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# The prognostic value of the grey-to-white matter ratio in cardiac arrest patients treated with extracorporeal membrane oxygenation☆

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ABSTRACT

*Aim:* The grey-to-white matter ratio (GWR) is a reliable predictor of the neurological outcome of out-of-hospital cardiac arrest (OHCA). However, the reliability in patients receiving extracorporeal membrane oxygenation-assisted cardiopulmonary resuscitation (ECPR) remains unknown. We evaluated the utility of the GWR in predicting neurological outcomes in ECPR-treated patients.
*Methods:* This single-centre retrospective study was conducted from July 2009 to January 2014. Patients who received ECPR for OHCA were classified into two groups: Cerebral performance category(CPC) 1–2 was defined as good, CPC 3–5 as poor outcome. Four GWR (GWR-AV[average], GWR-CO[cortex], GWR-BG[basal ganglia], and GWR-SI [simplified])were evaluated and compared between the groups.
*Results:* Of 38 patients who received ECPR for OHCA, 30 patients were enrolled. Five (16.7%) had a good outcome and 25(83.3%) a poor outcome. All GWR were significantly higher in the good outcome group than in the poor outcome group. ROC curve analysis produced the following areas under the curve: GWR-AV = 0.920 (95% CI 0.761 to 0.987), GWR-BG = 0.872 (95%CI 0.699 to 0.965), GWR-CO = 0.952 (95% CI 0.806 to 0.997), and GWR-SI = 0.848(95% CI 0.670 to 0.962). The cut-off value with 100% specificity for the prediction of the poor outcome was 1.23 for GWR-AV (sensitivity: 76%), 1.24 for GWR-BG (sensitivity: 88.0%), 1.22 for GWR-CO (sensitivity: 64%), and 1.21 for GWR-SI (sensitivity: 76%).
*Conclusions:* In ECPR, GWR of patients with poor outcome was significantly lower than that of patients with good outcome.



## Introduction

Cardiopulmonary resuscitation (CPR) is the treatment of choice for cardiopulmonary collapse and has been developed and modified to achieve better survival and good neurological outcome. Despite the major advances in resuscitation practice, the survival rate after out-of-hospital cardiac arrest (OHCA) has remained poor for over 30 years,[1,2] and most regions report a survival rate to hospital discharge of less than 10%.[3] Moreover, the rate of good neurological outcome (cerebral performance category (CPC) 1 or 2 at hospital discharge) is reported to be only 0.98% to 5.1%.[4,5]

Extracorporeal membrane oxygenation (ECMO) can facilitate the return of spontaneous circulation (ROSC) and provides adequate organ perfusion, especially to the brain, during resuscitation. ECMO has been used since 1976 as a therapeutic option during

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refractory cardiac arrest, the so-called extracorporeal CPR (ECPR).[6] In the 2010 AHA guideline, ECPR is an alternative method for patients who have a brief no-flow time and a reversible cause of cardiac arrest who are classified as Class IIb.[7–9] There are many cases with a favourable outcome after ECPR.[10–12] To avoid unnecessary prolongation of intensive care unit (ICU) admission when neurological recovery is unlikely, early prediction of outcome is an important aspect of post-resuscitation care in OHCA patients. Various serum markers, such as S-100 and neuron-specific enolase (NSE),[13] and bilaterally absent somato-sensory evoked potentials[14] appear to have the prognostic ability to predict a poor outcome after cardiac arrest. These methods often have limitations in predicting neurologic outcome, and cannot be used as a sole modality to predict the neurologic outcome. Brain imaging may also be helpful for predicting outcome. Brain magnetic resonance imaging (MRI) can evaluate the severity of global cerebral hypoxic–ischaemic injury after cardiac arrest,[15] but MRI is an expensive and time-consuming procedure.[16] Brain computed tomography (CT) obtained from OHCA patients treated with conventional CPR immediately after resuscitation may be useful in predicting their outcomes.[17] In particular, loss of the differentiation between grey matter and white matter on the brain CT is considered a marker of cerebral oedema in the post-cardiac arrest patient.[16–19] However, the reliability of this measure as a neurological predictor after ECPR remains unknown. We evaluated the association between the grey-to-white matter ratio (GWR) and the outcomes of patients treated with ECPR.

## Methods

### *Study population*

This study was retrospective study in a single institution, which is a tertiary referral centre and that covers the local population of about 280,000. This study was approved by our institutional review boards, which exempted informed consent. Between July 2009 and January 2014, 30 patients were treated with venoarterial ECMO using the femoral vein and artery. CPR for cardiac arrest patients was performed following the latest advanced cardiac life-support guidelines.

We included OHCA patients older than 18 years who had received ECMO and a brain CT to exclude intracranial haemorrhage. We excluded patients who had poor baseline neurology (CPC $\geq$ 3), patients with on-going intracranial haemorrhage or terminal malignancy.

