLS procedures has been initiated. Selig et al.[14] started BIS and SR monitoring as soon as possible after initiation of advanced life support, and if possible, during CPR (25/89); and this was continued for up to 72 hours. The average BIS and SR within the first 4 hours of resuscitation was able to predict an unfavourable neurological outcome, with a specificity of 89.5% and a sensitivity of 85.7%.

Several case reports have positively used the BIS monitor during cardiac arrest to monitor cerebral perfusion during

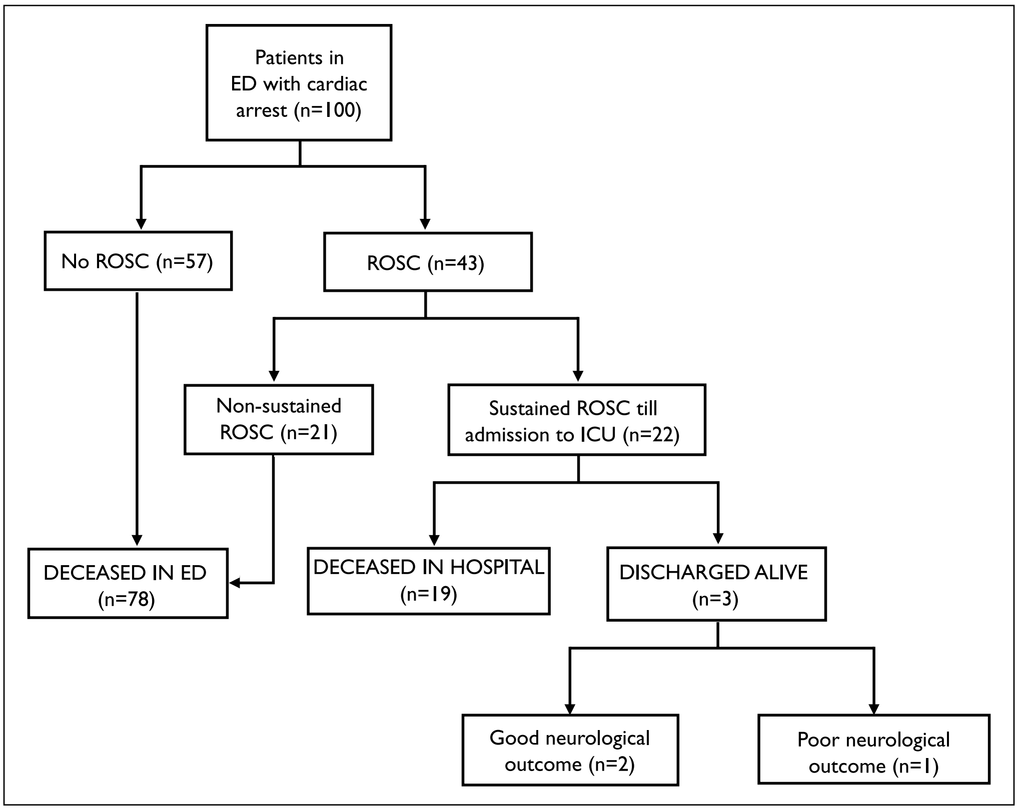

Figure 1. Flow chart of recruited participants.

Table 3. Comparison of patients with sustained and non-sustained ROSC.

Characteristics	With ROSC (%) (*n* = 43)	No ROSC (%) (*n* = 57)	*p* value
Out-of-hospital cardiac arrest	37 (86.0)	51 (89.5)	0.81
[a]Cardiac history	34 (79.1)	36 (63.2)	0.34
Witnessed arrest	31 (72.1)	36 (63.2)	0.28
Presence of bystander CPR	13 (30.2)	13 (22.8)	0.36
Downtime to CPR (≤ 10 min) by medical personnel. Median (IQR)	10.5 (5 – 21.5)	15 (7.5 – 24.5)	0.12
Initial rhythm			
Asystole	17 (39.5)	36 (63.2)	0.02
PEA	17 (39.5)	9 (15.8)	
VF/VT	9 (20.1)	12 (21.1)	

[a]Documented ischemic heart disease, diabetes or hypertension.
CPR: Cardiopulmonary resuscitation; IQR: interquartile range; min: minutes; PEA: pulseless electrical activity; ROSC: return of spontaneous circulation; VF/VT: ventricular fibrillation/ventricular tachycardia.

