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## Clinical paper

# Intra-aortic balloon pump and survival with favorable neurological outcome after out-of-hospital cardiac arrest: A multicenter, prospective propensity score-matched study



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## Abstract

**Objectives:** This study aimed to evaluate whether intra-aortic balloon pump (IABP) use in nontraumatic out-of-hospital cardiac arrest (OHCA) patients who achieved return of spontaneous circulation (ROSC) is associated with favorable neurological outcome after OHCA.

**Background:** The association between the IABP use in OHCA patients and favorable neurological outcome has not been extensively evaluated.

**Methods:** The Comprehensive Registry of Intensive Cares for OHCA Survival (CRITICAL) study, a multicenter, prospective observational registry in Osaka, Japan, included consecutive nontraumatic OHCA patients aged  $\geq 18$  years who achieved ROSC from July 2012 to December 2016. The primary outcome was 1-month survival with favorable neurological outcome. Logistic regression analysis was used to evaluate the association between the IABP use or non-IABP use and favorable neurological outcome using one-to-one propensity score (PS) matching analysis.

**Results:** Among the 2894 eligible patients, 10.4% used IABP, and 89.6% did not use IABP. In all patients, the proportion of 1-month survival with favorable neurological outcome was higher in the IABP use group than in the non-IABP use group (30.7% [92/300] vs. 13.2% [342/2594]). However, in PS-matched patients, the proportions of 1-month survival with favorable neurological outcome were almost consistent, and there were no significant differences between the IABP use group and the non-IABP use group (37.3% [59/158] vs. 41.1% [65/158]; adjusted odds ratio, 0.97; 95% confidence interval, 0.48–1.96).

**Conclusions:** In this population, the current PS matching analysis did not reveal any association between the IABP use and 1-month survival with favorable neurological outcome among adult patients with ROSC after OHCA.

**Keywords:** Out-of-hospital cardiac arrest, Intra-aortic balloon pump, Percutaneous mechanical circulatory support, Post-Cardiac arrest syndrome

## Introduction

Out-of-hospital cardiac arrest (OHCA) is one of the critical public health problems, occurring for over 350,000 in the United States and over 120,000 in Japan every year.<sup>1–5</sup> Although the outcome in OHCA patients has been improving with continuous improvements in the chain of survival, it is still low, only approximately 10% even among bystander-witnessed OHCA patients.<sup>5</sup>

Recently, the importance of post-cardiac arrest care for OHCA patients who achieved return of spontaneous circulation (ROSC) has been recognized.<sup>6–8</sup> In post-cardiac arrest syndrome (PCAS), low cardiac output and high systemic vascular resistance may cause multiple organ failure and brain dysfunction.<sup>6</sup> Since intra-aortic balloon pump (IABP) modestly enhances cardiac output, increases coronary artery perfusion, decreases afterload, and maintains organ perfusion,<sup>9</sup> it might improve the neurological outcome of OHCA patients who achieved ROSC. Therefore, IABP has been used as one of the percutaneous mechanical circulatory supports (pMCSs) for OHCA patients who achieved ROSC in post-cardiac arrest care.<sup>6,10</sup> In a multicenter, prospective observational study, the IABP use in patients with acute myocardial infarction (AMI) complicated by cardiac arrest did not improve 1-month survival, whereas in a single-center retrospective observational study, the IABP use for OHCA patients as post-cardiac arrest care was associated with improved functional outcomes.<sup>11,12</sup> Thus, whether the use of IABP would improve the outcomes among OHCA patients who achieved ROSC is still controversial.

The CRITICAL study is a multicenter, prospective observational data registry in Osaka, Japan, designed to accumulate both pre- and in-hospital data on OHCA treatments.<sup>13</sup> Using this database, we evaluated whether the IABP use for nontraumatic OHCA patients who achieved ROSC would be associated with favorable neurological outcome after OHCA, based on a propensity score (PS)-matched method.

