Chapter 17
Changes of Cerebral Oxygen Metabolism and Hemodynamics During ECPR with Hypothermia Measured by Near-Infrared Spectroscopy: A Pilot Study

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Abstract (Background) The 2010 CPR Guidelines recommend that extracorporeal cardiopulmonary resuscitation (ECPR) using an emergency cardiopulmonary bypass (CPB) should be considered for patients with cardiac arrest. However, it is not yet clear whether this therapy can improve cerebral circulation and oxygenation in these patients. To clarify this issue, we evaluated changes of cerebral blood oxygenation (CBO) during ECPR using near-infrared spectroscopy (NIRS). (Methods) We employed NIRS to measure CBO in the bilateral frontal lobe in patients transported to the emergency room (ER) after out-of-hospital cardiac arrest between November 2009 and June 2011. (Results) Fifteen patients met the above criteria.

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The tissue oxygenation index (TOI) on arrival at the ER was 36.5 %. This increased to 67.8 % during ECPR ($P<0.001$). The one patient whose TOI subsequently decreased had a favorable neurological outcome. (Conclusion) Increase of TOI during ECPR might reflect an improvement in cerebral blood flow, while decrease of TOI after ECPR might reflect oxygen utilization by the brain tissue as a result of neuronal cell survival. NIRS may be useful for monitoring cerebral hemodynamics and oxygen metabolism during CPR.

17.1 Introduction

Cardiac arrest is a major public health problem worldwide. Despite decades of efforts to promote cardiopulmonary resuscitation (CPR) science and education, the survival rate for out-of-hospital cardiac arrest remains low [1–3]. In Japan, the SOS-KANTO study showed that a favorable neurological outcome at 30 days was extremely rare in patients with out-of-hospital cardiac arrest who arrived at the emergency hospital in cardiac arrest [3–6]. The 2010 CPR Guidelines indicated that organized post-cardiac arrest care with an emphasis on multidisciplinary programs that focus on optimizing hemodynamic, neurologic, and metabolic function (including therapeutic hypothermia (TH)) may improve survival to hospital discharge among victims who achieve return of spontaneous circulation (ROSC) following cardiac arrest either in- or out-of-hospital [2]. TH is one intervention that has been shown to improve outcome for comatose adult victims of witnessed out-of-hospital

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cardiac arrest when the presenting rhythm was ventricular fibrillation (VF) [7, 8]. The 2010 CPR Guidelines recommended that comatose adult patients with ROSC after out-of-hospital VF cardiac arrest should be cooled to 32–34 °C for 12–24 h (Class I) [2] and that extracorporeal CPR (ECPR) using an emergency cardiopulmonary bypass (CPB) should be considered for patients with inhospital cardiac arrest when the duration of the no-flow arrest was brief, and the condition leading to the cardiac arrest was reversible or amenable to heart transplantation or revascularization (Class IIb) [2]. Since 1996, we have performed ECPR using emergency CPB with TH, followed by percutaneous coronary intervention (PCI) if necessary, on patients who arrive at the emergency room (ER) in cardiac arrest [9, 10]. Our preliminary study indicated that early attainment of a core temperature of 34 °C during cardiac arrest had neurological benefits for patients with out-of-hospital cardiac arrest who underwent CPB and PCI [10]. However, it is not yet clear whether this therapy can improve cerebral circulation and oxygenation in these patients. To clarify this issue, we evaluated changes of cerebral blood oxygenation (CBO) during ECPR using near-infrared spectroscopy (NIRS). NIRS, an optical technique, is an attractive tool for this purpose because it allows noninvasive, continuous measurements of CBO changes with high time resolution and is easy to use [11, 12].

17.2 Methods

17.2.1 Patients

Between November 2009 and June 2011, we employed NIRS (NIRO-200NX, Hamamatsu Photonics, Japan) to measure CBO in the bilateral frontal lobe in patients transported to the ER after out-of-hospital cardiac arrest. The patients were included in a prospective observational study. They were enrolled in this study when they met the following criteria: aged 18–74 years, cardiac arrest witnessed by bystanders, presumed cardiac etiology of cardiac arrest according to the Utstein style guidelines [13], defibrillation using automated external defibrillator by bystander and/or emergency medical personnel, and persistent cardiac arrest on arrival at the ER [10]. Exclusion criteria were a tympanic-membrane temperature below 30 °C on arrival at the ER, successful ROSC within 10 min of arrival at the ER with conventional ALS; non-cardiac etiology of cardiac arrest; or pregnancy. Patients were also excluded if their families refused to give informed consent for participation in this study [10].

