

## Prognostic value of blood gas parameters and end-tidal carbon dioxide values in out-of-hospital cardiopulmonary arrest patients

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**Background/aim:** This study aimed to evaluate the usefulness of blood gas and end-tidal carbon dioxide (EtCO<sub>2</sub>) measurements for predicting return of spontaneous circulation (ROSC) and for evaluating post-ROSC neurological survival.

**Materials and methods:** This was a prospective case control study utilizing Atatürk University's database of adult nontraumatic patients (over 18 years old) with out-of-hospital cardiac arrest (OHCA) over the course of a year. The neurological status of the patients was evaluated after 1 h at ROSC and at hospital discharge, as defined by the cerebral performance category score. The blood gas parameters pH, PO<sub>2</sub>, PCO<sub>2</sub>, lactate, and BE were compared with EtCO<sub>2</sub> from capnography and arteriol/alveolar carbon dioxide difference (AaDCO<sub>2</sub>) by using both blood gas and capnography upon admission to the emergency department and at ROSC.

**Results:** A total of 155 patients were included in the study to form the control group with ROSC. The PO<sub>2</sub>, PCO<sub>2</sub>, and AaDCO<sub>2</sub> values showed a prognostic marker for the supply of ROSC (P < 0.05). The EtCO<sub>2</sub>, lactate, and BE values measured by the blood gas were found to be insignificant in the prediction of ROSC (P > 0.05). Conversely, AaDCO<sub>2</sub> was found to be significant in ROSC estimation (P < 0.05), but not in neurological evaluation (P > 0.05).

**Conclusion:** Blood gas parameters and EtCO<sub>2</sub> are sufficient in predicting ROSC. The value of AaDCO<sub>2</sub> calculated using EtCO<sub>2</sub> and PO<sub>2</sub> may be used in predicting the prognosis of OHCA patients, but this value does not provide any conclusions concerning neurological survival.

**Key words:** Arteriol/alveolar carbon dioxide difference, blood gas, end-tidal carbon dioxide, out of hospital cardiopulmonary arrest, resuscitation

### 1. Introduction

#### 1.1. Background

Mortality rates after sudden cardiac arrest are high, even when return of spontaneous circulation (ROSC) is provided [1,2]. Arrest interventions aim at ensuring ROSC and minimizing neurological damage after ROSC. Many prognostic factors exist, such as cardiac output, ventilation status, and tissue perfusion; these are closely related to the discharge of cardiac arrest patients. Elevated mortality after ROSC may be associated with postcardiac arrest syndrome, including anoxic neurological damage, myocardial dysfunction, and systemic ischemic/reperfusion response [3].

#### 1.2. Goals of this investigation

The first aim of the study was to investigate whether arteriole/alveolar carbon dioxide difference (AaDCO<sub>2</sub>), which is calculated using blood gas parameters, and

end-tidal carbon dioxide (EtCO<sub>2</sub>), which is measured by capnography, could be used as prognostic markers for patients with cardiac arrest in which ROSC is provided. The second aim was to examine whether these markers played a role in short-term neurological evaluation.

### 2. Methods

#### 2.1. Study design and setting

This was a prospective case control clinical study of out-of-hospital cardiac arrest (OHCA) patients' prognostic value on ROSC and neurological recovery by blood gas analyses and EtCO<sub>2</sub> values. Patients who were admitted to the clinic's emergency department with cardiopulmonary arrest from February 2016 to February 2017 were enrolled in the study. Study approval was obtained from the coordinating center's Institutional Editorial Board with a waiver of informed consent.

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## 2.2. Patient selection

Patients were included in the study who were 18 years of age or older and were nontraumatic patients admitted to the emergency department with OHCA. Despite the planned inclusion of pregnant arrest patients, pregnant cardiopulmonary arrest patient entry into the clinic did not occur during the study's time interval.