## Methods

### Study design and settings

We analyzed the database of the Comprehensive Registry of Intensive Cares for OHCA Survival (CRITICAL) study, which is a

multicenter, prospective observational data registry, designed to accumulate both pre- and in-hospital data on OHCA treatments. A complete description of the study methodology was previously provided.<sup>13</sup>

### Patient registry

The target area of the CRITICAL study is the Osaka Prefecture in Japan, which has an area of 1905 km<sup>2</sup> with a residential population of 8,839,469 inhabitants as of 2015.<sup>14,15</sup> In the Osaka Prefecture, there are 535 hospitals with 108,481 beds in 2012.<sup>16</sup> A total of 276 hospitals accept emergency patients from ambulances. Of them, 15 hospitals have critical care medical centers (CCMCs) that can accept emergency severely ill patients.<sup>17</sup> The CRITICAL study group consists of 13 CCMCs and 1 non-CCMC with a department of emergency treatments in the Osaka Prefecture in Japan. As many as 30% of OHCA patients in Osaka were transported to CCMCs and treated.<sup>18</sup>

In the CRITICAL study, we registered all consecutive patients suffering from OHCA, resuscitated by emergency medical service (EMS) personnel or bystander, and transported at the participating institution. This registry excluded patients with OHCA who were not performed cardiopulmonary resuscitation (CPR) by physicians after their arrival at the hospital and who or whose family members refused to participate in our registry. Additionally, OHCA patients who were transported at the participating institution after receiving any procedures in another hospital were excluded. Personal identifiers were removed from the CRITICAL study. Finally, in this study analyses, we included adult patients aged 18 years or over who had cardiac arrests of nontraumatic cause and who achieved ROSC between July 2012 and December 2016. The registry was approved by the Ethics Committee of Kyoto University as the corresponding institution, and each hospital also approved the CRITICAL study protocol as necessary.

### EMS systems in Osaka

Details of the EMS system in Osaka were described previously.<sup>19,20</sup> The 119 emergency telephone number is accessible anywhere in Japan including the Osaka Prefecture, and upon receipt of a 119 call, an emergency dispatch center sends the nearest available ambulance

to the site. Emergency services are provided 24 h every day; the system is single-tiered in 32 stations and two-tiered in two stations. The latter uses medics followed by physicians. Each ambulance includes a three-person unit providing life support. Most highly trained EMS personnel are called emergency life-saving technicians. They are allowed to insert an intravenous line and an adjunct airway and to use a semiautomated external defibrillator for OHCA patients. Emergency life-saving technicians are permitted to provide shocks without consulting a physician, and specially trained emergency life-saving technicians are allowed to perform tracheal intubation and to administer adrenaline for OHCA patients. All EMS providers performed CPR, basically according to the Japanese CPR guidelines.<sup>21</sup>

### **Prehospital and in-hospital measurements**

We obtained anonymized prehospital data from the All-Japan Utstein Registry of the Fire and Disaster Management Agency (FDMA), which is a prospective, population-based, nationwide registry of OHCA that uses the data recommended by the Utstein-style international guideline.<sup>22</sup> The detail of this registry has been described previously.<sup>23,24</sup>

In the CRITICAL study, detailed in-hospital data were prospectively collected for consecutive patients with OHCA after their arrival at the participating institution. These data were systemically merged with prehospital data from the All-Japan Utstein Registry of the FDMA using the following five items in both data: prefectures, emergency call time, age, gender, and the cerebral performance category (CPC) score.

The following in-hospital data of patients with OHCA after their arrival at the participating institution were collected prospectively: ROSC, first documented rhythm, actual detailed treatments for a patient with OHCA, causes of arrest, and outcome data. The cause of arrest was divided into cardiac and noncardiac cause. The diagnosis of cardiac or noncardiac cause was clinically determined by the physicians at the hospital where the patient was transported. The presumed cardiac cause was a diagnosis by exclusion. All patients who achieved ROSC were followed up 1 month after OHCA. As outcome data, 1-month survival and neurological status were collected. Neurological status was evaluated by the physician responsible for treating the patient using the CPC score with the following categories: category 1, good cerebral performance; category 2, moderate cerebral disability; category 3, severe cerebral disability; category 4, coma or vegetative state; and category 5, death or brain death.

### **Outcome measures**

The primary outcome measure was 1-month survival with favorable neurological outcome after OHCA. A favorable neurological outcome was defined as CPC score of 1 or 2. The secondary outcome measure was 1-month survival.