17.2.2 Procedures

Our treatment protocol of extracorporeal CPR for induction of hypothermia with PCI is shown in Fig. 17.1 [10]. On arrival at the ER, the attending physicians

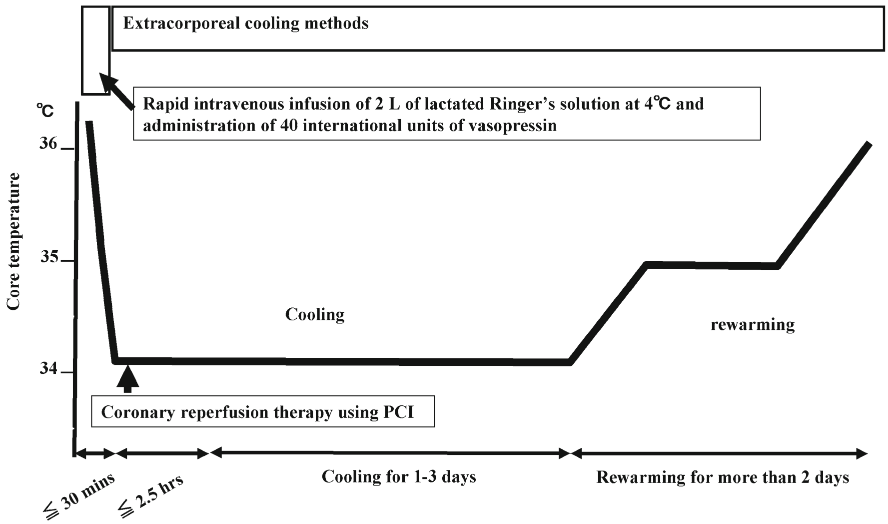

Fig. 17.1 Protocol of extracorporeal cardiopulmonary resuscitation (*CPR*) for induction of hypothermia with percutaneous coronary intervention (*PCI*). On arrival of the patient at the emergency room (*ER*), extracorporeal CPR using emergency cardiopulmonary bypass plus intra-aortic balloon pumping was immediately performed. Subsequently, emergency coronary angiography with PCI was performed in cases of suspected acute coronary syndrome

assessed as soon as possible whether a patient was eligible for this study after conventional ALS, including rapid intravenous infusion of 2 L of lactated Ringer's solution at 4 °C and the administration of 40 international units (IU) of vasopressin, and employed NIRS to measure CBO in the bilateral frontal lobe in patients. CPB plus intra-aortic balloon pumping was initiated when ROSC could not be achieved within 10 min of arrival. After implementation of CPB plus intra-aortic balloon pumping, emergency coronary angiography was performed during cardiac arrest in cases of suspected acute coronary syndrome (ACS). Subsequently, coronary reperfusion therapy using PCI during extracorporeal CPR was performed immediately.

17.2.3 Statistical Analysis

All analyses were performed using the SPSS software package (version 16.0 J SPSS, Chicago, IL, USA). Continuous variables are expressed as mean ± SD. Differences in the mean levels of tissue oxygenation index (TOI) between arrival at the ER, administration of 40 IU of vasopressin, and implementation of CPB were tested by Mann–Whitney *U* test for unpaired values with two-tailed *P* values of <0.05.

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17.3 Results

During the study period, 15 patients met the above criteria. Characteristics of these patients are presented in Table 17.1. The mean age was 57.0 ± 12.6 years. The proportion of male patients was 93.3 %. The mean time interval from collapse to the implementation of CPB was 51.6 ± 16.6 min, and the mean time interval from arrival at the ER to implementation of CPB was 17.9 ± 7.7 min. The proportion of patients due to ACS was 66.6 %.

The TOI on arrival at the ER was 36.5 ± 7.0 % (Fig. 17.2). This increased to 42.3 ± 6.9 % following administration of 40 IU of vasopressin ($P < 0.001$) and to 67.8 ± 7.9 % following implementation of CPB ($P < 0.001$). Moreover, oxyhemoglobin (Oxy-Hb) increased by 14.1 ± 6.3 μM, and deoxyhemoglobin (Deoxy-Hb) decreased by 16.8 ± 8.4 μM. After the implementation of CPB, the one patient whose TOI subsequently decreased had a favorable neurological outcome at 30 days after cardiac arrest (Fig. 17.3).

17.4 Discussion

This study shows that ECPR with TH can improve cerebral circulation and oxygenation in these patients. In cardiac arrest patients, clinically relevant recovery depends strongly on the restoration of cerebral function, which in turn depends on two major

Table 17.1 Baseline characteristics of the study populations

Characteristics	Patients ($n = 15$)
Age (years)	57.0 ± 12.6
Male sex (no. (%))	14 (93.3)
Prehospital treatment (no. (%))	
Defibrillations	14 (93.3)
Administration of intravenous epinephrine	7 (46.7)
Initial cardiac rhythm	
VF/pulseless VT	14 (93.3)
PEA	1 (6.7)
Asystole	0
Time interval (min)	
From collapse to implementation of CPB	51.6 ± 16.6
From arrival at the ER to implementation of CPB	17.9 ± 7.7
Cause of cardiac arrest	
Acute coronary syndrome	10 (66.6)
Cardiomyopathy	2 (13.3)
Others	3 (20.0)

