Original Article

Effectiveness of the hemoglobin index for screening of subarachnoid hemorrhage in out-of-hospital cardiopulmonary arrest patients: a retrospective observational study

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Aim: The hemoglobin index (HbI) represents the amount of hemoglobin, which reflects regional tissue blood volume. The HbI is calculated in real time by a regional oxygen saturation (rSO_2) monitor. For the hypothesis of our HbI project, we theorized that HbI could be a new method for the screening of subarachnoid hemorrhage (SAH) in overcrowded emergency departments. As a first step, this study aimed to clarify the effectiveness of HbI in screening SAH in out-of-hospital cardiopulmonary arrest (OHCA) patients using the rSO_2 data of our previous studies.

Methods: In this single-center, retrospective, observational study, we examined HbI in patients with OHCA transferred to the Trauma and Acute Critical Care Center at Osaka University Hospital (Osaka, Japan) during the period between April 2013 and December 2015. A sensor attached to the patient's forehead monitored HbI continuously.

Results: Among 63 patients (40 men and 23 women; mean age, 76 [interquartile range (IQR), 66–85] years) with OHCA, five were diagnosed as having SAH (SAH group) and 58 were not (non-SAH group). The HbI values were significantly higher in the SAH group than in the non-SAH group (1.35 [IQR: 0.80–2.69] versus 0.41 [IQR: 0.32–0.61]), $P = 0.0042$). In the SAH group, with an HbI cut-off value of 1.18, the specificity and sensitivity were 96% and 80%, respectively, and the area under the receiver operating characteristic curve of HbI was 0.89.

Conclusions: The HbI might be useful for the screening of SAH in patients with OHCA. The application of HbI in the emergency department could be expected in the future.

Key words: Emergency medicine, near-infrared spectroscopy, out-of-hospital cardiac arrest, regional oxygen saturation, resuscitation

BACKGROUND

MOST SUBARACHNOID HEMORRHAGE (SAH) is caused by ruptured intracranial aneurysms or arteriovenous malformations. Subarachnoid hemorrhage can lead

to severe disability or death.[1] If there was a way to easily predict SAH non-invasively, it could help physicians to quickly predict SAH in the prehospital setting or emergency department.

In recent years, measurement of cerebral regional oxygen saturation (rSO_2) by near-infrared spectroscopy has attracted attention in many fields.[2–6] Our group has reported the effect of cerebral rSO_2 monitoring in patients with out-of-hospital cardiac arrest (OHCA) in resuscitation situations for several years.[6–10] In addition to cerebral rSO_2, we have also recorded the hemoglobin index (HbI). The HbI is the amount of hemoglobin measured by near-infrared radiation and is determined by the measurement of light intensity received at 805 nm. It also correlates with the regional blood volume. For the hypothesis of our HbI project, we theorized that the HbI might be effective in the screening of SAH,

especially in crowded emergency departments. Therefore, as a first step, using the rSO$_2$ data of our previous studies, we attempted in the present study to retrospectively clarify the effectiveness of HbI for the diagnosis of SAH in OHCA patients.

METHODS

Study design and data collection

THIS WAS A retrospective observational study that was approved by the Ethics Committee of Osaka University Graduate School of Medicine (No. 15599). The subjects were all patients with cardiopulmonary arrest (CPA) who were transferred to Osaka University Graduate School of Medicine (Osaka, Japan). The local institutional review board waived the need for informed consent because all subjects were in CPA. The sensor of the rSO$_2$ monitor described below was attached to the patient's forehead in the emergency department (Fig. 1A). During resuscitation, the medical staff could see the rSO$_2$ and HbI values displayed on the monitor, which were automatically recorded. However, they did not change the treatment according to the cerebral rSO$_2$ and HbI data. We retrospectively collected and analyzed data from these patients with CPA.