### **Statistical analysis**

Pre- and in-hospital information and outcomes were evaluated between the IABP use group and the non-IABP use group. We also assessed the trend in the proportion of the IABP use. To reduce the potential confounding effects in the comparison between the IABP use and the non-IABP use, we estimated a PS by using a logistic

regression model that adjusted for the following 20 variables: year (2012–2016), gender (male, female), age (continuous value), witness status (no, yes), bystander CPR (no, yes), public-access defibrillation (no, yes), dispatcher instruction (no, yes), first documented rhythm at prehospital (shockable, non-shockable, presence of pulse), adrenaline administration at prehospital (no, yes), tracheal intubation at prehospital (no, yes), time from call to hospital arrival (continuous value), first documented rhythm after hospital arrival (shockable, non-shockable, presence of pulse), adrenaline administration at in-hospital (no, yes), amiodarone administration at in-hospital (no, yes), lidocaine administration at in-hospital (no, yes), coronary angiography (no, yes), percutaneous coronary intervention (PCI) (no, yes), target temperature management (no, yes), extracorporeal membrane oxygenation (no, yes), and cause of arrest (cardiac, noncardiac). We performed a receiver operating characteristic curve analysis with an area under the curve of PS for predicting IABP use in patients with OHCA. One-to-one pair matching between the IABP use group and the non-IABP use group was performed using nearest neighbor matching without replacement, using calipers of width equal to 0.2 of the standard deviation of the logit of the PS. In order to measure covariate balance, we checked the standardized mean difference (SMD) of before and after matching. When the SMD is less than 0.25,<sup>25</sup> it means that there is a negligible imbalance between the two groups.

We investigated the association between the IABP use or non-IABP use and the favorable neurological outcome using the univariable and multivariable logistic regression analyses. Based on these analyses, we calculated the crude or adjusted odds ratio (OR) and their 95% confidence intervals (CIs). In multivariable logistic regression models, we adjusted for the above 20 variables used in the PS calculation. Moreover, we performed subgroup analyses by cause of arrest (cardiac, noncardiac), first documented rhythm after hospital arrival (shockable, non-shockable), or reperfusion therapy (PCI, non-PCI), using the univariable and multivariable logistic regression analyses.

All statistical analyses were performed using the SPSS statistical package version 24.0J (IBM Corp.) and R version 3.2.0 (The R Foundation for Statistical Computing). All tests were two-tailed, and P values <0.05 were considered statistically significant.