## 2.3. Measurements and variables

Patients were taken to the resuscitation room after emergency department entry. Monitorization and heart rate monitoring were initiated with supraglottic airway supplies, such as balloon-masked ambu, until oxygen was provided with an endotracheal tube (ETT). Simultaneous chest compressions were started. The blood gas sample was then taken with a suitable heparinized syringe at the same time as EtCO<sub>2</sub> measurement. The samples were sent to the laboratory in 2 min to prevent the blood from clotting. In the blood gas analysis, pH, PO<sub>2</sub>, PCO<sub>2</sub>, lactate, and BE values were measured. The same procedure was repeated again after the patient's ROSC was obtained. Resuscitation was applied according to the 2015 AHA guidelines until ROSC was provided. After ROSC was provided, the cerebral performance category (CPC) score was noted, during the first hour and at discharge, for neurological evaluation.

## 2.4. Biochemical analysis

EtCO<sub>2</sub> values from the patient and control groups were measured after admission to the hospital by capnography without stopping resuscitation. Simultaneously, blood was drawn to analyze the femoral artery with the help of a heparinized blood gas injector. No medication was given that could affect blood gas parameters of the patients, such as NaHCO<sub>3</sub>. After the air inside the injector was thoroughly evacuated, the sample was delivered to University Research Hospital Central Laboratories at room temperature with the help of the hospital pneumatic system. If the system was not available, the sample was delivered by the emergency staff. After the blood reached the laboratory, it was taken to the device to be analyzed quickly. Within 3 to 5 min, the analysis results were available.

PCO<sub>2</sub>, PO<sub>2</sub>, pH, lactate, and BE levels from the blood samples were measured using the ABL 800 Basic Auto check radiometer, according to the directions provided by the manufacturer. For patients with ROSC, the same procedure was repeated again within 5 min of the patient's pulse and rhythm control.

## 2.5. Statistical analysis

Statistical analysis of the study was performed with SPSS 20.0 (SPSS Inc, Chicago, IL, USA) and Med Calc for sensitivity, specificity, and positive and negative likelihood ratios. The results were expressed as percentages for categorical variables and as medians (interquartile ranges), mean  $\pm$  standard deviation, minimum, and maximum for the continuous variables. Categorical data were compared

using the chi-square test. The Saphiro–Wilk test was used to evaluate normality with a significance level of 0.05. Continuous variables were compared using the independent sample t-test or the Mann–Whitney U test, as appropriate. Univariate and multivariate regression analyses were performed to investigate the relationship between significant parameters and ROSC. The predictive significance of variables were measured with receiver operating characteristic (ROC) curves, namely PO<sub>2</sub>, PCO<sub>2</sub>, and AaDCO<sub>2</sub> with cardiopulmonary resuscitation (CPR) before the EMS team reached the hospital, by emergency physicians in the hospital, and by adrenaline doses. The sensitivity, specificity, and positive and negative likelihood ratios (+LR and –LR) were calculated for cutoff values. A value of  $P < 0.05$  was considered statistically significant

## 3. Results

During the course of the study, 249 cardiopulmonary arrest patients came to the emergency department. Of these patients, 94 were traumatic arrest patients and were excluded from the study. A total of 155 outpatients, who were nontraumatic and over 18 years old, were included in the study.

The blood gases, EtCO<sub>2</sub>, and AaDCO<sub>2</sub> values before and after the resuscitation of the patients are shown in Table 1. When the relationship between blood gas parameters and the values of EtCO<sub>2</sub> and AaDCO<sub>2</sub> were investigated, in terms of the availability of ROSC and short-term neurological evaluation, PO<sub>2</sub> ( $P = 0.0006$ ), PCO<sub>2</sub> ( $P = 0.0012$ ), and AaDCO<sub>2</sub> ( $P = 0.0003$ ) were found to be statistically significant.

The sensitivity, specificity, positive, and negative predictive values, and positive and negative likelihood ratios of all useful values are shown in Table 2. The same table shows the importance of CPR before EMS providers arrived ( $P = 0.0006$ ), in the ambulance ( $P < 0.0001$ ), in the hospital ( $P < 0.0001$ ), and upon administration of adrenaline ( $P < 0.0001$ ).

## 4. Discussion

The prognostic value of blood gas analyses, EtCO<sub>2</sub> values, and AaDCO<sub>2</sub> values for the ROSC and short-term neurological recovery were prospectively analyzed.