VF/pulseless VT ventricular fibrillation/pulseless ventricular tachycardia, *PEA* pulseless electrical activity, *CPB* cardiopulmonary bypass, *ER* emergency room

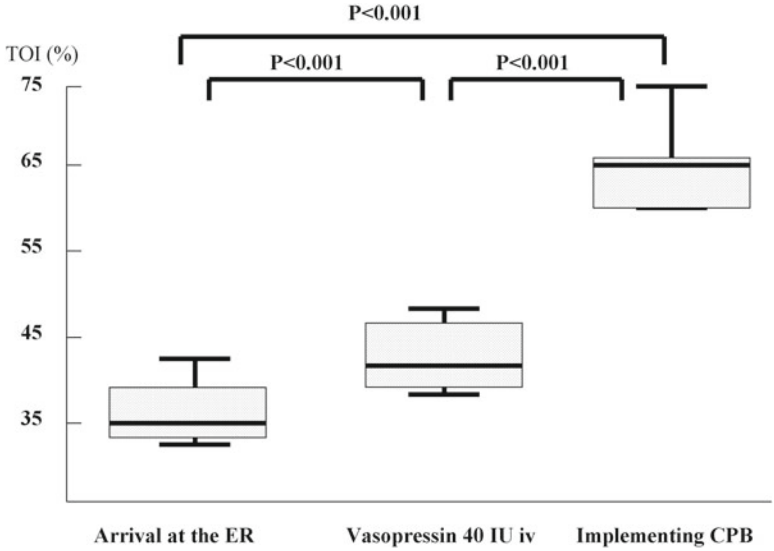

Fig. 17.2 The value of tissue oxygenation index (*TOI*) on arrival at the emergency room (*ER*) was 36.5 ± 7.0 %. This increased to 42.3 ± 6.9 % following administration of 40 IY of vasopressin ($P < 0.001$) and to 67.8 ± 7.9 % following implementation of cardiopulmonary bypass (CPB) ($P < 0.001$)

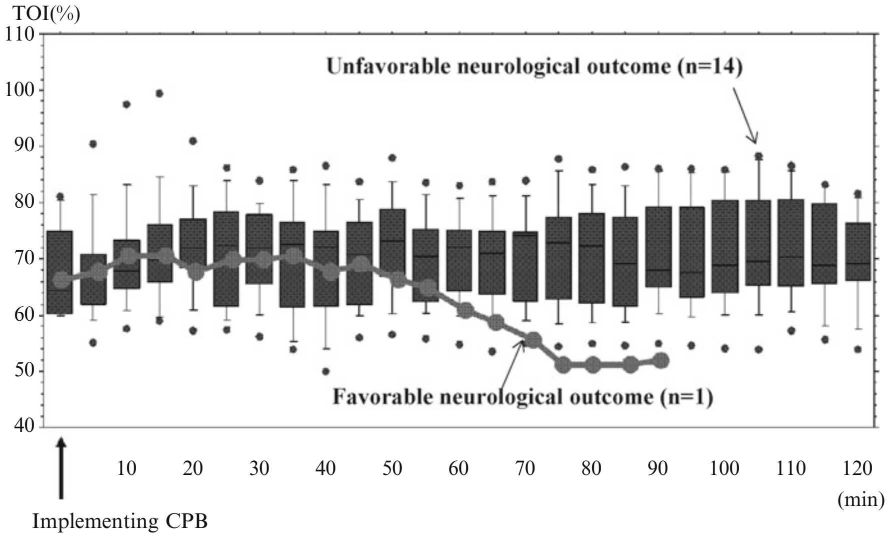

Fig. 17.3 After the implementation of cardiopulmonary bypass (*CPB*), the one patient whose tissue oxygenation index (*TOI*) subsequently decreased had a favorable neurological outcome at 30 days after cardiac arrest

factors, i.e., prevention or alleviation of global ischemia during the "no-flow time" and "low-flow (CPR) time" and minimization of post-reperfusion injury of the brain [14]. We speculated that the TOI on arrival at the ER may reflect the degree of global ischemia that persisted during the prehospital period. Increase of TOI by the implementation of CPB might reflect an improvement in cerebral blood flow, while decrease of TOI after the implementation of CPB might reflect oxygen utilization of the brain tissue as a result of neuronal cell survival. However, it should be noted that changes of TOI could be caused by other factors such as cerebral metabolic rate of oxygen ($CMRO_2$), arteriovenous (AV) volume ratio, and systemic oxygen saturation. Further studies are necessary to clarify these issues.

17.4.1 Study Limitations

There are several limitations to our study. First, it was not a multicenter study for resuscitation after out-of-hospital cardiac arrest. Second, our findings should be considered preliminary because of small sample size: there were only 15 patients in the present study, and there was only one patient with a favorable neurological outcome at 30 days after cardiac arrest.

17.5 Conclusions

We suggest that NIRS may be useful for monitoring cerebral hemodynamics and oxygen metabolism during ECPR.

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