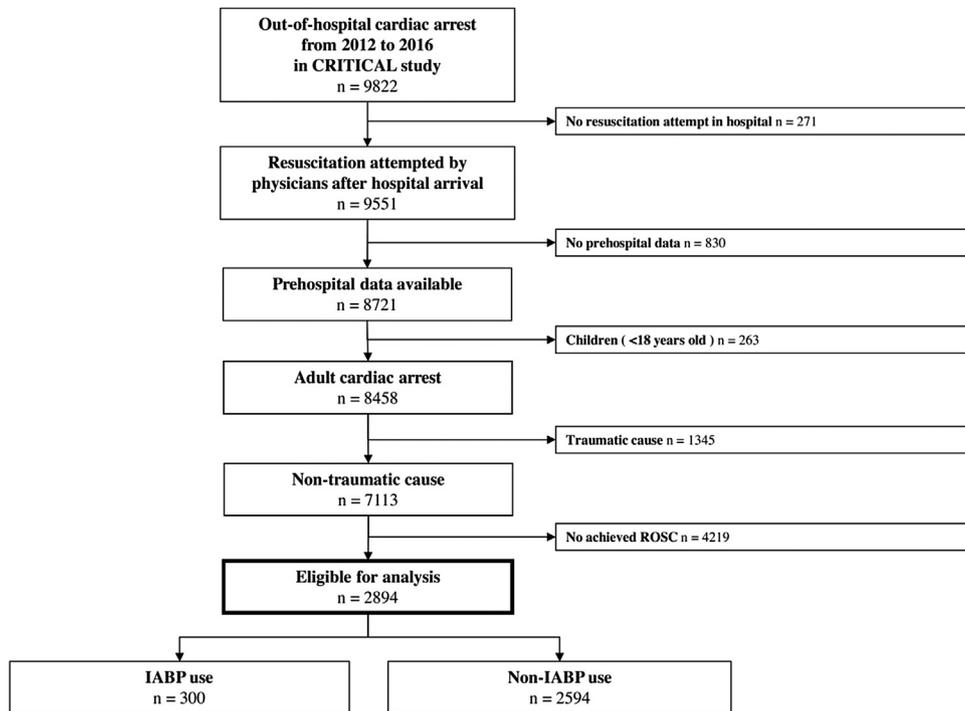
## **Results**

### **Study population**

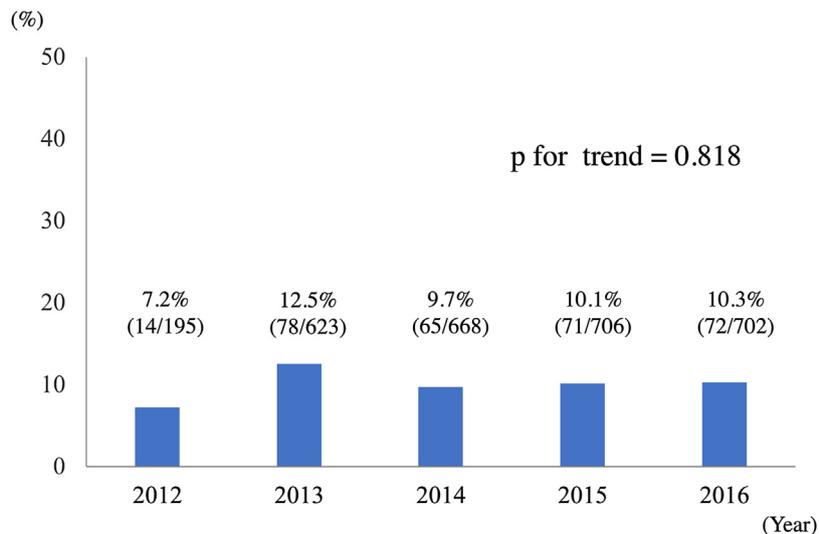
During the study period, 9822 patients with OHCA were documented (Fig. 1). Of the 9551 patient data in whom resuscitation was attempted at the hospitals, 8721 patient data were combined with the prehospital data. Of these, we excluded 263 children aged under 18 years, 1345 patients with traumatic OHCA, and 4219 patients who did not achieve ROSC. A total of 2894 patient (300 in the IABP use group [10.4%] and 2594 in the non-IABP use group [89.6%]) was eligible for our analysis. The proportion of the IABP use remained stable during the study period (from 7.2% in 2012 to 10.3% in 2016; p for trend=0.818) (Fig. 2).

### **Patient characteristics**

Patient characteristics, prehospital information, and in-hospital information of adult patients who achieved ROSC after nontraumatic



**Fig. 1 – Overview of out-of-hospital cardiac arrests from 2012 to 2015 in CRITICAL study. IABP = intra-aortic balloon pump.**



**Fig. 2 – Temporal trend in the proportion of the IABP use during the study period. IABP = intra-aortic balloon pump.**

OHCA by the IABP use or non-IABP use before and after PS matching are shown in Table 1. In all patients before PS matching, the IABP use group was more likely younger, male, to have shockable rhythm as the first documented rhythm by EMS personnel, to have shockable rhythm as the first documented rhythm after hospital arrival, administered with amiodarone and lidocaine, performed with coronary angiography, to undergo target temperature management and extracorporeal membrane oxygenation, and to have cardiac cause. After PS matching, 158 patients in each group were selected, and the area under the

receiver operating characteristic curve of PS was 0.967. The covariate balance between the groups in the score-matched patients was well improved.