Near-infrared spectroscopy rSO$_2$ and HbI monitoring system

An rSO$_2$ monitor (TOS-OR; Fujita Medical Co., Tokyo, Japan)[6,9,10] was used to measure the cerebral rSO$_2$ and HbI values. The TOS-OR system measures the oxygen saturation based on the Beer–Lambert law, using three different wavelengths of near-infrared LED light, which has specific absorbance to oxyhemoglobin and deoxyhemoglobin. The degree of oxygen saturation is calculated using the correlation of oxygen saturation with the ratio R/IR of the absorbance of two wavelengths (R and IR) of oxyhemoglobin and deoxyhemoglobin, respectively. The 800–810-nm wavelengths show the same degree of absorbance in both oxyhemoglobin and deoxyhemoglobin. Therefore, we could measure the changes in the amount of total hemoglobin (oxyhemoglobin
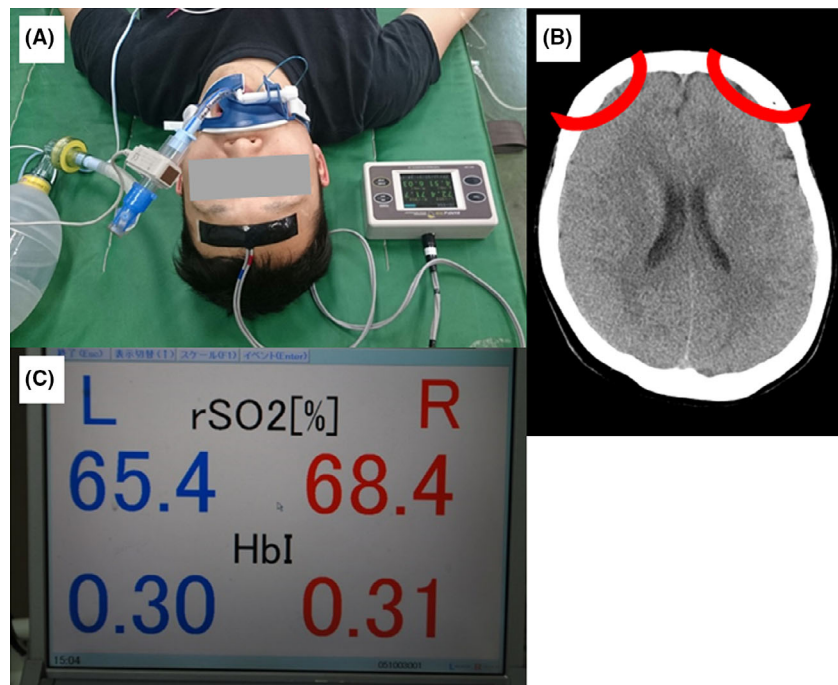

Fig. 1. Photographs showing measurement of a mock patient, the field of regional oxygen saturation (rSO$_2$) measurement, and the screen of the near-infrared spectroscopy unit (rSO$_2$ monitor). A, The detector consists of two sensors placed on the forehead of the patient to monitor the bilateral frontal lobes. B, Lights pass through the skin to a depth of approximately 3 cm, and the reflected lights are sensed by a photodiode. Therefore, we think that the monitor measures within the range indicated by the red lines on a head computed tomography scan. C, The screen of the rSO$_2$ monitor simultaneously shows the values of rSO$_2$ and the hemoglobin index (HbI) on left (L) and right (R) sides of the patient's forehead.

and deoxyhemoglobin) using these wavelengths even if the oxygen saturation changed. The lights pass through the skin to a depth of approximately 3 cm, and the reflected lights are sensed by a photodiode (Fig. 1B). The reflected lights represent the hemoglobin information mainly in the cerebral cortex. The system can measure rSO_2 data every second without the need for cardiac pulsations.

Hemoglobin index

If we measure the degree of absorption using the 800–810-nm wavelengths with the same degrees of absorbance of both oxyhemoglobin and deoxyhemoglobin, we can obtain information proportional to the amount of hemoglobin present, regardless of the oxygen saturation. If the light-receiving element receives a large amount of light, then the output voltage will be high. With larger amounts of hemoglobin, an increased amount of light is absorbed, which results in less reflected light and thus a lower output voltage. Output voltage is thus inversely proportional to the amount of hemoglobin present. To convert the measured voltage by wavelength to a value that correlates with the hemoglobin amount, the use of the reciprocal of the measured value (measured voltage) allows us to obtain the proportionate value. In the TOS, the reciprocal of the measured voltage is calculated and displayed as the HbI (Fig. 1C).[11] The HbI is the relative value of an abstract number and thus has no units. Moreover, the HbI represents the amount of hemoglobin that is present just beneath the sensor and does not represent the local hemoglobin concentration around the entire brain cortex.