Acidosis, peripheral vasodilation, reduction of the preload of the heart, and inability to effectively perform CPR increased PCO<sub>2</sub>. Reasons for this value can be both patient-originated and nonpatient-originated. Therefore, the use of PCO<sub>2</sub> with a value such as EtCO<sub>2</sub> might strengthen the ROSC estimate [4]. In this study, the value of PCO<sub>2</sub> measured from the bloodstream was in agreement with previous studies and could be used in predicting the ROSC of the patient ( $P = 0.0012$ ).

PO<sub>2</sub> was not a reliable indicator of tissue hypoxia in blood gases from cardiac arrest patients. This effect was due

**Table 1.** Values of blood gases, EtCO<sub>2</sub>, and AaDCO<sub>2</sub> before and after the resuscitation of the patients.

	ROSC	EXITUS	P-value
Age (year)			
Median	65	67.50	0.312
Percentiles 25	55	58.25	
Percentiles 75	78	76.75	
A-etCO <sub>2</sub> (mmHg)			<b>0.005</b>
Median	14.5	12	
Percentiles 25	10	7.25	
Percentiles 75	26.5	17	
A-ph			0.721
Median	6.97	6.99	
Percentiles 25	6.87	6.87	
Percentiles 75	7.11	7.12	
A-pCO <sub>2</sub> (mmHg)			<b>0.0012</b>
Median	54.55	68.5	
Percentiles 25	41.3	55.8	
Percentiles 75	73.27	87.72	
A-pO <sub>2</sub> (mmHg)			<b>0.0006</b>
Median	51.5	26.85	
Percentiles 25	28.2	18.65	
Percentiles 75	73.45	53.25	
A-BE			0.155
Median	-15.95	-12.8	
Percentiles 25	-21.75	-18.75	
Percentiles 75	-11.25	-8.7	
A-Lactat (mmol/L)			0.484
Median	11.6	12.4	
Percentiles 25	9.95	8.8	
Percentiles 75	14.7	16	
A-AapCO <sub>2</sub> (mmHg)			<b>0.0003</b>
Median	38.5	54.4	
Percentiles 25	22.35	41.6	
Percentiles 75	56.75	72.2	
B-ECPR (minute)			0.0006
Median	5	10	
Percentiles 25	3	5	
Percentiles 75	10	20	
B-HCPR (minute)			<b>&lt;0.0001</b>
Median	3	10	
Percentiles 25	0	5	
Percentiles 75	10	20	
HCPR (minute)			<b>&lt;0.0001</b>
Median	20	45	
Percentiles 25	10	35	
Percentiles 75	35	50	
Adrenalin Time (x1mg)			<b>&lt;0.0001</b>
Median	5	10	
Percentiles 25	3	9	
Percentiles 75	9	15	
Defibrillation time			0.773
Median	0	0	
Percentiles 25	0	0	
Percentiles 75	3	3	
Amiodaron Doze (mg)			0.902
Median	0	0	
Percentiles 25	0	0	
Percentiles 75	450	450	

NaHCO <sub>3</sub> Doze (x8,4%NaHCO <sub>3</sub> =1ml/kg)			
Median	0	0	0.225
Percentiles 25	0	0	
Percentiles 75	0	0	
O <sub>2</sub> (lt/dk)			0.394
Median	15	13	
Percentiles 25	10	10	
Percentiles 75	15	15	
R-etCO <sub>2</sub> (mmHg)			-
Median	26	-	
Percentiles 25	20.75	-	
Percentiles 75	37.75	-	
R-ph			-
Median	6.98	-	
Percentiles 25	6.85	-	
Percentiles 75	7.06	-	
R-pCO <sub>2</sub> (mmHg)			-
Median	61.1	-	
Percentiles 25	41.9	-	
Percentiles 75	75.55	-	
R-PO <sub>2</sub> (mmHg)			-
Median	79.8	-	
Percentiles 25	53.75	-	
Percentiles 75	129	-	
R-BE			-
Median	-15.1	-	
Percentiles 25	-19.2	-	
Percentiles 75	-9.95	-	
R-Lactat (mmol/L)			-
Median	11.5	-	
Percentiles 25	9	-	
Percentiles 75	14.15	-	
R-AapCO <sub>2</sub> (mmHg)			-
Median	32.6	-	
Percentiles 25	13.5	-	
Percentiles 75	46.8	-	