**Outcomes**

Table 2 shows the outcomes of adult patients who achieved ROSC after nontraumatic OHCA between the IABP use group and the non-IABP use group. In all patients before PS matching, the proportion of

**Table 1 – Characteristics of out-of-hospital cardiac arrest of non-traumatic origin having return of spontaneous circulation with or without IABP use.**

	All patients			Propensity score matched patients		
	IABP <sub>use</sub> (N = 300)	Non-IABP <sub>use</sub> (N = 2594)	SMD	IABP <sub>use</sub> (N = 158)	Non-IABP <sub>use</sub> (N = 158)	SMD
Year, n (%)						
2012	14 (4.7)	181 (7.0)	0.099	7 (4.4)	7 (4.4)	<0.001
2013	78 (26.0)	545 (21.0)	0.118	39 (24.7)	32 (20.3)	0.106
2014	65 (21.7)	603 (23.2)	0.038	33 (20.9)	34 (21.5)	0.015
2015	71 (23.7)	635 (24.5)	0.019	42 (26.6)	39 (24.7)	0.043
2016	72 (24.0)	630 (24.3)	0.007	37 (23.4)	46 (29.1)	0.130
Age, median (IQR)	64 (50-72)	74 (63-82)	0.653	65 (50-73)	65 (51-74)	0.012
Adults aged 18–64 years old, n (%)	156 (52.0)	724 (27.9)		75 (47.5)	77 (48.7)	
Elderlies aged ≥65 years old, n (%)	144 (48.0)	1870 (72.1)		83 (52.5)	81 (51.3)	
Male, n (%)	242 (80.7)	1649 (63.6)	0.388	128 (81.0)	129 (81.6)	0.016
Witnessed, n (%)	238 (79.3)	1778 (68.5)	0.248	123 (77.8)	121 (76.6)	0.030
Bystander CPR, n (%)	122 (40.7)	956 (36.9)	0.078	72 (45.6)	71 (44.9)	0.013
Public-access defibrillation, n (%)	16 (5.3)	61 (2.4)	0.156	13 (8.2)	11 (7.0)	0.048
Dispatcher instruction, n (%)	105 (35.0)	939 (36.2)	0.025	59 (37.3)	59 (37.3)	<0.001
First documented rhythm by EMS, n (%)						
Shockable	221 (73.7)	430 (16.6)	1.401	112 (70.9)	112 (70.9)	<0.001
Non-shockable	61 (20.3)	1998 (77.0)	1.377	35 (22.2)	36 (22.8)	0.015
Presence of pulse	18 (6.0)	166 (6.4)	0.017	11 (7.0)	10 (6.3)	0.025
Adrenaline administration at pre-hospital, n (%)	77 (25.7)	629 (24.2)	0.033	42 (26.6)	41 (25.9)	0.014
Tracheal intubation, n (%)	73 (24.3)	746 (28.8)	0.100	40 (25.3)	39 (24.7)	0.015
Time from call to hospital arrival, mins, median (IQR)	30 (23-38)	32 (26-40)	0.013	29 (23-38)	31 (24-38)	0.044
First documented rhythm after arrived hospital, n (%)						
Shockable	126 (42.0)	113 (4.4)	0.997	55 (34.8)	46 (29.1)	0.122
Non-shockable	121 (40.3)	1818 (70.1)	0.627	56 (35.4)	55 (34.8)	0.013
Presence of pulse	53 (17.7)	663 (25.6)	0.193	47 (29.7)	57 (36.1)	0.135
Adrenaline administration at in-hospital, n (%)	227 (75.7)	1845 (71.1)	0.103	104 (65.8)	86 (54.4)	0.234
Amiodarone administration at in-hospital, n (%)	106 (35.3)	86 (3.3)	0.887	39 (24.7)	33 (20.9)	0.091
Lidocaine administration at in-hospital, n (%)	25 (8.3)	42 (1.6)	0.313	11 (7.0)	9 (5.7)	0.052
Coronary angiography, n (%)	286 (95.3)	377 (14.5)	2.782	144 (91.1)	148 (93.7)	0.096
Percutaneous coronary intervention, n (%)	171 (57.0)	136 (5.2)	1.348	78 (49.4)	75 (47.5)	0.038
Target temperature management, n (%)	189 (63.0)	429 (16.5)	1.079	96 (60.8)	92 (58.2)	0.052
Extracorporeal membrane oxygenation, n (%)	211 (70.3)	106 (4.1)	1.882	69 (43.7)	61 (38.6)	0.103
Cardiac cause, n (%)	281 (93.7)	1382 (53.3)	1.029	146 (92.4)	150 (94.9)	0.104

IABP, intra-aortic balloon pump; SMD, standardized mean difference; IQR, interquartile range; CPR, cardiopulmonary resuscitation; EMS, emergency medical service.

