Intra-arrest Partial Carbon Dioxide Level and Favorable Neurological Outcome after Out- of-Hospital Cardiac Arrest: A Nationwide Multicenter Observational Study in Japan (the JAAM-OHCA Registry)

Tasuku Matsuyama (task-m@koto.kpu-m.ac.jp)
Kyoto Prefectural University of Medicine
Bon Ohta
Kyoto Prefectural University of Medicine
Kosuke Kiyohara
Otsuma Women's University
Tetsuhisa Kitamura
Osaka University

Research Article

Keywords: Out-of-hospital cardiac arrest, ventilation, carbon dioxide, neurological outcomes

Posted Date: May 20th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1659359/v1

Abstract

Background: Little is known about whether guideline-recommended ventilation during cardiopulmonary resuscitation results in optimal partial carbon dioxide (pCO2) levels or favorable outcomes after out-of-hospital cardiac arrest (OHCA). This study aimed to evaluate the association between pCO2 levels and outcomes.

Methods: We performed a secondary analysis of a multicenter observational study, including adult patients with OHCA who did not achieve a return of spontaneous circulation (ROSC) upon hospital arrival and whose blood gas analysis was performed before the ROSC between June 2014 and December 2017. The primary exposure in this study was the intra-arrest pCO2 value obtained from a blood gas analysis performed upon hospital arrival. The patients were categorized into four quartiles based on their intra-arrest carbon dioxide levels: quartiles 1 (<66.0 mmHg), 2 (66.1–87.2 mmHg), 3 (87.3–113.5 mmHg), and 4 (≥113.6 mmHg). The primary outcome was 1-month survival with favorable neurological outcomes defined as cerebral performance category 1 or 2. Multivariate logistic regression analysis was used to evaluate the association between pCO2 and favorable neurological outcomes. We also investigated the association between pCO2 and favorable neurological outcomes stratified using the method of ventilation (bag-mask ventilation, supraglottic airway, or tracheal intubation) and the etiology of the arrest (cardiac, respiratory, or other etiology of arrest).

Results: During the study period, 23,803 patients were eligible for the analysis. The proportion of favorable neurological outcomes was 0.7% (153/20,913), 1.8% (90/5,133), 0.7% (35/5,232), 0.4% (19/5,263), and 0.2% (9/5,285) in quartiles 1 (<66.0 mmHg), 2 (66.1–87.2 mmHg), 3 (87.3–113.5 mmHg), and 4 (≥113.6 mmHg), respectively. Multivariable logistic regression analysis demonstrated that the probability of favorable neurological outcome decreased with increased intra-arrest carbon dioxide levels (i.e., Q1 versus Q4, adjusted odds ratio 0.25, 95% confidence interval 0.16–0.55, P for trend <0.001). Stratified analyses showed that a higher intra-arrest pCO2 level was associated with a decreased probability of favorable neurological outcomes in any method of ventilation and cause of arrests.

Conclusion: We observed that patients with higher intra-arrest pCO2 levels were less likely to achieve a favorable neurological outcome, regardless of the method of ventilation and cause of arrests.

Introduction

Despite the accumulation of evidence regarding resuscitation medicine in recent decades, the probability of favorable outcomes after out-of-hospital cardiac arrest (OHCA) remains low [1–3]. High-quality cardiopulmonary resuscitation (CPR), including high-quality chest compression and optimal ventilation, is an essential component for improving outcomes after OHCA [4, 5]. Regarding the quality of chest compression, the international CPR guidelines suggest a definite target regarding the compression rate, depth, and recoil to deliver oxygenated blood to vital organs [4, 5].

The aim of ventilation is to increase arterial oxygen levels, decrease arterial carbon dioxide levels, and alleviate respiratory acidosis. On the other hand, the current recommendation of the compression-to-ventilation ratio for patients with OHCA has been made to balance the risk of increasing intrathoracic pressure and decreasing coronary perfusion pressure by hyperventilation or severe respiratory acidosis by hypoventilation [4, 5]. However, this recommendation is based on limited evidence [6, 7]. Furthermore, very few studies have reported whether guideline-recommended CPR results in optimal partial carbon dioxide (pCO2) levels or whether it is associated with favorable outcomes after OHCA, suggesting important knowledge gaps [6, 7].

The Japanese Association for Acute Medicine (JAAM)-OHCA registry is a nationwide hospital-based prospective observational data registry that includes 137 medical institutions in Japan. Using this registry, this study aimed to evaluate (1) the distribution of intra-arrest pCO2 levels upon hospital arrival and (2) the association between each pCO2 level and the outcome after OHCA.

Methods

Study Design and Setting

This study was a retrospective analysis of the JAAM-OHCA registry [8]. The study period was from June 2014 to December 2017. The complete study methodology has been previously described [8,9]. In brief, pre-hospital data collection was conducted by emergency medical service (EMS) personnel according to the Utstein-style template [10,11], whereas the physicians of each participating institution collected in-hospital data, including information on the etiology of arrests, treatments, and outcomes. The registry is ongoing without setting the end date of the registry period. The registry was approved by the ethics committee of each participating hospital.

Study Patients

This study included adult patients aged ≥18 years with OHCA for whom resuscitation was attempted by bystanders or EMS personnel who were then transported to participating institutions without achieving a return of spontaneous circulation (ROSC) upon hospital arrival. The exclusion criteria were patients (1) for whom resuscitation was not attempted, (2) whose pre-hospital data were not available, and (2) whose pre-ROSC pCO2 value was not available.

