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Prospective Analysis of Pre-Hospital Cerebral Oxygen Saturation Monitoring During CPR by Emergency Personnel

Tessa Wright[1]*, Chloe Matthews[1]

[1]*Department of Family Nursing, School of Health, University of Auckland, Auckland, New Zealand.*

Abstract

Regional cerebral oxygen saturation (rSO_2) offers a non-invasive indicator of brain perfusion. Despite its potential, the dynamics of rSO_2 during pre-hospital management of out-of-hospital cardiac arrest (OHCA) patients remain poorly understood. This study explored whether different temporal patterns of rSO_2 were linked to clinical outcomes. Between June 2013 and December 2019 in Osaka City, Japan, emergency life-saving technicians (ELTs) used portable devices to measure rSO_2 in OHCA patients. Serial changes were classified as type 1 (progressively increasing) or type 2 (stable or decreasing). Cases where monitoring began after return of spontaneous circulation (ROSC) were excluded. Outcomes included prehospital ROSC, survival to hospital admission, 1-month survival, and favorable neurological status (Cerebral Performance Category [CPC] 1–2). Among 87 patients analyzed, 40 exhibited type 1 patterns (median age 80.5 years, 50% male) and 47 type 2 patterns (median age 81 years, 59.6% male). After adjusting for potential confounders, type 1 patients were significantly more likely to achieve prehospital ROSC (27.5% vs. 4.3%; adjusted odds ratio [AOR] 5.67, 95% CI 1.04–30.96, $p = 0.045$) and survive to hospital admission (42.5% vs. 12.8%; AOR 3.56, 95% CI 1.11–11.43, $p = 0.033$). No statistically significant differences were observed in 1-month survival or neurological outcomes. An increasing trend in rSO_2 during pre-hospital resuscitation correlates with higher rates of ROSC and survival to admission. Real-time cerebral oxygen monitoring in the field may help optimize resuscitation approaches.

Keywords: Out-of-hospital cardiac arrest, Cerebral oxygenation, Near-infrared spectroscopy, Pre-hospital care, Emergency life-saving technicians, Portable monitoring

Introduction

Regional cerebral oxygen saturation (rSO_2) is a non-invasive indicator of cerebral perfusion that has been widely studied in resuscitation research [1–3]. Unlike single measurements, tracking the serial changes in rSO_2 over time may provide more meaningful insights into a patient's condition [4–6]. Although several studies have suggested that measuring rSO_2 at hospital arrival can help predict neurological outcomes in out-of-hospital cardiac arrest (OHCA) patients [7–9], our previous work has shown that rSO_2 values can fluctuate considerably depending on the patient's status at the time of measurement [3, 5, 6].

Most commercially available near-infrared spectroscopy (NIRS) devices are designed based on Ito *et al.*'s model, which assumes a fixed venous-to-arterial ratio in the cerebral cortex of roughly 70/30% or 75/25% [10–12]. However, evidence indicates that this ratio is not constant across patients [13], suggesting that using a fixed model may be suboptimal for device validation. Furthermore, rSO_2 values are affected by physiological variables such as cardiac output, $PaCO_2$, and pH, and measurements can differ between devices even for the same patient [14, 15]. Therefore, assessing relative changes from an individual patient's baseline is considered more reliable.

Corresponding author: Tessa Wright
Address: Department of Family Nursing, School of Health, University of Auckland, Auckland, New Zealand
E-mail: ✉ t.wright.familycare@yahoo.com
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In the prehospital setting, there is limited evidence on how rSO_2 changes during cardiopulmonary resuscitation (CPR) in OHCA patients [16,17]. To address this, we developed a portable rSO_2 monitor (HAND ai TOS®; TOSTEC CO., Tokyo, Japan), small enough for use in the field (170 × 100 × 50 mm; 600 g). Since 2013, emergency life-saving technicians (ELTs) have been able to perform prehospital rSO_2 monitoring, marking the first such implementation worldwide [5, 18]. Preliminary findings published in 2016 highlighted the importance of monitoring serial rSO_2 changes during prehospital CPR and suggested its potential for informing new resuscitation strategies [5]. Building on this growing registry of OHCA patients, the present study aims to investigate the association between patterns of serial rSO_2 changes in the prehospital setting and patient outcomes.