CPR.[5,6,12] Leary et al.[15] indicated that a BIS score of > 45 yielded the highest positive likelihood ratio for a favourable neurological outcome. Both Leary et al.[15] and Stammet et al.[16] also found that a BIS score of zero is uniformly predictive of poor outcomes, in 100% of the cases. Our study did not show any correlation between BIS scores and a favourable outcome. Of the two survivors with good outcomes (CPC 1), one of them had a BIS score of zero during resuscitation. Interestingly, this patient also received therapeutic hypothermia post-resuscitation, before admission to the ICU.

Therapeutic hypothermia (TH) is now recognised as an integral component of the complex bundle of post-resuscitation care. During CPR and ROSC, there are a multitude of complex physiological changes that occur stemming from an increase in cytokines and inflammatory mediators. This leads to increased activation of neutrophils and the vascular endothelium, resulting in a potent pro-inflammatory response.[17] Therapeutic hypothermia alters the pathophysiology of post-cardiac arrest syndrome, and it is possible that it affects BIS readings during ROSC. Others have studied the performance of BIS monitoring in patients using therapeutic hypothermia after successful CPR, cautiously showing positive results.[11,15,16,18–20] Furthermore, the physiological and inflammatory response during CPR and after achieving ROSC may have differing pathophysiological mechanisms, which could alter cerebral perfusion and BIS readings; however, we did not find any significant difference in BIS readings during the phases of resuscitation (with the initial reading during

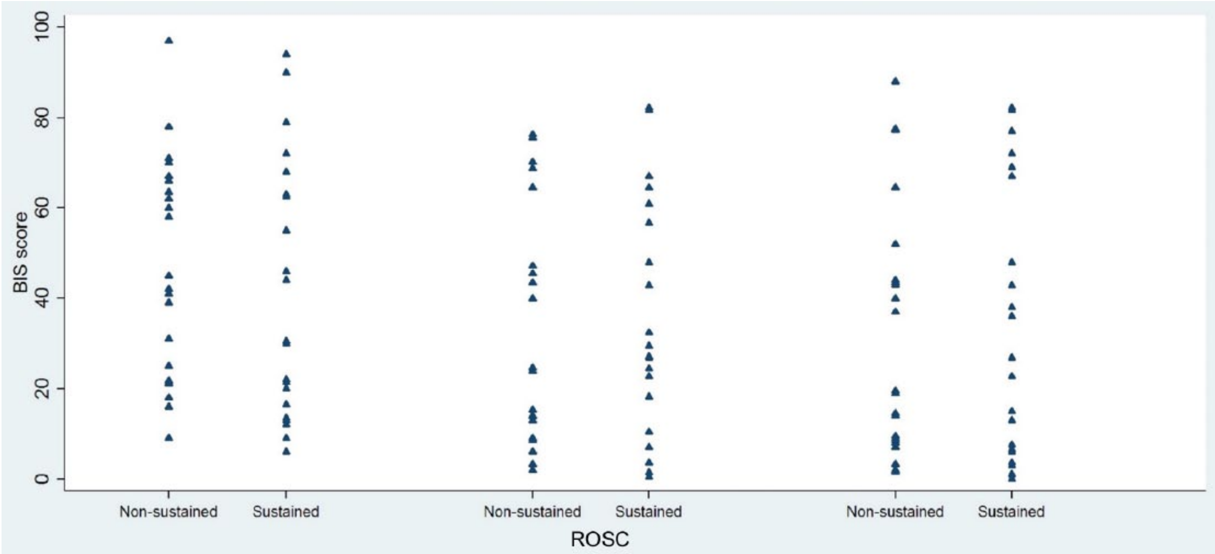

Figure 2. BIS values between sustained and non-sustained ROSC.
BIS: bispectral index; ROSC: return of spontaneous circulation.