EMS System in Japan

A detailed description of the EMS system in Japan has been provided previously. The EMS system in Japan has been provided elsewhere [12,13]. Emergency services are provided 24 h a day. After receiving an emergency call, an ambulance is dispatched from the nearest center. The most highly trained emergency care providers are called emergency life-saving technicians (ELSTs) and permit the insertion of an intravenous line and supraglottic airway device for patients with OHCA. In addition, specially trained ELSTs were permitted to perform tracheal intubation and administer intravenous adrenaline. Generally, a crew of three emergency providers, including at least one ELST, is in each ambulance. CPR is performed based on the Japanese CPR guidelines, which are similar to other international guidelines, especially regarding the ventilation strategy: 30:2 compression-ventilation ratio if there is no advanced airway and 10 breaths/min after advanced airway placement [14]. In Japan, termination of resuscitation in pre-hospital settings by EMS personnel is prohibited [14,15]. Therefore, except for cases of decapitation, incineration, decomposition, rigor mortis, or dependent cyanosis, EMS personnel transport almost all patients with OHCA to the hospitals.

Data Collection and Primary Exposure

We collected the following data from the JAAM-OHCA registry: age, sex, causes of arrest, witness status, bystander CPR, a first documented rhythm at the scene or after hospital arrival, pre-hospital epinephrine administration, pre-hospital airway management, blood gas analysis, actual treatments for patients with OHCA (e.g., targeted temperature management, coronary angiography, and percutaneous coronary intervention), and outcome data. The etiologies of cardiac arrest were divided into three categories: cardiac (or presumed cardiac) and respiratory (respiratory disease, hanging, drowning, or asphyxia), or others. Respiratory etiology was kept as a separate category because patients with these etiologies of cardiac arrest might have a basic high pCO2 level; therefore, they should be analyzed separately. The presumed cardiac cause category was determined by exclusion (i.e., the diagnosis was made when there was no evidence of a noncardiac cause) [10,11].

The primary exposure in this study was the intra-arrest pCO2 value obtained from a blood gas analysis performed upon hospital arrival. The patients were categorized into four quartiles based on their intra-arrest pCO2 levels: quartiles 1 (<66.0 mmHg), 2 (66.1–87.2 mmHg), 3 (87.3–113.5 mmHg), and 4 (≥113.6 mmHg).

Outcome Measurements

The primary outcome of this study was 1-month survival with a neurologically favorable outcome. The secondary outcome was 1-month survival. The neurological status of the survivors was evaluated by medical staff at each institution 1 month after the event. Neurologically favorable outcomes were defined as cerebral performance category (CPC) 1 or 2 [10,11,16].

Statistical Analyses

Patient characteristics and outcomes were compared among the four groups using the Kruskal–Wallis rank test for continuous variables and the chi-square test for categorical variables. To evaluate the association between intra-arrest pCO2 levels and favorable neurological outcomes, we applied univariable and multivariable logistic regression analyses with odds ratios as the effect variables. We selected the following potential confounders: age (continuous), sex (male or female), etiology of cardiac arrest (cardiac, respiratory, or other), bystander witness (yes or no), bystander CPR (yes or no), first documented rhythm (shockable, non-shockable, or other), pre-hospital advanced airway method (bag-mask ventilation, supraglottic airway, or tracheal intubation), pH level, the interval between the call, and time of blood gas sampling [17-20]. As stratified analyses using the method of ventilation and etiology of arrests, we visually described the nonlinear relationship between the intra-arrest pCO2 level and the estimated probability of favorable neurological outcome using a restricted cubic spline with the univariable logistic regression model. In addition, to minimize the impact of "no ventilation time," we focused on witnessed arrests and performed univariable and multivariable logistic regression analyses using the same covariates as the main ones. All P-values were two-sided, and values <0.05 were considered statistically significant. All statistical analyses were performed using Statistical Product and Service Solutions (version 25 J; IBM Corp. Armonk, NY, USA) and R software (R Foundation for Statistical Computing, version 3.4.3).

Results

During the study period, 34,754 patients with OHCA were registered. After excluding those who met the exclusion criteria, 20,913 patients were eligible for analysis (Fig. 1). Of these, 5,133 patients were included in quartile 1, 5,232 in quartile 2, 5,263 in quartile 3, and 5,285 in quartile 4 (Table 1).

Table 1 presents the basic and pre-/in-hospital information stratified by the pCO2 level. The proportion of men was approximately 60%, and the median age was 75 years. Quartile 1 was more likely to have witnessed arrests, shockable rhythm as the first documented rhythm at the scene, higher pH upon hospital arrival, target temperature management (TTM), and percutaneous coronary intervention (PCI) compared with quartile 4. In addition, the median pCO2 level was higher in patients with respiratory causes than in those with cardiac causes (Supplementary Figure).