Materials and Methods

Study design, participants, and setting

We conducted a prospective observational study enrolling adults (≥18 years) who experienced out-of-hospital cardiac arrest (OHCA) and had measurable cerebral rSO_2, treated by emergency life-saving technicians (ELTs) in Osaka City, Japan, between June 2013 and December 2019. Osaka City, situated in central Japan, spans 225.30 km^2 and had a population of 2,746,983 in 2020 [19]. Of the city's 63 EMS ambulance teams, nine were gradually equipped with portable rSO_2 monitoring devices, beginning with a single unit and expanding as the study progressed. Patients whose rSO_2 measurements began after return of spontaneous circulation (ROSC) were excluded from the analysis.

CPR was administered by ELTs according to the Japan Resuscitation Council Guidelines (2010 or 2015), which are based on the International Liaison Committee on Resuscitation recommendations [20, 21]. The rSO_2 sensor was applied to the patient's forehead by the ELTs, and treatment decisions were made independently of the rSO_2 readings.

We collected detailed pre-hospital information from EMS records, including age, sex, initial cardiac rhythm, bystander CPR status, and ambulance response times. Corresponding in-hospital outcomes were obtained from the treating facilities in accordance with the Utstein reporting style. Pre-hospital rSO_2 data were subsequently merged with the clinical database for analysis. The study protocol was approved by the Ethics Committee of Osaka University Graduate School of Medicine (No. 12446-7), and the requirement for informed consent was waived due to the patients' critical condition.

Portable rSO_2 monitoring system

For this study, we used a portable near-infrared spectroscopy (NIRS) device, HAND ai TOS® (TOSTEC CO., Tokyo, Japan), previously developed for field use [5, 18]. This device has not received regulatory approval from the Medicines and Healthcare Products Regulatory Agency (MHRA) or the U.S. Food and Drug Administration (FDA). HAND ai TOS measures cerebral oxygen saturation by emitting three near-infrared wavelengths that are selectively absorbed by oxyhemoglobin and deoxyhemoglobin. The light penetrates roughly 3 cm beneath the skin, and a photodiode captures the reflected signal, providing an estimate of hemoglobin oxygenation primarily in the cerebral cortex.

Evaluation of serial rSO_2 changes

The portable monitoring system allows rSO_2 measurements every second without requiring arterial pulsation, enabling continuous assessment in patients with cardiopulmonary arrest (CPA). Two rSO_2 readings, one from each hemisphere, were recorded simultaneously, and the mean value was used for analysis. In a prior study involving 15 healthy adults (10 men, 5 women; mean age 43.2 ± 8.9 years), the normal cerebral rSO_2 range was established as 71.2 ± 3.9% on room air [22]. For this study, serial rSO_2 patterns were classified into two categories: type 1, defined as an increase of at least 5% from the initial measurement, and type 2, defined as a non-increasing pattern.

Endpoints

The primary outcome was prehospital return of spontaneous circulation (ROSC). Secondary outcomes included survival to hospital admission, 1-month survival, and favorable neurological outcome, defined as Cerebral Performance Category (CPC) 1 or 2.

Drop phenomenon

During monitoring, we observed instances of a sudden, marked decrease in rSO_2, which we termed the "drop phenomenon," potentially reflecting acute cerebral circulatory failure. Patients exhibiting this phenomenon were analyzed separately to evaluate its clinical significance.

Statistical analysis

Continuous variables were compared using the Wilcoxon rank-sum test, while categorical variables were analyzed with the chi-square or Fisher's exact test, as appropriate. Multivariable logistic regression was performed to identify factors associated with study outcomes, with adjusted odds ratios (AORs) and 95% confidence intervals (CIs) reported. Potential confounders—selected based on prior literature and biological plausibility—included age, sex, witness status, and bystander CPR. Statistical significance was defined as $p < 0.05$. All analyses were conducted using JMP Pro 13 (SAS Institute Inc., Cary, NC, USA).

Results and Discussion

Patient characteristics

Figure 1 illustrates the flow of patients included in this study. During the study period, a total of 18,123 OHCA cases occurred in Osaka City, of which 94 patients were enrolled for rSO_2 monitoring. Seven patients were excluded because measurements began after return of spontaneous circulation (ROSC). Representative examples of type 1 and type 2 serial rSO_2 patterns are shown in **Figure 2**.