In the TOS, a calculation method that uses a combination of a calibration curve and phantom (calibrator) is adopted based on the abovementioned facts, which results in a system with reliably reproducible values and also enables correction of variation in the elements of the sensor. We assumed a phantom standard of 1. The TOS can compare HbI values between patients by using a phantom.

Data analysis

Two HbI values were acquired continuously from the left side and right side of the forehead. The average of those two values was calculated.

Statistical analysis

Patient characteristics and outcomes were evaluated between the two groups using the Wilcoxon rank-sum test for continuous variables and Fisher's exact test for categorical variables. Continuous variables are presented as the median and interquartile range (IQR). To analyze the effectiveness of diagnosing SAH, we described a receiver operating characteristic (ROC) curve and calculated the cut-off value for HbI. All statistical analyses were undertaken with JMP Pro 13 for Windows (SAS Institute, Cary, NC, USA).

RESULTS

Patient characteristics

AMONG THE 63 patients (40 men and 23 women; mean age, 76 [IQR 66–85] years) with OHCA, five were diagnosed as having SAH (SAH group), and 58 were not diagnosed as having SAH (non-SAH group). Characteristics of the OHCA patients are shown in Table 1.

Hemoglobin index

Characteristics and HbI of the SAH patients are shown in Table 2. The values of HbI were significantly higher in the SAH group than in the non-SAH group of patients with OHCA (1.35 [IQ, 0.80–2.69] versus 0.41 [IQR, 0.32–0.61]), $P = 0.0042$) (Fig. 2). The values of HbI were not significantly different between the survivor group ($n = 8$) and the non-survivor group ($n = 55$) (0.67 [IQR, 0.44–0.80] versus 0.41 [IQR, 0.32–0.61]), $P = 0.06$).

Area under the ROC curve

In the SAH group, with an HbI cut-off value of 1.18, the specificity and sensitivity were 96% and 80%, respectively. The area under the ROC curve of HbI was 0.89 (Fig. 3). With an HbI cutoff value of 1.18, the diagnosis of SAH was

Table 1. Characteristics of out-of-hospital cardiopulmonary arrest patients with or without subarachnoid hemorrhage (SAH)

	SAH ($n = 5$)	Non-SAH ($n = 58$)	P-value
Sex, n (%)			1.0000
Female	2 (40.0)	21 (36.2)	–
Male	3 (60.0)	37 (63.8)	–
Age, years; median (IQR)	57 (46.0–60.5)	78 (69.5–86)	0.0009
Prognosis, n (%)			1.0000
Survival	0 (0.0)	8 (13.8)	–
Death	5 (100.0)	50 (86.2)	–

IQR, interquartile range.

Table 2. Characteristics and hemoglobin index (HbI) of out-of-hospital cardiopulmonary arrest patients with subarachnoid hemorrhage

Patient	Age	Sex	Enhanced CT	Angiography	Location of rupture	Location of hemorrhage	Extravasation into subdural space	Outcome	HbI
1	57	Male	+	+	A-com An.	Basicranial area to brain surface	None	Death	3.85
2	64	Female	+	−	Lt VA dissection	Basicranial area to brain surface	None	Death	1.18
3	57	Female	+	−	Lt PCA An.	Basicranial area to brain surface	None	Death	1.53
4	40	Male	+	−	Rt VA dissection	Only basicranial area	None	Death	0.41
5	52	Male	−	−	s/o Rt MCA An.	Basicranial area to brain surface	None	Death	1.35