After arriving at the hospital, the patients received CPR under the supervision of emergency medicine staff. If ROSC was not achieved within 10 min of CPR, the ECMO team reassessed each patient's status. If the status indicated ECMO, the ECMO was implanted immediately in the catheterisation laboratory during cardiac compressions. A brain CT scan was obtained within 1 h after pump on and just before ICU admission.

We obtained data retrospectively. The following variables were recorded after chart review: age, sex, witnessed arrest, bystander CPR, initial shockable rhythm, ROSC before ECMO pump on, collapse to ECMO pump-on time, Simplified Acute Physiologic Score II(SAPS II) after ECPR, ECMO duration, therapeutic hypothermia, and CPC at hospital discharge.[20–23]

### *ECMO system*

ECMO support comprises a polymethylpentene oxygenator. Three types of centrifugal pumps were used for ECMO. From 2007 to May 2010, a Capiox Emergency Bypass System (Terumo, Inc., Tokyo, Japan) or a Bio-Pump (Medtronic Inc., Minneapolis, MN, USA) were used; after June 2010, a ROTAFLOW Centrifugal Pump (Maquet Inc., Hirrlingen, Germany), was used. Venoarterial ECMO was performed using a Bio-Medicus17-Fr arterial cannula (Medtronic Inc.) and a 21-Fr venous cannula (Bio-Medicus Multistage Femoral Venous Cannula; Medtronic Inc.). The technique of choice was peripheral vessel cannulation using a modified Seldinger technique through the femoral vein and femoral artery. The dimension of the catheters was selected based on the patient's body size.

ECMO was started by an ECMO team, which comprised a cardiac anaesthesiologist, cardiac surgeon, perfusionist, and nurse from the cardiac surgical ICU. The ECMO team was alerted by the emergency physician. While the cardiac surgeon initiated the cannulation, the perfusionist assembled the circuit and primed it with Ringer's lactate solution. After ECMO initiation, coronary angioplasty was performed if the cause was suspected to be of cardiac origin or to the cardiac surgery operating room. Withdrawal of ECMO for life-sustaining care was considered when there was irreversible multiple organ failure or severe neurologic damage equivalent to brain death after sufficient ECMO therapy. However, weaning off ECMO should only be considered after obtaining consent from the patient's relatives.

### *Determination*

Participants were scanned using a SOMATOM Sensation 64 CT scanner (Siemens, Erlangen, Germany) with 5 mm slices. Regions of interest (ROI) were placed independently by two readers who were radiologists. Investigators blinded to the clinical information opened the CT scans for each patient using commercial image-viewing software (PiView STAR;INFINITT Healthcare, Seoul, South Korea) with the window adjusted to "brain" and identified comparable brain slices at the level of the basal ganglia(BG) and two levels of the superior cortex as described previously.[21] Circular regions of measurement (0.1–0.15 $cm^2$) were placed over these ROI, and the average attenuation in Hounsfield units (HU) was recorded. At the BG level, the values were recorded bilaterally for the caudate nucleus (CN), putamen (PU), corpus callosum (CC), and posterior limb of the internal capsule (PIC). (Fig. 1). The GWR in the BG(GWR-BG) was calculated according to a previously reported equation as

$$\mathrm{GWR-BG} = \frac{(\mathrm{CN}+\mathrm{PU})}{(\mathrm{CC}+\mathrm{PIC})}.$$

We recorded values bilaterally for the medial cortex and medial white matter at the level of the centrum semiovale (MC1 and MWM1, respectively) and high convexity area (MC2 and MWM2, respectively). The cerebrum GWR was calculated as

$$\mathrm{GWR-cortical\,(CO)} = \frac{(\mathrm{MC1}+\mathrm{MC2})}{(\mathrm{MWM1}+\mathrm{MWM2})}.$$

The ratio of the sum of all ROI was calculated as follows:

$$\mathrm{GWR-average\,(AV)} = \frac{(\mathrm{CN}+\mathrm{PU}+\mathrm{MC1}+\mathrm{MC2})}{(\mathrm{CC}+\mathrm{PIC}+\mathrm{MWM1}+\mathrm{MWM2})}.$$

The GWR-BG was calculated using a simplified method as reported previously[16]:

$$\mathrm{GWR-simplified\,(SI)} = \frac{\mathrm{PU}}{\mathrm{PIC}}.$$

The ROI were measured and averaged to yield the mean value, and the four GWR (GWR-BG, GWR-CO, GWR-AV, and GWR-SI) were calculated as described above. Increasing cerebral oedema results in less attenuation in the grey matter and a lower GWR.

### *Outcome measurement*

We divided patients into two groups: (1) good outcome group was defined as patients who survived and were conscious and able