Table 1 summarizes the characteristics of patients who had not achieved ROSC at the start of rSO_2 monitoring. In total, 87 patients were included in the analysis: 40 patients exhibited type 1 (increasing rSO_2) patterns (median age 80.5 years [IQR 72–85.5], 50.0% male), and 47 patients exhibited type 2 (non-increasing rSO_2) patterns (median age 81 years [IQR 71–84], 59.6% male). The proportions of patients with witnessed arrest and those receiving adrenaline administration by ELTs were significantly higher in the type 1 group compared with type 2 ($p = 0.003$ and $p = 0.001$, respectively).

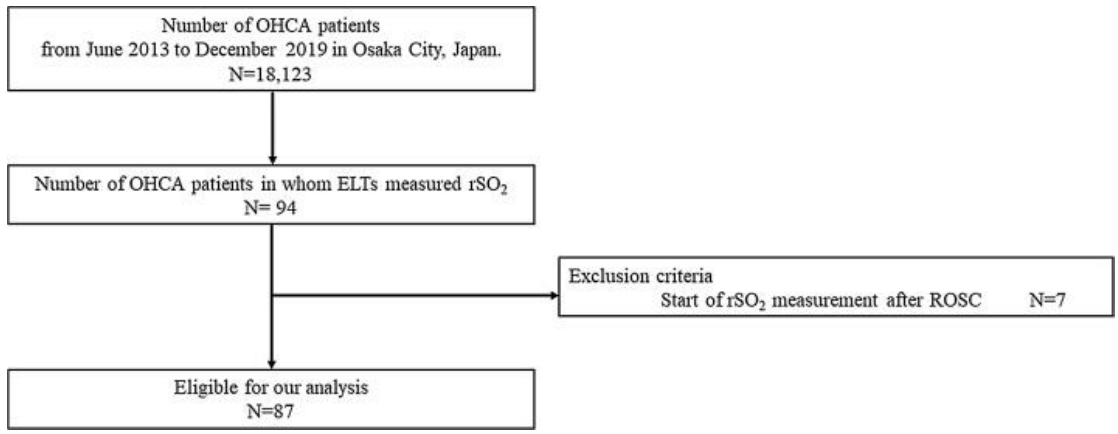

Figure 1. Patient flow, OHACA, out-of-hospital cardiac arrest; rSO_2, regional saturation of oxygen; ELTs, emergency life-saving technicians

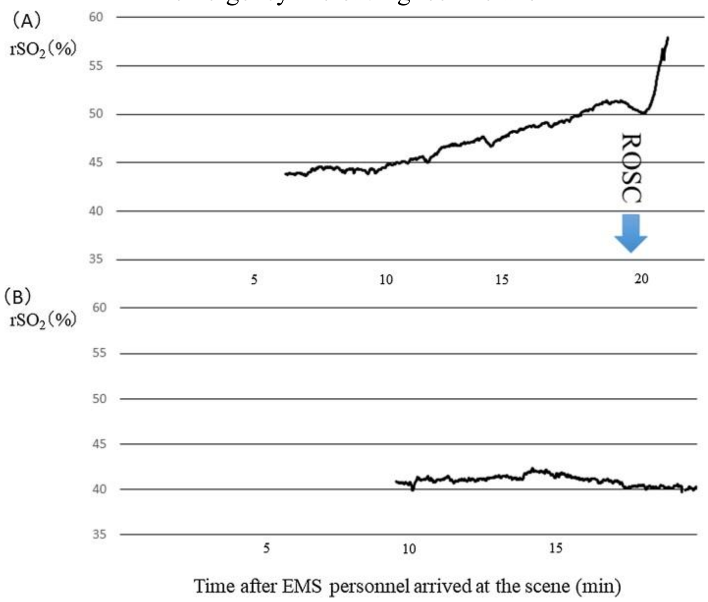

Figure 2. Representative examples of serial cerebral rSO_2 changes

(A) Type 1: Increasing pattern. A 95-year-old woman with pulseless electrical activity (PEA) on initial ECG (witnessed [+]; bystander CPR: unknown) showed gradually rising rSO_2 values, ultimately achieving ROSC. After ROSC, her rSO_2 increased more sharply than before.
(B) Type 2: Non-increasing pattern. A 33-year-old man with asystole on initial ECG (witnessed [–]; bystander CPR [–]) showed no rise in rSO_2 values and did not achieve ROSC in the prehospital setting.
Abbreviations: CPR, cardiopulmonary resuscitation; ECG, electrocardiogram; EMS, emergency medical service; PEA, pulseless electrical activity; ROSC, return of spontaneous circulation; rSO_2, regional cerebral oxygen saturation.