The area under receiver operating characteristic curve of the logistic regression model to calculate a propensity score was 0.967.

**Table 2 – Outcomes of out-of-hospital cardiac arrest of non-traumatic origin having return of spontaneous circulation with or without IABP use.**

	Total	IABP use	Non-IABP use	Crude OR	(95% CI)	Adjusted OR	(95% CI)
All patients <sup>a</sup>	(N = 2894)	(N = 300)	(N = 2594)				
One-month survival	764 (26.4%)	135 (45.0%)	629 (24.2%)	2.56	(2.00–3.26)	0.78	(0.48–1.26)
CPC 1 or 2	434 (15.0%)	92 (30.7%)	342 (13.2%)	2.91	(2.22–3.82)	0.93	(0.54–1.59)
Propensity score-matched patients <sup>a</sup>	(N = 316)	(N = 158)	(N = 158)				
One-month survival	170 (53.8%)	81 (51.3%)	89 (56.3%)	0.82	(0.52–1.27)	0.90	(0.49–1.62)
CPC 1 or 2	124 (39.2%)	59 (37.3%)	65 (41.1%)	0.85	(0.54–1.34)	0.97	(0.48–1.96)

IABP, intra-aortic balloon pump; CPC, cerebral performance category; OR, odds ratio; CI, confidence interval.

ORs were calculated for IABP use versus non-IABP use.

<sup>a</sup> Adjusted for year, gender, age, witness status, bystander CPR, public-access defibrillation, dispatcher instruction, first documented rhythm at pre-hospital, adrenaline administration, at pre-hospital, tracheal intubation, time from call to hospital arrival, first documented rhythm after arrived hospital, adrenaline administration at in-hospital, amiodarone administration, at in-hospital, lidocaine administration at in-hospital, coronary angiography, percutaneous coronary intervention, target temperature management, extracorporeal membrane oxygenation, cause of arrest.

1-month survival with a favorable neurological outcome was higher in the IABP use group than in the non-IABP use group (30.7% [92/300] vs. 13.2% [342/2594]). However, in PS-matched patients, the proportions of 1-month survival with favorable neurological outcome were almost consistent between the IABP use group and the non-IABP use group (37.3% [59/158] vs. 41.1% [65/158]). In adjusted logistic regression analysis, there were no significant differences between the IABP use group and the non-IABP use group (adjusted OR, 0.97; 95% CI, 0.48–1.96).

Table 3 shows the results of the subgroup analyses. In the subgroup analysis on the cause of arrest, among cardiac cause, the proportion of 1-month survival with favorable neurological outcome was 32.0% among the IABP use group and 20.2% among the non-IABP use group (adjusted OR, 1.18; 95% CI, 0.66–2.11). Among noncardiac cause, the proportion was 10.5% and 5.2%, respectively (adjusted OR, 0.15; 95% CI, 0.02–1.43). In the subgroup analysis on the first documented rhythm after hospital arrival, as for shockable rhythm, the proportions of 1-month survival with favorable neurological outcome were 41.3% for the IABP use group and 32.7% for the non-IABP use group (adjusted OR, 1.84; 95% CI, 0.72–4.67). As for non-shockable rhythm, the proportions were 5.8% and 2.3% for the IABP use group and the non-IABP use group, respectively (adjusted OR, 0.43; 95% CI, 0.13–1.48). In the subgroup analysis on the reperfusion therapy, regarding PCI, the proportions were 35.7% for the IABP use group and 60.3% for the non-IABP use group, respectively (adjusted OR, 1.06; 95% CI, 0.47–2.42). Regarding non-PCI, the proportions were 24.0% for the IABP use group and

10.6% for the non-IABP use group, respectively (adjusted OR, 0.72; 95% CI, 0.33–1.57).

## Discussion

In this multicenter, prospective observational study, the IABP use for adult patients who achieved ROSC after non-traumatic OHCA was not associated with improved 1-month survival with favorable neurological outcome compared with the non-IABP use, and the adjusted OR from matched cohort after PS matching was similar to one from all patient cohort before PS matching. Our findings provide implication for the CPR guidelines regarding the use of pMCS in the treatments of PCAS.