A-EtCO<sub>2</sub>: admission endtidal carbon dioxide, A-ph: admission ph, A-PCO<sub>2</sub>: admission PCO<sub>2</sub>, A-PO<sub>2</sub>: admission PO<sub>2</sub>, A-BE: admission BE, A- lactat: admission lactat, A-AaDCO<sub>2</sub>: admission AaDCO<sub>2</sub>, R-EtCO<sub>2</sub>: ROSC EtCO<sub>2</sub>, R-ph: ROSC ph, R-PCO<sub>2</sub>: ROSC PCO<sub>2</sub>, R-O<sub>2</sub>: ROSC O<sub>2</sub>, R-BE: ROSC BE, R-lactat: ROSC lactat, R-AaDCO<sub>2</sub>: ROSC AaDCO<sub>2</sub>, ROSC: return of spontaneous circulation

to arterial, venous, or mix formation and was affected by the intake site of the bloodstream, as well as whether CPR was effective and complete perfusion was not provided. For example, values measured from the fingertip were lower than values measured in the blood gas due to low cardiac output and poor circulation [5]. A statistically significant relationship was established between PO<sub>2</sub> values measured from blood gases and ROSC at the time of admission to the emergency clinic. This evaluation showed that PO<sub>2</sub> values could be used in ROSC estimation, in agreement with previous studies (P = 0.0006).

**Table 2.** The sensitivity, specificity, positive and negative predictive values, and positive and negative likely ratios of significant values.

Parameter	A-PCO <sub>2</sub>	A-PO <sub>2</sub>	A-AaDCO <sub>2</sub>	B-ECPR	B-HCPR	HCPR	Adrenalin Doze
P-value	0.0012	0.0006	0.0003	0.0006	<0.0001	<0.0001	<0.0001
Cutoff	≤53.6	>27.9	≤45.2	≤10	≤2	≤25	≤7
Sensitivity	50	76.92	66.04	83.05	49.15	66.1	69.49
95%CI	36.1–63.9	63.2–87.5	51.7–78.5	71.0–91.6	35.9–62.5	52.6–77.9	56.1–80.8
Specificity	77.78	54.4	68.97	39.58	83.33	91.67	86.46
95%CI	67.8–85.9	43.6–65	58.1–78.5	29.7–50.1	74.4–90.2	84.2–96.3	78–92.6
+LR	2.25	1.69	2.13	1.37	2.95	7.93	5.13
95%CI	1.4–3.6	1.3–2.2	1.5–3.1	1.1–1.7	1.8–4.9	4–15.8	3–8.7
-LR	0.64	0.42	0.49	0.43	0.61	0.37	0.35
95%CI	0.5–0.9	0.2–0.7	0.3–0.7	0.2–0.8	0.5–0.8	0.3–0.5	0.2–0.5
+PV	57.4	49.4	56.5	45.8	64.4	83	75.9
95%CI	45.8–68.3	42.7–56.1	47.3–65.2	40.9–50.8	51.9–75.2	71–90.7	64.9–84.3
-PV	72.2	80.3	76.9	79.2	72.7	81.5	82.2
95%CI	66–77.6	70.6–87.4	69.1–83.3	67.2–80.6	67.2–80.6	75.4–86.3	75.7–87.2

A-PCO<sub>2</sub>: admission PCO<sub>2</sub>, A-PO<sub>2</sub>: admission PO<sub>2</sub>, A-AaDCO<sub>2</sub>: admission AaDCO<sub>2</sub>, B-ECPR: CPR before EMS providers, B-HCPR: CPR in ambulance, HCPR: CPR in hospital

Many respiratory, metabolic, and circulatory factors cause the measured lactate value to be high in blood gas analysis. The basis of these values are the onset of anaerobic metabolic activities in tissues experiencing decreased tissue perfusion, increased tissue oxygen demand, and insufficient oxygen during resuscitation of cardiac arrest patients. According to previous studies, a lactate value higher than 2, more pronounced tissue hypoxia, and the presence of 4 or more are indications of higher risk of patient mortality [6]. In this study, the mean lactate levels in arrest patients were measured as 12.7 ± 4.49 (1.6–29), and lactate levels after ROSC administration were measured as 11.78 ± 4.84. The maximum lactate level was 29, and the maximum lactate level of ROSC patients was 24. No significant correlation was found between the elevated prognostic value of the lactate levels and ROSC (P = 0.484), and no statistically significant effect of lactate as a prognostic marker was found.