Regarding outcomes, the proportion of favorable neurological outcomes was 0.7% (153/20,913), 1.8% (90/5,133), 0.7% (35/5,232), 0.4% (19/5,263), and 0.2% (9/5,285) in quartiles 1 (< 66.0 mmHg), 2 (66.1–87.2 mmHg), 3 (87.3–113.5 mmHg), and 4 (≥ 113.6 mmHg) (Table 2). The probability of favorable neurological outcomes decreased with increased intra-arrest pCO2 levels (Fig. 2). This association was consistently observed after adjusting for potential confounding factors using multivariable logistic regression analysis (i.e., Q1 versus Q4, adjusted odds ratio 0.25, 95% confidence interval 0.16–0.55, P for trend < 0.001) (Table 2).

In addition, in the stratified analyses, we observed that a higher intra-arrest pCO2 level was associated with a decreased probability of favorable neurological outcomes in any method of ventilation and cause of arrests (Figs. 3a and b). The sensitivity analyses focusing on witnessed arrests showed the same trend as the main analyses (Table 3).

Discussion

Using the nationwide multicenter OHCA registry, we observed that higher intra-arrest pCO2 levels were associated with a decreased probability of favorable neurological outcomes among patients with OHCA in a dose-dependent manner. Moreover, the same trend was observed after stratifying the ventilation method and etiology of arrests or focusing on witnessed arrests.

No studies have assessed whether intra-arrest pCO2 is associated with long-term outcomes such as 1 month survival and 1 month survival with favorable neurological outcomes. Regarding short-term outcomes, two studies investigated the unadjusted association between intra-arrest pCO2 levels and hospital admission [6, 7]. These previous studies observed no significant association between them. However, these studies included only 83 and 145 patients, which was too small to draw a conclusion. This study, including the overwhelmingly larger number of patients with OHCA, may provide important information about ventilation strategies during CPR.

Our study found that most patients were hypercapnic during CPR regardless of the method of airway management, although there were substantial variations with regard to each group. A previous study observed that the mean pCO2 level of 18 samples obtained under ongoing CPR was 67 mmHg, which was much lower than that in this study [7]. Experts have assumed that pCO2 levels increase after cardiac arrest and are maintained or gradually decrease after the initiation of CPR [21]. However, based on the observed much higher pCO2 levels in this study, ventilation is unlikely to decrease pCO2 levels in the real world. The exact reason for this is unknown, but it may result from dead space ventilation caused by reduced lung volume and perfusion during CPR or due to hypoventilation. Although the actual minute volume delivered to the patients or the change in pCO2 level during CPR could not be obtained from our study, the currently recommended quantity of ventilation may not be sufficient. In addition, we found that patients with respiratory causes were more likely to have higher pCO2 levels than those with cardiac causes. This is the first study to demonstrate a higher level of pCO2 in patients with respiratory causes, which may suggest the need for alternation of ventilation strategies for these patients.

Acidosis was present in all patients in this study. A previous study evaluating intra-arrest blood gas analysis reported that the pH levels ranged from 7.0–7.1, which was higher than that in our study. Importantly, although pH gradually decreased from Q1 to Q4, metabolic acidosis was conversely less severe, indicating that hypercarbia was the main contributor to acidosis. These results were similar to those of a previous study [6]. Surprisingly, the accumulation of acid metabolites does not necessarily appear to occur during CPR. Rather, we might have observed compensatory metabolic alkalosis for respiratory acidosis, even during CPR. Acidosis of any kind can be harmful to circulation because it results in negative inotropy, vasodilatation, and impaired oxygen uptake in the lungs. Higher volume ventilation leads to a decrease in pCO2 and the normalization of pH. In contrast, a previous study demonstrated that hyperventilation during CPR induced hypotension by increasing intrathoracic pressure and decreasing coronary perfusion pressure, which resulted in worse outcomes [22]. Hence, it is currently considered that by reducing the number of ventilation, cardiac output and pulmonary blood flow may be increased with no compromise of oxygenation or acid-base balance [23]. Our observations demonstrate that carbon dioxide excretion during CPR should receive more attention, along with balancing the circulatory effects of positive pressure ventilation.

International CPR guidelines emphasize that hyperventilation must be avoided [4, 5]. However, we observed that almost all patients with OHCA had hypercapnia during CPR, which contributed mainly to severe acidosis. Therefore, we suggest that the ventilation strategy during CPR should be reconsidered, and further efforts to determine the target pCO2 level and ventilation volume during CPR should be made. Moreover, the optimal ventilation strategy may vary from person to person [24], and real-time physiological monitoring to evaluate respiratory and circulatory dynamics is needed.

Limitation

This study has several inherent limitations. First, we did not have information about each patient's comorbidities or activities of daily living before arrest. Second, we did not obtain important physiological data such as baseline pCO2 level, end-tidal carbon dioxide, quality of CPR, and change in pCO2 level during CPR. Finally, as with other observational studies, there may be possible residual confounders.

Conclusion

From the nationwide OHCA registry in Japan, we observed that those with higher intra-arrest pCO2 levels were less likely to achieve a favorable neurological outcome, regardless of the method of ventilation and cause of arrests. Therefore, further studies are warranted to determine the optimal ventilation strategy for patients with OHCA.

Abbreviations

OHCA: Out-of-hospital cardiac arrest; CPR: cardiopulmonary resuscitation; partial carbon dioxide: pCO2; JAAM : The Japanese Association for Acute Medicine; EMS: emergency medical service; ROSC: return of spontaneous circulation; ELST: emergency life-sving technician; CPC: cerebral performance category; IQR: interquartile range; OR: odds ratios; CI: confidence interval; AED, automated external defibrillator; pCO2, partial carbon dioxide; TTM, target temperature management; PCI, percutaneous coronary intervention.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of each institution. The research was carried out following a named standard. Because of the observational study and de-identification of personal data, each committee waived the need for informed consent.