In this study, no associations between the IABP use and favorable neurological outcome were observed among OHCA patients who achieved ROSC. There were some preceding studies assessing the association between the IABP use and neurological outcomes after OHCA by using the PS method. In a multicenter, prospective observational study for patients with AMI complicated by cardiac arrest in Korea,<sup>11</sup> the IABP use was not associated with 1-month all-cause mortality, and this result was consistent with ours. On the other hand, in a single-center, retrospective observational study in patients with cardiac arrest due to cardiac cause in the United Kingdom,<sup>12</sup> the IABP use as post-cardiac arrest care was associated with favorable functional status at discharge, which is different from ours. Compared with our study population, subjects from the United Kingdom were more likely to have some factors related to better outcome after OHCA such

**Table 3 – Subgroup analysis of out-of-hospital cardiac arrest of non-traumatic origin having return of spontaneous circulation with or without IABP use.**

	Total	IABP use	Non-IABP use	Crude OR	(95% CI)	Adjusted OR	(95% CI)
<b>Cause of arrest<sup>a</sup></b>							
Cardiac cause	(N = 1663)	(N = 281)	(N = 1382)				
CPC 1 or 2	369 (22.2%)	90 (32.0%)	279 (20.2%)	1.86	(1.40 - 2.47)	1.18	(0.66 - 2.11)
Non-cardiac cause	(N = 1231)	(N = 19)	(N = 1212)				
CPC 1 or 2	65 (5.3%)	2 (10.5%)	63 (5.2%)	2.15	(0.49 - 9.49)	0.15	(0.02 - 1.43)
<b>First documented rhythm after arrived hospital<sup>b</sup></b>							
Shockable	(N = 239)	(N = 126)	(N = 113)				
CPC 1 or 2	89 (37.2%)	52 (41.3%)	37 (32.7%)	1.44	(0.85 - 2.45)	1.84	(0.72 - 4.67)
Non-shockable	(N = 1939)	(N = 121)	(N = 1818)				
CPC 1 or 2	49 (2.5%)	7 (5.8%)	42 (2.3%)	2.60	(1.14 - 5.91)	0.43	(0.13 - 1.48)
<b>Reperfusion therapy<sup>c</sup></b>							
PCI	(N = 307)	(N = 171)	(N = 136)				
CPC 1 or 2	143 (46.6%)	61 (35.7%)	82 (60.3%)	0.37	(0.23 - 0.58)	1.06	(0.47 - 2.42)
Non-PCI	(N = 2587)	(N = 129)	(N = 2458)				
CPC 1 or 2	291 (11.2s%)	31 (24.0%)	260 (10.6%)	2.67	(1.75 - 4.09)	0.72	(0.33 - 1.57)

IABP, intra-aortic balloon pump; CPC, cerebral performance category; OR, odds ratio; CI confidence interval; PCI, percutaneous coronary intervention.

ORs were calculated for IABP use versus non-IABP use.

<sup>a</sup> Adjusted for year, gender, age, witness status, bystander CPR, public-access defibrillation, dispatcher instruction, first documented rhythm at pre-hospital, adrenaline administration at pre-hospital, tracheal intubation, time from call to hospital arrival, first documented rhythm after arrived hospital, adrenaline administration at in-hospital, amiodarone administration at in-hospital, lidocaine administration at in-hospital, coronary angiography, percutaneous coronary intervention, target temperature management, extracorporeal membrane oxygenation.

<sup>b</sup> Adjusted for year, gender, age, witness status, bystander CPR, public-access defibrillation, dispatcher instruction, first documented rhythm at pre-hospital, adrenaline administration at pre-hospital, tracheal intubation, time from call to hospital arrival, adrenaline administration at in-hospital, amiodarone administration at in-hospital, lidocaine administration at in-hospital, coronary angiography, percutaneous coronary intervention, target temperature management, extracorporeal membrane oxygenation, cause of arrest.