A-com, anterior communicating artery; An, aneurysm; CT, computed tomography; Lt, left; MCA, middle cerebral artery; PCA, posterior cerebral artery; Rt, right; s/o, suspect of; VA, vertebral artery.
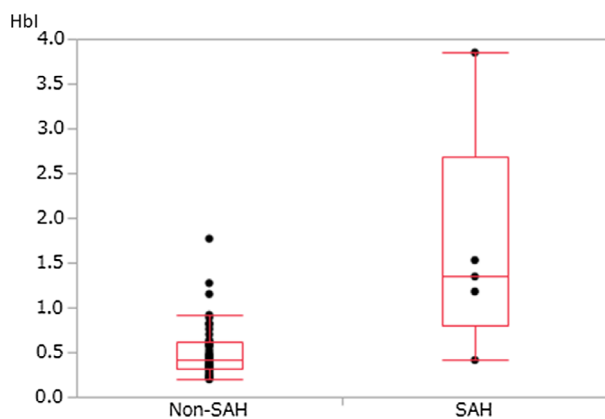

Fig. 2. Comparison of hemoglobin index (HbI) values between the subarachnoid hemorrhage (SAH) group and non-SAH group of patients with out-of-hospital cardiopulmonary arrest. The HbI values are significantly higher in the SAH group than in the non-SAH group (1.35 [interquartile range, 0.80–2.69] versus 0.41 [interquartile range, 0.32–0.61]), $P = 0.0042$).

Fig. 3. Area under the receiver operating characteristic curve of the hemoglobin index (HbI) in out-of-hospital cardiopulmonary arrest patients with subarachnoid hemorrhage. With an HbI cut-off value of 1.18, the specificity and sensitivity were 96% and 80%, respectively, and the area under the receiver operating characteristic curve of HbI was 0.89.

significantly different between the patients with HbI ≥ 1.18 and those with HbI < 1.18 ($P = 0.0001$) (Table 3).

DISCUSSION

FROM THE RETROSPECTIVE analysis of our rSO$_2$ study data, this study revealed that the values of HbI in patients with OHCA were significantly higher in the SAH group than non-SAH group and that the area under the ROC curve indicated high accuracy for the diagnosis of SAH. To
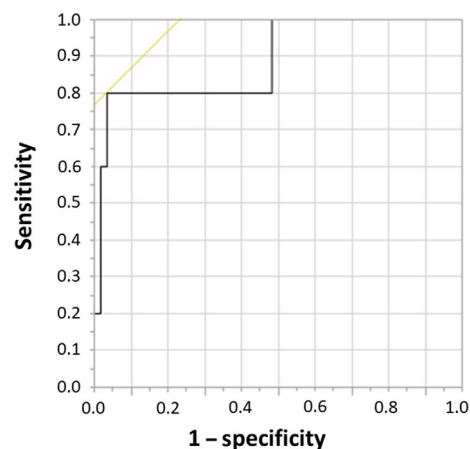
our knowledge, this is the first report to assess the effectiveness of the HbI for the diagnosis of SAH in patients with OHCA. A previous study reported that HbI values of 20 adults were distributed between 0.8 and 1.2.[12] The values of HbI in four of the five SAH patients with OHCA in the present study were higher than those in the 20 adults. We have no HbI data on general patients with SAH; therefore, we will also need to collect HbI data from these patients with SAH. The true purpose of our HbI project is not to screen for SAH in OHCA patients but rather to screen for SAH in patients

Table 3. Number of out-of-hospital cardiopulmonary arrest patients with and without a diagnosis of subarachnoid hemorrhage (SAH) based on hemoglobin index (HbI) value

	Non-SAH	SAH	Total
HbI ≥ 1.18	2	4	6
HbI < 1.18	56	1	57
Total	58	5	63

suspected of having SAH in overcrowded emergency departments. Our findings not only provide basic HbI data on OHCA patients but could also help to improve the ability to screen for SAH in patients who walk into an emergency department.

In this study, we evaluated the average of two HbI values obtained from the left side and right side of the forehead, not trend data. The rSO$_2$ values indicate the overall oxygen saturation including the arteries, veins, and capillaries. Therefore, the values of rSO$_2$ change depending on the circulation or oxygenation. Although we have reported trend data of rSO$_2$ in our previous studies,[6–10] HbI represents the amount of hemoglobin present, so we thought that it would be reasonable to evaluate the average HbI.