Table 1. Characteristics of patients without ROSC when ELT started rSO_2 monitoring

Characteristic	Type 1: Increasing pattern (n = 40)	Type 2: Non-increasing pattern (n = 47)	p-value
Sex, male	20 (50.0%)	28 (59.6%)	0.395
Age, years, median (IQR)	80.5 (72–85.5)	81 (71–84)	0.932
Initial cardiac rhythm, n (%)			0.097
Venticular fibrillation (VF)	5 (12.5%)	3 (6.4%)	
Pulseless electrical activity (PEA)	16 (40.0%)	11 (23.4%)	
Asystole	19 (47.5%)	33 (70.2%)	
Witnessed arrest, n (%)			0.003
Yes	25 (62.5%)	14 (29.8%)	
No	15 (37.5%)	33 (70.2%)	
Bystander CPR, n (%)			0.735
Yes	21 (52.5%)	21 (44.7%)	
No	16 (40.0%)	21 (44.7%)	
Unknown	3 (7.5%)	5 (10.6%)	
Adrenaline (epinephrine) administered by ELT, n (%)			0.001
Yes	16 (40.0%)	4 (8.5%)	
No	24 (60.0%)	41 (87.2%)	
Unknown	0 (0%)	2 (4.3%)	
Initial rSO_2, %, median (IQR)	42.1 (35.6–47.8)	45.6 (40.1–49.7)	0.114
"Drop phenomenon" observed, n (%)			0.330
Yes	3 (7.5%)	1 (2.1%)	
No	37 (92.5%)	46 (97.9%)	

CPR, cardiopulmonary resuscitation; ELT, emergency life-saving technician; IQR, interquartile range; PEA, pulseless electrical activity; ROSC, return of spontaneous circulation; rSO_2, regional saturation of oxygen; VF, ventricular fibrillation.

Comparison of Outcomes by Serial rSO_2 Pattern

Table 2 presents the outcomes according to the type of serial cerebral rSO_2 change, analyzed using multivariable logistic regression. Patients with type 1 (increasing) rSO_2 patterns had significantly higher rates of prehospital ROSC (11/40 [27.5%] vs. 2/47 [4.3%]; adjusted odds ratio [AOR] 5.67, 95% CI 1.04–30.96, p = 0.045) and survival to hospital admission (17/40 [42.5%] vs. 6/41 [12.8%]; AOR 3.56, 95% CI 1.11–11.43, p = 0.033) compared with type 2 (non-increasing) patterns. No significant differences were observed for 1-month survival (5/40 [12.5%] vs. 1/47 [2.1%]; AOR 3.21, 95% CI 0.32–32.72, p = 0.324) or favorable neurological outcome (CPC 1–2: 3/40 [7.5%] vs. 0/47 [0%]).

Table 2. Outcomes by type of serial change in cerebral rSO_2

Outcome	Type 1: Increasing pattern (n = 40)	Type 2: Non-increasing pattern (n = 47)	Crude OR (95% CI)	p-value	Adjusted OR* (95% CI)	p-value
Pre-hospital ROSC	27.5% (11/40)	4.3% (2/47)	8.53 (1.76–41.32)	0.008	5.67 (1.04–30.96)	0.045
Alive at hospital admission	42.5% (17/40)	12.8% (6/47)	5.05 (1.75–14.60)	0.003	3.56 (1.11–11.43)	0.033
1-Month survival	12.5% (5/40)	2.1% (1/47)	6.57 (0.73–58.81)	0.092	3.21 (0.32–32.72)	0.324
Favorable neurological outcome (CPC 1–2)	7.5% (3/40)	0% (0/47)	Not calculable	–	Not calculable	–

ORs were calculated for Increasing type vs. Non-increasing type.
CPR, cardiopulmonary resuscitation; CPC, Cerebral Performance Category; OR, odds ratio; CI, confidence interval; ROSC, return of spontaneous circulation; rSO_2, regional saturation of oxygen.
*Adjusted for age, sex, witness and bystander CPR.