Consent for publication

Not applicable.

Availability of data and material

Please contact the author for data requests.

Competing interests

The authors declare that they have no competing interests.

Source of funding

This study was supported by Japan Society for the Promotion of Science KAKENHI Grant Numbers 21K16576.

Authors' contributions

Matsuyama had full access to all the data in the study and take responsibility for the integrity of the data and accuracy of the data analysis.

Study concept and design: Matsuyama, Kitamura, Kiyohara.

Acquisition, analysis, and interpretation of data: All authors.

Drafting of the manuscript: Matsuyama, Kitamura.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Matsuyama.

Obtained funding: Matsuyama and Kitamura.

Study supervision: Ohta

Acknowledgments

We are deeply indebted to all members and institutions of the JAAM-OHCA Registry for their contributions. The participating institutions of the JAAM-OHCA Registry are listed at the following URL: http://www.jaamohca-web.com/list/.

References

1. Hasselqvist-Ax I, Riva G, Herlitz J, et al. Early cardiopulmonary resuscitation in out-of-hospital cardiac arrest. N Engl J Med. 2015; 372: 2307-15
2. Wissenberg M, Lippert FK, Folke F, et al. Association of national initiatives to improve cardiac arrest management with rates of bystander intervention and patient survival after out-of-hospital cardiac arrest. JAMA 2013; 310: 1377-84.
3. Okubo M, Gibo K, Wallace DJ, Komukai S, Izawa J, Kiyohara K et al. Regional variation in functional outcome after out-of-hospital cardiac arrest across 47 prefectures in Japan. Resuscitation.

2018;124:21-28.

4. Merchant RM, Topjian AA, Panchal AR, Cheng A, Aziz K, Berg KM et al. Part 1: Executive Summary: 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2020;142:S337-s357.
5. Perkins GD, Graesner JT, Semeraro F, Olasveengen T, Soar J, Lott C et al. European Resuscitation Council Guidelines 2021: Executive summary. Resuscitation. 2021;161:1-60.
6. Spindelboeck W, Schindler O, Moser A, Hausler F, Wallner S, Strasser C, Haas J, Gemes G, Prause G (2013) Increasing arterial oxygen partial pressure during cardiopulmonary resuscitation is associated with improved rates of hospital admission. Resuscitation 84:770–775
7. Spindelboeck W, Gemes G, Strasser C, Toescher K, Kores B, Metnitz P, Haas J, Prause G (2016) Arterial blood gases during and their dynamic changes after cardiopulmonary resuscitation: a prospective clinical study. Resuscitation 106:24–29
8. Kitamura T, Iwami T, Atsumi T, Endo T, Kanna T, Kuroda Y et al. The profile of Japanese Association for Acute Medicine - out-of-hospital cardiac arrest registry in 2014-2015. Acute medicine & surgery. 2018;5:249-258.
9. Matsuyama T, Iwami T, Yamada T, Hayakawa K, Yoshiya K, Irisawa T, et al. Effect of serum albumin concentration on favorable neurological outcome after out-of-hospital cardiac arrest (From the CRITICAL Study in Osaka, Japan). The American Journal of Cardiology. 2018;121:156-161.
10. Jacobs I, Nadkarni V, Bahr J, Berg RA, Billi JE, Bossaert L et al. Cardiac arrest and cardiopulmonary resuscitation outcome reports: update and simplification of the Utstein templates for resuscitation registries. A statement for healthcare professionals from a task force of the international liaison committee on resuscitation (American Heart Association, European Resuscitation Council, Australian Resuscitation Council, New Zealand Resuscitation Council, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Council of Southern Africa). Resuscitation. 2004;63:233-49.
11. Perkins GD, Jacobs IG, Nadkarni VM, Berg RA, Bhanji F, Biarent D et al. Cardiac arrest and cardiopulmonary resuscitation outcome reports: update of the Utstein Resuscitation Registry Templates for Out-of-Hospital Cardiac Arrest: a statement for healthcare professionals from a task force of the International Liaison Committee on Resuscitation (American Heart Association, European Resuscitation Council, Australian and New Zealand Council on Resuscitation, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Council of Southern Africa, Resuscitation Council of Asia); and the American Heart Association Emergency Cardiovascular Care Committee and the Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation. Circulation. 2015;132:1286-300.
12. Kitamura T, Iwami T, Kawamura T, Nagao K, Tanaka H, Hiraide A, Implementation Working Group for the All-Japan Utstein Registry of the F and Disaster Management A. Nationwide public-access defibrillation in Japan. N Engl J Med. 2010;362:994-1004.