BE is the amount of acid or base added to bring the pH to 7.40 at 37 °C and 40 mm Hg partial CO<sub>2</sub> pressure. The normal value is between -2.5 and +2.5 mmol/L. In this study, the lowest and highest BE values measured were -28 and 17.5, respectively, and the average was -14.37 ± 6.96. Some studies mentioned BE as a predictor of ROSC, but in this study, statistical data to support this was not reached (P = 0.155).

EtCO<sub>2</sub> followed by capnography is a useful monitoring option for cardiac arrest patients in which follow-up of patients' resuscitation can be done. This process has the

important advantage of being easy to implement; it does not require experience or special skills for application. It is low-cost and noninvasive. During resuscitation, effective ventilation and effective chest pressure increase the measured EtCO<sub>2</sub> value. A sudden increase in the EtCO<sub>2</sub> value during resuscitation can be interpreted as providing ROSC [7–9]. In this study, the arrival of the emergency clinic arrest patients with an average of 15.66 ± 10.15 mm Hg EtCO<sub>2</sub> average value for patients provided ROSC was measured as the average of 29.48 ± 14.98 mm Hg. The minimum EtCO<sub>2</sub> values were 2 mm Hg for the acceptance of arrest patients and 6 mm Hg after ROSC was given. In this study, a statistically significant correlation between EtCO<sub>2</sub> and ROSC as shown by the literature was not found (P = 0.005).

Because resuscitation is a dynamic process, and hardness of arterial blood gas is present in cardiac arrest patients, resuscitation needs more prognostic and neurological indicators independent from patient and devices which cannot be affected PCO<sub>2</sub> measurements. The most beneficial methods for the follow-up and prognosis of patients undergoing resuscitation are EtCO<sub>2</sub> measured by capnography, and PCO<sub>2</sub> and lactate levels measured by blood gas. There has not yet been much research to back the notion that AaDCO<sub>2</sub>, the difference between PCO<sub>2</sub> measured from arterial blood gas and EtCO<sub>2</sub> measured by capnography, could be used as a follow-up and prognostic indicator of resuscitated cardiac arrest patients. Some studies have mentioned that the value of AaDCO<sub>2</sub> might

have an effect on mortality and ROSC and, in some cases, may be indicative of CPR activity and organ perfusion [10, 11]. In this study, the mean AaDCO<sub>2</sub> value was calculated as 52.77 ± 30.49 mm Hg (-4.9 to 153 mm Hg) on admission to the emergency clinic, and 6.02 ± 39.73 mm Hg after ROSC admission, parallel to the study by Spindelboeck et al. [12]. The maximum value at admission to the emergency room was 153 mm Hg, and the maximum value after ROSC was given was 148 mm Hg. According to the statistical analysis performed, a significant relationship was found between ROSC and AaDCO<sub>2</sub> values, which were calculated when the patients came to the emergency clinic (P = 0.0003). The AaDCO<sub>2</sub> values calculated before and after ROSC delivery were found to be useful in predicting the likelihood of ROSC formation.

In this study, CPC was used as the measurement of neurological survival and follow-up of the groups. The CPC value measured during the first hour of patients'

ROSC was defined as the short-term symptomatology, and the CPC value at the patients' discharge was recorded. The mean CPC of ROSC patients was 4.54 ± 0.7. According to the results of statistical analysis, no significant relationship was found between AaDCO<sub>2</sub> values and CPC (P = 0.19).

In conclusion, PCO<sub>2</sub>, PO<sub>2</sub>, and AaDCO<sub>2</sub> can be used as prognostic markers of OHCA patients returning to spontaneous circulation when they are admitted to emergency services. PCO<sub>2</sub> values were calculated from arterial blood gas, and AaDCO<sub>2</sub> values were calculated by EtCO<sub>2</sub> measured by capnography; these were shown to have a more significant statistical value in the prediction of ROSC. Blood gas parameters and EtCO<sub>2</sub> values did not show any activity as neurological improvement markers in the short term, opposite to Hope Kilgannon J et al.'s study [13], and the AaDCO<sub>2</sub> value calculated using these 2 assessments showed that neurological improvement could not be used as a prognostic marker.

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