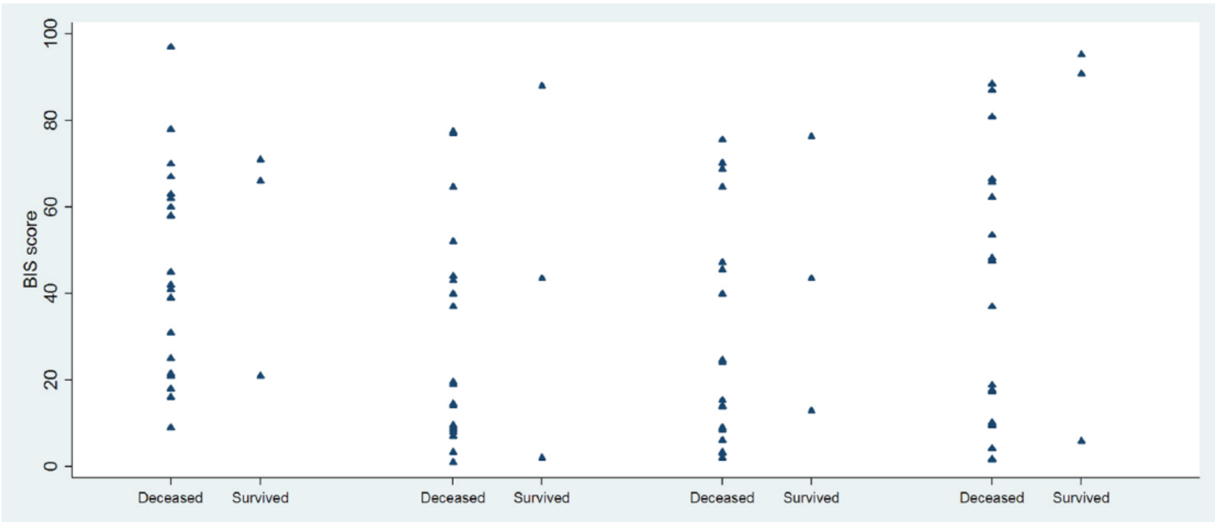

Figure 3. BIS values between the deceased and discharged live patients.
BIS: bispectral index.

CPR, during ROSC, 10 minutes after ROSC and 10 minutes prior to admission to the ICU).

Another factor that may affect BIS readings is a movement artefact, particularly during chest compressions. Fatovich et al.[7] conclude, in their case series, that movement during external chest compressions has a major impact on BIS values. This was further reinforced because their one case involving internal cardiac massage did not show a movement artefact. Also, they applied a BIS monitor on a cadaver and recorded BIS readings when they rocked the head side to side, mimicking head movements during CPR. All of our cases had their BIS monitor applied during ongoing CPR. These, and also the quality of CPR, are one of many possible confounding factors of patients with cardiac arrest in the ED that we were unable to stratify, due to the small sample size.

Our study had some limitations. There were heterogeneous characteristics of events surrounding cardiac arrest that may have affected the outcomes, for example, whether the cardiac arrest was witnessed, the presence of bystander CPR, and the downtime before CPR by medical personnel; however, as mentioned, we were unable to stratify according to such characteristics, because of the small sample size. Also, the very limited number of survivors raised the possibility of a Type 2 error. Also, we do not have data on the average time to obtain the first BIS value nor at which stage of the resuscitation the BIS monitor applied. Most of our patients had asystole as their presenting rhythm; and it is well established that asystole confers the poorest prognosis. With very poor cerebral perfusion and oxygenation in asystole, BIS values may not be accurate.

While BIS has been validated to be reflective of neurological activity during surgical anaesthesia, it might not be able to monitor neurological activity due to cerebral ischemia during cardiac arrest; however, a recent study by Stammet et al.[16] was able to show that the combination of the serum level of S100B and BIS monitoring accurately predicts outcome, in patients treated using therapeutic hypothermia after successful CPR. Perhaps this is the future direction for prognostication of cardiac arrest patients, by utilising a combination of tests.

In conclusion, our results showed that early BIS values do not predict ROSC, survival nor neurological recovery in patients presenting to the ED with cardiac arrest. In addition, a BIS score of zero may not indicate a poor prognosis, especially in patients undergoing therapeutic hypothermia.

Conflict of interest

The authors declare that there are no conflicts of interest.

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