13. Iwami T, Nichol G, Hiraide A, Hayashi Y, Nishiuchi T, Kajino K, et al. Continuous improvements in "chain of survival" increased survival after out-of-hospital cardiac arrests: a large-scale population-based study. Circulation. 2009;119:728-34.
14. Japan Resuscitation Council. 2020 Japanese Guidelines for Emergency Care and Cardiopulmonary Resuscitation. TokyoJapan: Igaku-Shoin, 2021
15. Fire and Disaster Management Agency. Report on a study on social system development to improve survival from emergency cardiovascular disease (in Japanese). https://www.fdma.go.jp/publication/#rescue Accessed April 1, 2022
16. Becker LB, Aufderheide TP, Geocadin RG, Callaway CW, Lazar RM, Donnino MW, et al. Primary outcomes for resuscitation science studies: a consensus statement from the American Heart Association. Circulation. 2011;124:2158-77.
17. Matsuyama T, Komukai S, Izawa J, Gibo K, Okubo M, Kiyohara K et al. Pre-Hospital Administration of Epinephrine in Pediatric Patients With Out-of-Hospital Cardiac Arrest. Journal of the American College of Cardiology. 2020;75:194-204.
18. Izawa J, Komukai S, Gibo K, Okubo M, Kiyohara K, Nishiyama C, et al. Pre-hospital advanced airway management for adults with out-of-hospital cardiac arrest: nationwide cohort study. BMJ. 2019;364:l430.
19. Iwami T, Kitamura T, Kiyohara K, Kawamura T. Dissemination of Chest Compression-Only Cardiopulmonary Resuscitation and Survival After Out-of-Hospital Cardiac Arrest. Circulation. 2015;132:415-22.
20. Kitamura T, Kiyohara K, Sakai T, Matsuyama T, Hatakeyama T, Shimamoto T et al. Public-Access Defibrillation and Out-of-Hospital Cardiac Arrest in Japan. N Engl J Med. 2016;375:1649-1659.
21. Skrifvars MB, Olasveengen TM, Ristagno G. Oxygen and carbon dioxide targets during and after resuscitation of cardiac arrest patients. Intensive Care Med. 2019;45:284–286
22. Aufderheide TP, Sigurdsson G, Pirrallo RG, Yannopoulos D, McKnite S, vonBriesen C, et al. Hyperventilation- induced hypotension during cardiopulmonary resuscitation. Circulation. 2004;109:1960–1965
23. Yannopoulos D, Tang W, Roussos C, Aufderheide TP, Idris AH, Lurie KG. Reducing ventilation frequency during cardiopulmonary resuscitation in a porcine model of cardiac arrest. Respir Care. 2005;50:628–635
24. Friess SH, Sutton RM, Bhalala U, Maltese MR, Naim MY, Bratinov G, et al. Hemodynamic directed cardiopulmonary resuscitation improves short-term survival from ventricular fibrillation cardiac arrest. Crit Care Med. 2013;41:2698-704.

Tables

Table 1

Patient characteristics and pre-/in-hospital information among OHCA patients by CO2 level

	Quartile 1 (<66.0 mmHg)		Quartile 2 (66.1-87.2 mmHg)		Quartile 3 (87.3-113.5 mmHg)		Quartile 4 (≥113.6 mmHg)		*P* Value
	(n=5133)		(n=5232)		(n=5263)		(n=5285)		
Basic information									
Men	3108	(60.5)	3278	(62.7)	3233	(61.4)	3038	(57.5)	<0.001
Age, median (IQR) (Years)	74	(64-84)	75	(65-84)	75	(65-84)	74	(61-83)	<0.001
Cause of arrest									<0.001
Cardiac cause	2827	(55.1)	2865	(25.1)	2948	(56.0)	2753	(52.1)	
Respiratory cause	496	(9.7)	735	(14.0)	1097	(20.8)	1482	(28.0)	
Other	1810	(35.3)	1632	(31.2)	1218	(23.1)	1050	(19.9)	
Prehospital information									
Bystander witness	2842	(55.4)	2736	(52.3)	2182	(41.5)	1178	(22.3)	<0.001
Bystander CPR	2036	(39.7)	2219	(42.4)	2362	(44.9)	2569	(48.6)	<0.001
First documented rhythm at the scene									<0.001
Ventricular fibrillation/pulseless ventricular tachycardia	488	(9.5)	460	(8.8)	410	(7.8)	164	(3.1)	
Pulseless electric activity/asystole	4348	(84.7)	4543	(86.8)	4708	(89.5)	5041	(3.1)	
Other	297	(5.8)	229	(4.4)	145	(2.8)	80	(1.5)	
Epinephrine	1319	(25.7)	1318	(25.2)	1454	(27.6)	1407	(26.6)	0.025
Airway management									<0.001
Bag Mask Ventilation	2221	(43.3)	2395	(45.8)	2423	(46.0)	2713	(51.3)	
Supraglottic airway	2157	(42.0)	2262	(43.2)	2317	(44.0)	2190	(41.4)	
Endotracheal	755	(14.7)	575	(11.0)	523	(9.9)	382	(7.2)	