Drop phenomenon

The "drop phenomenon" was observed in 6 of the 94 OHCA patients. A representative case is illustrated in **Figure 3**: an 82-year-old woman presenting with pulseless electrical activity (PEA) on initial ECG (witnessed [+]; bystander CPR [+]) exhibited gradually increasing rSO_2 values and initially achieved ROSC. However, during transport, despite the presence of QRS complexes on her ECG, her rSO_2 suddenly decreased. This prompted the ELT to recognize recurrent PEA and resume CPR.

Similarly, the other five patients initially achieved ROSC but experienced a sudden decline in rSO_2, after which the ELTs identified PEA and restarted resuscitation. Notably, the drop phenomenon occurred only in patients who had already achieved ROSC. **Table 3** summarizes the characteristics of these six patients who experienced this phenomenon.

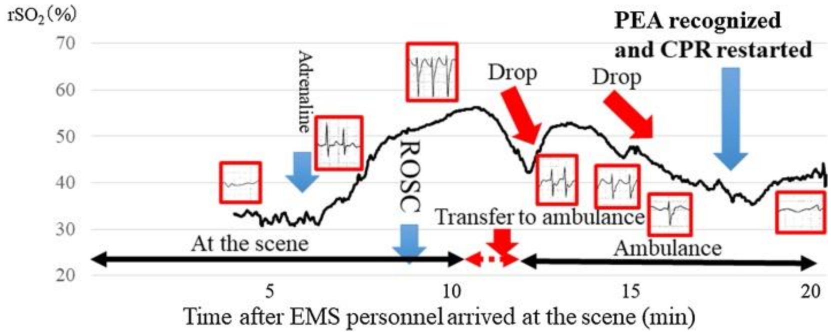

Figure 3. Representative case of the "drop phenomenon" in serial rSO_2 monitoring

An 82-year-old woman with pulseless electrical activity (PEA) on initial ECG (witnessed [+]; bystander CPR [+]) showed a gradual increase in rSO_2 and initially achieved ROSC. During transport, although her ECG still displayed QRS complexes, her rSO_2 suddenly dropped. The ELT recognized recurrent PEA and resumed CPR.

Abbreviations: CPR, cardiopulmonary resuscitation; ECG, electrocardiogram; ELT, emergency life-saving technician; PEA, pulseless electrical activity; ROSC, return of spontaneous circulation; rSO_2, regional cerebral oxygen saturation.

Table 3. Characteristics of the 6 patients with 'Drop phenomenon' in the serial change of rSO_2 values

Case	Sex	Age	Bystander CPR	Administration of adrenaline by ELT	Initial rSO_2 value	Prehospital ROSC	Alive at hospital admission	1-month survival	CPC 1 or 2	Initial rhythm	Witness
1*	Female	82	–	+	31.0	Yes	Yes	No	No	PEA	+
2	Male	64	–	+	40.5 (after ROSC)	Yes	No	No	No	PEA	+
3	Male	58	–	–	50.3	Yes	Yes	No	No	PEA	+
4	Male	81	+	–	40.0	Yes	Yes	No	No	PEA	+
5	Male	79	–	–	53.3	Yes	No	No	No	PEA	+
6	Male	95	–	–	51.5 (after ROSC)	Yes	Yes	No	No	PEA	+

CPR, cardiopulmonary resuscitation; CPC, Cerebral Performance Category; ELT, emergency life-saving technician; PEA, pulseless electrical activity; ROSC, return of spontaneous circulation; rSO_2, regional saturation of oxygen **(*Figure 3)**.

In this study, we found that the pattern of serial changes in cerebral rSO_2, as measured by emergency life-saving technicians (ELTs) in the prehospital setting, was significantly associated with prehospital ROSC and survival to hospital admission. To our knowledge, this is the first study to examine serial rSO_2 patterns in OHCA patients outside the hospital. Our findings provide insight into dynamic cerebral oxygenation changes during resuscitation and may inform new prehospital strategies, such as real-time monitoring to guide triage or the selection of the most appropriate receiving hospital.