<sup>c</sup> Adjusted for year, gender, age, witness status, bystander CPR, public-access defibrillation, dispatcher instruction, first documented rhythm at pre-hospital, adrenaline administration at pre-hospital, tracheal intubation, time from call to hospital arrival, first documented rhythm after arrived hospital, adrenaline administration at in-hospital, amiodarone administration at in-hospital, lidocaine administration at in-hospital, coronary angiography, target temperature management, extracorporeal membrane oxygenation, cause of arrest.

as first documented shockable rhythm and witness and CPR by bystanders. Thus, the difference in the selection of the target population might have caused the difference in the effect of the IABP use. For example, in the subgroup analysis of our study, the IABP use tended to be associated with favorable neurological outcome among patients who presented shockable rhythm after hospital arrival, although it was statistically insignificant. Further observational studies or randomized controlled trials are essential to verify the effects of the IABP use on OHCA patients who achieved ROSC and to test our results.

In the preceding studies, there were few studies suggesting the effectiveness of the IABP use among patients with cardiovascular diseases including ischemic heart disease. Importantly, a landmark clinical trial (IABP SHOCK II trial) showed no superiority of the IABP use in 30-day all-cause mortality.<sup>26</sup> Similar results have been shown in a systematic review of 12 randomized trials and 15 observational studies, targeting patients with AMI.<sup>27</sup> In the subgroup analysis regarding AMI patients with non-cardiogenic shock (CS) from this review, the IABP use was associated with poor 30-day mortality. Findings that the IABP use was associated with poor prognosis have also been shown by a multicenter, prospective observational study in AMI patients in Japan.<sup>28</sup> These studies suggest that the IABP use might not contribute to the improvement of neurological outcomes in patients with myocardial dysfunction.

Why did the IABP use seem ineffective in OHCA patients with ROSC? When using IABP, the balloon deflation during systole causes a decreased afterload, enhances cardiac output, and decreases left ventricular stroke work index, and the balloon inflation during diastole causes an increased coronary artery perfusion and maintains vital organ perfusion.<sup>10</sup> However, IABP provides less hemodynamic support than other pMCSs, and cardiac flows of IABP, Impella, and TandemHeart are 0.3–0.5 L/min, 1.0–5.0 L/min, and 2.5–5.0 L/min, respectively.<sup>29</sup> For example, a clinical trial reported that the IABP use increased cerebral blood flow among patients with impaired left ventricular function,<sup>30</sup> whereas in IABP SHOCK I trial, there were no differences in cardiac output, left ventricular stroke work index, and systemic vascular resistance with or without the IABP use among AMI patients complicated by CS.<sup>31</sup> Furthermore, IABP SHOCK II trial reported that a positive effect of IABP in maintaining multiple organ perfusion did not continue for a long time,<sup>26</sup> and some papers reported that IABP had no effect on increasing microvascular perfusion,<sup>32,33</sup> and CRISP AMI trial showed no association of the IABP use with infarct size for AMI patients without shock.<sup>34</sup> These studies suggest that the effect of enhancing cardiac output and increasing coronary artery perfusion by the IABP use for AMI patients with or without CS might be small. Thus, even among OHCA patients complicated by PCAS, the IABP use might be insufficient as a pMCS.

In this decade, recommendations of IABP on the guidelines for myocardial infarction in the United States have lowered from Class I to Class IIa.<sup>35,36</sup> Although there was no description on the recommendations of IABP in the CPR guidelines for PCAS care,<sup>6–8</sup> our results would not positively recommend the IABP use. However, there are several pMCSs that increase cardiac flow to high level such as Impella and TandemHeart other than IABP.<sup>26,37</sup> Therefore, further studies are needed to verify the effect of these pMCSs on AMI patients or OHCA patients.

## Limitations

There were several limitations in this study. First, we did not obtain information on the timing of the IABP insertion. Second, vital data such

as blood pressure and heart rate, cardiac function, hemodynamic status, and records of inotropes used after ROSC were also lacking.<sup>31</sup> Third, although this study also eliminated the imbalance between the IABP use group and the non-IABP use group using PS matching analysis, unmeasured confounding factors such as past medical history including coronary artery disease, heart failure classification before cardiac arrest<sup>11,26,28</sup> may have influenced the association between the IABP use and the OHCA outcomes. Finally, this study was observational and therefore cannot establish causal relationships.

## Conclusions

From the CRITICAL study, the current propensity-score matching analysis did not reveal any association between the IABP use and 1-month survival with favorable neurological outcome among adult patients who achieved ROSC after nontraumatic OHCA.

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## Disclosures

None declared.

## Conflict of interest statement

All the authors declare that they have no potential conflict of interest.

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