intubation									
EMS resuscitation times, median (IQR), (minutes)									
EMS response time (call to contact with a patient)	8	(7-10)	8	(7-10)	8	(7-10)	9	(7-10)	<0.001
Hospital arrival time (call to hospital arrival)	32	(25-39)	31	(26-39)	32	(26-39)	33	(27-41)	<0.001
In-hospital information									
First documented rhythm after hospital arrival									<0.001
Ventricular fibrillation/pulseless ventricular tachycardia	335	(6.5)	301	(5.8)	224	(4.3)	104	(2.0)	
Pulseless electric activity/asystole	4770	(92.9)	4904	(93.7)	5015	(95.3)	5171	(97.8)	
Presence of pulse	28	(0.5)	27	(0.5)	24	(0.5)	10	(0.2)	
Blood gas analysis									
pH	7.01	(6.90-7.12)	6.95	(6.86-7.03)	6.89	(6.81-6.96)	6.79	(6.71-6.87)	<0.001
HCO3	11.9	(8.8-15.0)	15.7	(12.4-19.4)	17.5	(14.4-21.1)	18.5	(15.4-21.9)	<0.001
Time from call to blood gas analysis	40	(32-51)	39	(32-49)	39	(32-49)	40	(33-50)	0.002
Targeted temperature management	259	(5.0)	206	(3.9)	158	(3.0)	82	(1.6)	<0.001
Coronary angiography	326	(6.4)	256	(4.9)	158	(3.0)	54	(1.0)	<0.001
Percutaneous coronary intervention	173	(3.4)	127	(2.4)	77	(1.5)	15	(0.3)	<0.001

OHCA indicates out-of-hospital cardiac arrests; AED, automated external defibrillator; CPR, cardiopulmonary resuscitation; EMS, emergency medicine personnel, and IQR, interquartile range.

Table 2

Outcomes after OHCA by CO2 quartile

	Total	Survival case	(%)	Crude OR	(95% CI)	Adjusted OR	(95% CI)
1-month survival							
Quartile 1 (<66.0 mmHg)	5133	188	(3.7)	Reference		Reference*	
Quartile 2 (66.1-87.2 mmHg)	5232	115	(2.2)	0.59	(0.47-0.75)	0.66	(0.51-0.86)
Quartile 3 (87.3-113.5 mmHg)	5263	96	(1.8)	0.49	(0.38-0.63)	0.76	(0.57-1.02)
Quartile 4 (≥113.6 mmHg)	5285	36	(0.7)	0.18	(0.13-0.26)	0.58	(0.38-0.89)
P for trend				<0.001		<0.001	
Favorable neurological outcome							
Quartile 1 (<66.0 mmHg)	5133	90	(1.8)	Reference		Reference*	
Quartile 2 (66.1-87.2 mmHg)	5232	35	(0.7)	0.38	(0.26-0.56)	0.42	(0.27-0.64)
Quartile 3 (87.3-113.5 mmHg)	5263	19	(0.4)	0.20	(0.12-0.33)	0.24	(0.14-0.43)
Quartile 4 (≥113.6 mmHg)	5285	9	(0.2)	0.10	(0.48-0.19)	0.25	(0.16-0.55)
P for trend				<0.001		<0.001	

*Adjusted for age, sex, etiology of arrests, bystander witness, bystander CPR, first documented rhythm by emergency medical personnel,

prehospital airway management method, pH, and interval between call and time of blood gas sampling

OHCA indicates out-of-hospital cardiac arrest; CO2, carbon dioxide; OR, odds ratio; CI, confidence interval

Table 3

Outcomes after witnessed OHCA by CO2 quartile

	Total	Survival case	(%)	Crude OR	(95% CI)	Adjusted OR	(95% CI)
1-month survival							
Quartile 1 (<66.0 mmHg)	2842	151	(5.3)	Reference		Reference*	
Quartile 2 (66.1-87.2 mmHg)	2736	92	(3.4)	0.62	(0.48-0.81)	0.63	(0.47-0.85)
Quartile 3 (87.3-113.5 mmHg)	2182	77	(3.5)	0.65	(0.49-0.86)	0.75	(0.53-1.03)
Quartile 4 (≥113.6 mmHg)	1178	24	(2.0)	0.37	(0.24-0.57)	0.54	(0.33-0.90)
P for trend				<0.001		<0.001	
Favorable neurological outcome							
Quartile 1 (<66.0 mmHg)	2842	73	(2.6)	Reference		Reference*	
Quartile 2 (66.1-87.2 mmHg)	2736	30	(1.1)	0.42	(0.27-0.65)	0.40	(0.25-0.64)
Quartile 3 (87.3-113.5 mmHg)	2182	15	(0.7)	0.26	(0.15-0.46)	0.22	(0.12-0.41)
Quartile 4 (≥113.6 mmHg)	1178	5	(0.4)	0.16	(0.07-0.40)	0.19	(0.07-0.50)
P for trend				<0.001		<0.001	

*Adjusted for age, sex, etiology of arrests, bystander CPR, first documented rhythm by emergency medical personnel,

prehospital airway management method, pH, and interval between call and time of blood gas sampling

OHCA indicates out-of-hospital cardiac arrest; CO2, carbon dioxide; OR, odds ratio; CI, confidence interval