Despite the significantly higher values of HbI in the SAH group and the high diagnostic accuracy for SAH (Figs. 2 and 3), two patients were not diagnosed as having SAH in the HbI ≥ 1.18 group, and one patient was diagnosed as having SAH in the HbI < 1.18 group (Table 3). In the former two patients, head computed tomography (CT) showed acute subdural hematoma possibly due to trauma that occurred when the patients fell immediately after cardiac arrest. In the latter patient, the head CT showed SAH only in the basicranial area (Fig. 4). There was no hemorrhage on the brain surface that the TOS monitor could detect. The problem of the inability to detect hemorrhage in deeper areas of the brain needs to be examined in the future.

The HbI values were obtained within a few minutes after emergency department admission, indicating that the measurement of HbI is quick and easy. In recent years, emergency department crowding has become a big problem.[13,14] Therefore, HbI can be a very useful indicator in those emergency patients who are suspected of having SAH. The HbI could enable emergency physicians to prioritize between a medical examination or CT examination.

There are some limitations in this study. First, this was a single-center, retrospective study with a small sample size. Second, the HbI values of all CPA patients were not included during the study period. We only included patients with OHCA in whom a head CT and measurement of HbI were obtained. Third, the infrared lights of the TOS only pass through the skin to a depth of approximately 3 cm, so this monitor can only detect hemoglobin on the brain surface. Additional improvements in the rSO$_2$ and HbI monitor are required for its use in SAH screening in the emergency department, and these are currently underway. Finally, the
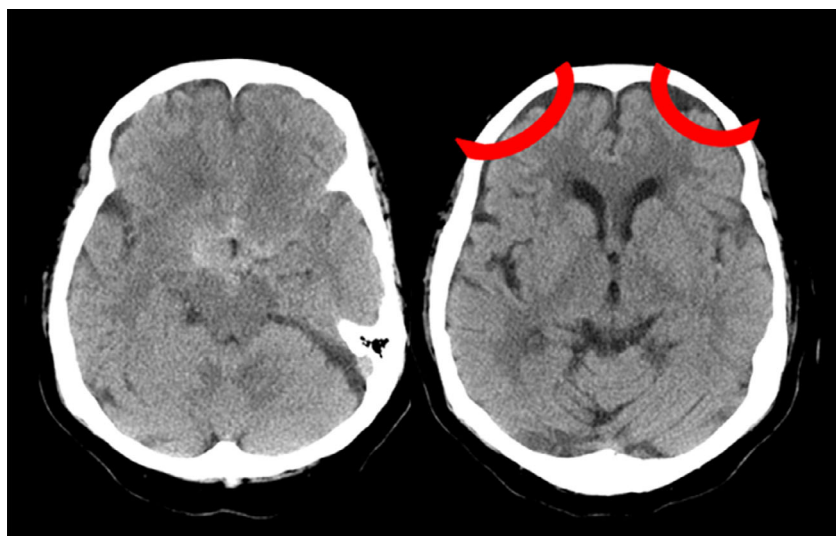

Fig. 4. Head computed tomography scan of a patient with subarachnoid hemorrhage, which shows subarachnoid hemorrhage only in the basicranial area. There was no hemorrhage on the brain surface that the monitor could detect. The problem is that hemorrhage in the deep brain area cannot be detected.

objective of this study was to evaluate only patients with OHCA. Therefore, a prospective study in the emergency department to evaluate patients suspected of having SAH will need to be undertaken with the improved monitor in the future.

CONCLUSION

THIS STUDY SHOWED that, among patients with OHCA, those with SAH had higher HbI values than those without SAH. The application of HbI to the emergency department could be expected in the future.

ACKNOWLEDGMENTS

DISCLOSURE

Approval of the research protocol: This study was approved by the Ethics Committee of Osaka University Graduate School of Medicine (No. 15599).
Informed consent: N/A.
Registry and the registration no. of the study/trial: N/A.
Animal studies: N/A.
Conflict of interest: None declared.

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