Multivariable logistic regression demonstrated that patients with type 1 (increasing) rSO_2 patterns had significantly higher rates of prehospital ROSC and survival to admission compared with type 2 (non-increasing) patterns **(Table 2)**. Previous studies have suggested that combining baseline rSO_2 with the magnitude of its rise over time may serve as a useful index for predicting ROSC and guiding CPR [3]. Increasing rSO_2 patterns during prehospital resuscitation have also been reported by Genbrugge *et al.* [16] and Prosen *et al.* [17]. However, Prosen *et al.* evaluated rSO_2 only in the five minutes preceding ROSC, limiting observations before patient transport. Unlike our portable monitor, the INVOS oximeter they used is not easily deployed in the field [5, 17]. Moreover, these prior studies focused primarily on absolute rSO_2 values, whereas our study emphasizes the trajectory and pattern of change rather than single measurements.

Our results, along with these previous reports [16,17], highlight the limitations of one-time rSO_2 measurements. Values fluctuate with the patient's physiological status even before hospital arrival, and initial rSO_2 values did not differ significantly between type 1 and type 2 patterns in our cohort ($p = 0.114$; **Table 1**).

Some studies suggest that rSO_2 increases before ROSC may reflect CPR quality [23, 24]. While small rises in rSO_2 may occur during effective CPR in patients who ultimately do not achieve ROSC [4], overall, pre-ROSC increases are not consistently linked to CPR performance. Parnia *et al.* reported that rSO_2 did not rise in non-ROSC in-hospital cardiac arrest patients, despite early high-quality CPR [25]. In our study, trained ELTs performed CPR, raising the question: what does an rSO_2 increase before ROSC signify? We hypothesize that such increases may indicate early cardiac activity, with a gradual return of spontaneous heartbeat preceding full ROSC. Once ROSC occurs, the pulse returns, and rSO_2 values rise sharply, as illustrated in **Figure 2**. Further studies are needed to confirm this hypothesis and elucidate the underlying physiological mechanisms.

In contrast, patients exhibiting a type 2 (non-increasing) rSO_2 pattern had very poor outcomes, with prehospital ROSC of 4.3%, survival to hospital admission of 12.8%, 1-month survival of 2.1%, and no patients achieving CPC 1–2 **(Table 2)**. Previous work by Takegawa *et al.* reported minimal rSO_2 increases during CPR in patients lacking sonographic cardiac activity or in those with Stanford type A aortic dissection [26]. We did not specifically assess whether such conditions were present among our type 2 patients. Further research is warranted to identify the clinical characteristics of patients displaying a non-increasing rSO_2 pattern. In the future, rSO_2-based transport criteria may help optimize hospital selection and resource allocation.

Another notable finding was the identification of the "drop phenomenon" **(Figure 3, Table 3)**, characterized by a sudden decrease in rSO_2 that may reflect abrupt cerebral hypoperfusion. **Figure 3** illustrates the relationship between ECG waveforms and serial rSO_2 changes. In the prehospital setting, ELTs can monitor ECG but cannot continuously assess pulse. Detecting a drop phenomenon could prompt more frequent pulse checks and earlier recognition of pulseless electrical activity (PEA), representing one of the most valuable potential benefits of prehospital rSO_2 monitoring.

This study has several limitations. First, rSO_2 monitoring was not blinded, raising the possibility that observed values could have influenced CPR performance. Second, the limited availability and high cost of monitors prevented universal monitoring of all CPA patients during the study period. Third, the low number of ventricular fibrillation cases limited analysis of initial ECG rhythms. Fourth, we could not compare rSO_2 measurements with alternative perfusion markers, such as end-tidal CO_2. Fifth, rSO_2 values may increase in the final 1–2 minutes before ROSC, potentially reflecting the onset of spontaneous circulation prior to measurement.

Conclusion

An increasing pattern of serial rSO_2 changes (type 1) was significantly associated with prehospital ROSC and survival to hospital admission. Continuous prehospital monitoring of cerebral rSO_2 may facilitate earlier recognition of resuscitation status and could inform the development of new strategies to improve outcomes in OHCA patients.

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Ethics statement: None.

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