Figures

Figure 1

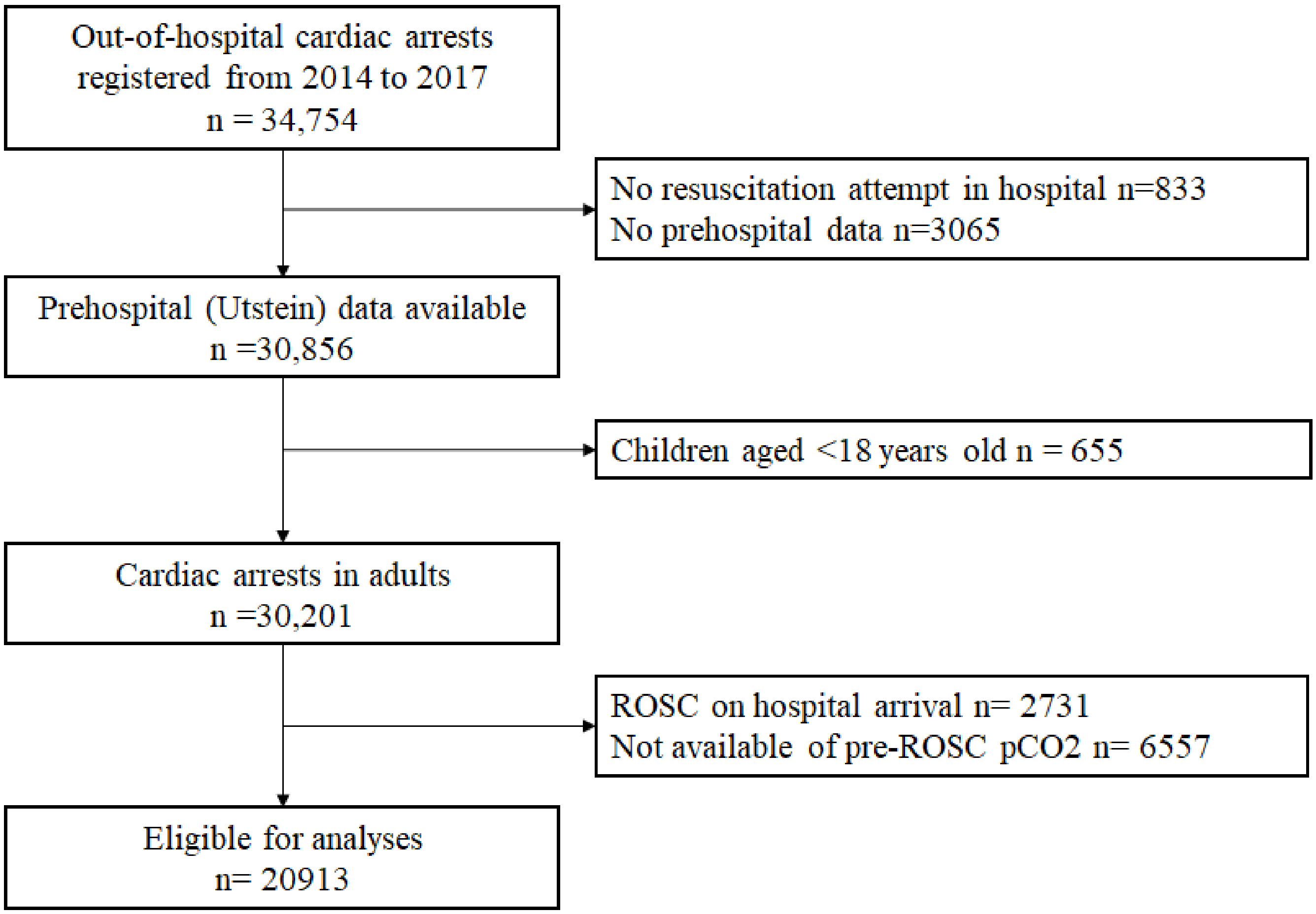

Figure 1

Patient flow of this study

ROSC: return of spontaneous circulation, pCO2: partial carbon dioxide

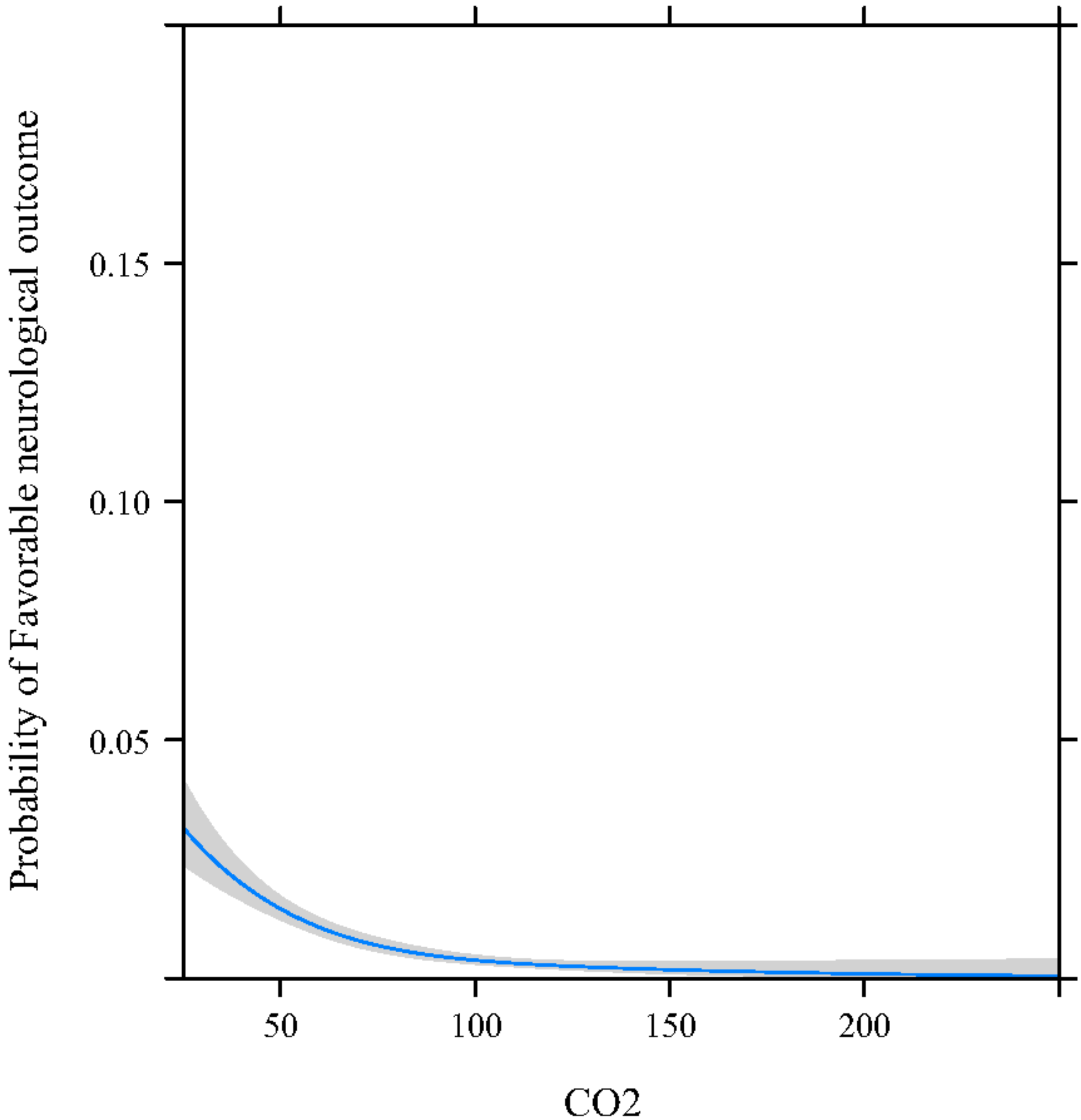

Figure 2

Probability of favorable neurological outcome by intra-arrest pCO2 level

pCO2: partial carbon dioxide

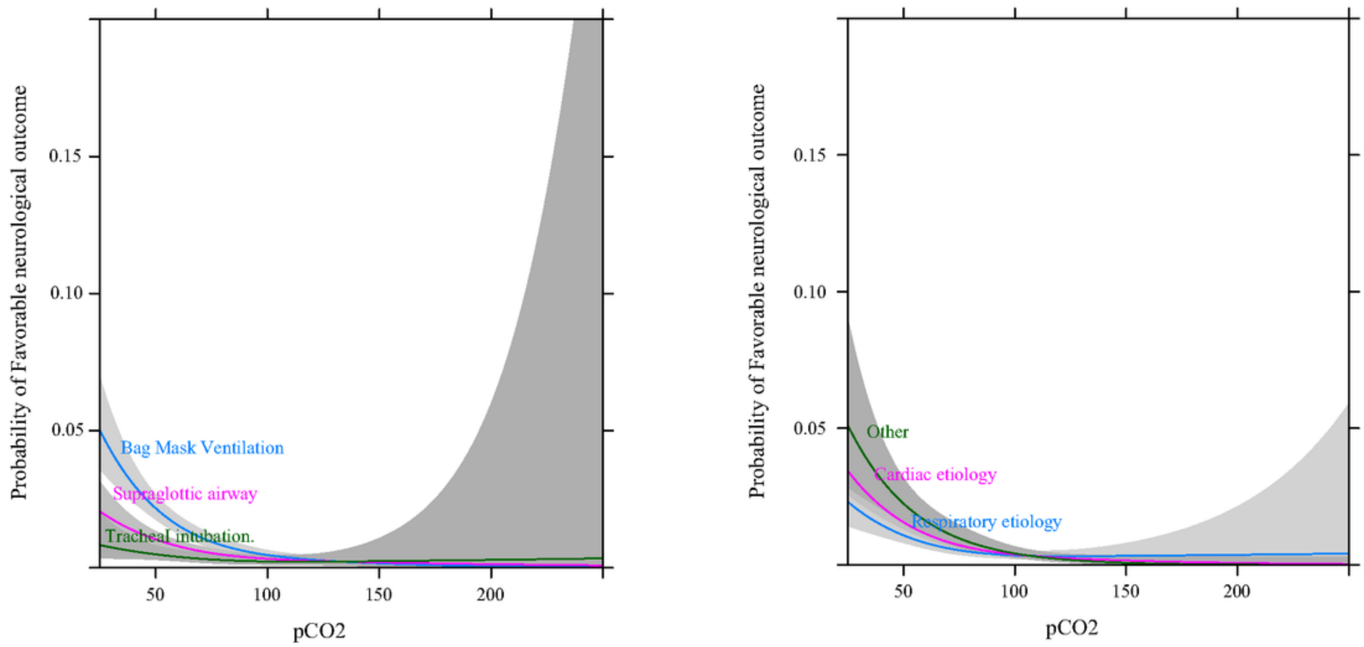

Figure 3

Probability of favorable neurological outcome by intra-arrest pCO2 level stratified by **(A)** method of ventilation; **(B)** etiology of arrests.

pCO2: partial carbon dioxide

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- PCO2SupplementalFigure1.pptx