HHS Public Access

Author manuscript

J Med Surg Public Health. Author manuscript; available in PMC 2025 January 24.

Published in final edited form as:

J Med Surg Public Health. 2024 December ; 4: . doi:10.1016/j.glmedi.2024.100143.

Temporal variations in and predictive values of ABG results prior to in-hospital cardiac arrest

Mina Attin[a,*], **Jie Ren**[b], **Chad Cross**[c], **Sidath Kapukotuwa**[d], **Ryan Shao**[e], **Peter G. Kaufmann**[f], **C.D. (Joey) Lin**[g], **Kim Arcoleo**[h]

[a]School of Nursing, University of Nevada, Las Vegas, 4505 S Maryland Pkwy, Las Vegas, NV 89154, USA

[b]Kirk Kerkorian School of Medicine, University of Nevada, Las Vegas, 625 Shadow Ln, Las Vegas, NV 89106, USA

[c]School of Public Health, University of Nevada, Las Vegas, 4505 S Maryland Pkwy, Las Vegas, NV 89154, USA

[d]School of Public Health, University of Nevada, Las Vegas, 4505 S Maryland Pkwy, Las Vegas, NV 89154, USA

[e]Kirk Kerkorian School of Medicine, University of Nevada, Las Vegas, 625 Shadow Ln, Las Vegas, NV 89106, USA

[f]School of Integrated Health Sciences, University of Nevada, Las Vegas, 4505 S Maryland Pkwy, Las Vegas, NV 89154, USA

[g]Department of Mathematics and Statistics, San Diego State University, 5500 Campanile Dr, San Diego, CA 92182, USA

[h]College of Nursing, Michigan State University, Michigan, Life Science, 1355 Bogue St Room A218, East Lansing, MI 48824, USA

Abstract

In-hospital cardiac arrest (IHCA) has been understudied relative to out-of-hospital cardiac arrest. Further, studies of IHCA have mainly focused on a limited number of pre-arrest patient characteristics (e.g., demographics, number and types of comorbidities). Arterial blood gas (ABG) analysis, one of the most common diagnostic tests for assessing and managing critically or acutely ill hospitalized patients, reflects pathophysiological changes associated with adverse events or complications, including IHCA. Yet the predictive and prognostic values of patterns of pre-arrest ABG parameters for IHCA have not been fully studied. The purpose of this retrospective pilot cohort study was to investigate temporal variations in and predictive values of pre-IHCA ABG values among patients with a history of cardiopulmonary diseases. Eligible patients had a history of structural heart disease, heart failure, or pulmonary diseases. Patients were excluded if their

*Corresponding author. Mina.Attin@unlv.edu (M. Attin).

Declaration of Competingt Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

IHCA was due to trauma, drug overdose, hypothermia, drowning, chronic terminal illness such as cancer or human immunodeficiency virus, or bleeding not caused by hemorrhage in the brain or heart. Also collected were dates, times, and causes of mechanical intubation prior to IHCA and causes of mortality. Co-primary outcomes were initial rhythms of IHCA and return of spontaneous circulation (ROSC). We conducted a pilot study and the ABG results (pH, partial pressure of carbon dioxide [$PaCO_2$], partial pressure of oxygen [PaO_2], bicarbonate [HCO_3^-], and lactate) from each of the 3 days prior to IHCA were extracted from the electronic health records (EHRs) of patients (N = 44) who had experienced IHCA at a single medical center. To characterize differences in ABG parameters among study days, coefficients of variation (CVs) were compared using the modified likelihood ratio test (MLRT) using the worst ABG values. Linear regression models were run for the continuous ABG parameters and logistic regression models for the dichotomous ABG variables. Overall model effect and least squares means, SDs, mean differences within and between days (with 95 % confidence intervals), *p*-values and effect sizes were reported for continuous variables. For categorical variables, estimates and standard errors, 95 % confidence intervals, Wald X2 variables and *p*-values were presented. The CVs for pH, $PaCO_2$, and HCO_3^- differed significant between study days ($p < .05$). The least squares means with 95 % confidence intervals for pH and lactate differed significantly in days ($p < .01$). Moderate to large effect sizes were obtained for all ABG parameters. Arterial lactate predicted initial rhythm (shockable versus non-shockable) and ROSC, while pH and HCO_3^- predicted ROSC. Results demonstrate, for the first time, the presence of significant variability in ABG parameters across 72 h prior to IHCA and the predictive potential of these parameters for initial rhythms of IHCA and ROSC. While validation in a larger sample is necessary, this study confirms the feasibility and potential value of exploring temporal patterns of pre-arrest ABG values from the EHRs. Findings of future larger studies on pre-arrest patterns of ABG parameters and other laboratory values may be used to design models that better predict risk for IHCA and guide patient care in the pre and intra-arrest periods.

Keywords

Resuscitation; Heart arrest; Laboratories; Hospital; In-hospital cardiac arrest; Arterial blood gas

1. Introduction

In-hospital cardiac arrest (IHCA) remains a significant public health challenge in the United States, with approximately 292,000 cases occurring annually and a 1-year survival rate of 13 % [1–3]. IHCA is defined as the absence of a pulse and need for defibrillator shocks and/or chest compressions in a patient who has been admitted to in-patient bed [4]. IHCA is associated with a high mortality rate and a 1-year survival of 13 % [2,3]. Researchers have increasingly noted the similarities and differences between patients with IHCA and out-of-hospital cardiac arrest (OHCA). For example, in a study conducted in Denmark, researchers noted similarities in demographics, comorbidities, and initial rhythms of cardiac arrest between patients with IHCA and those with OHCA [5], but found those with IHCA were sicker and had a higher prevalence of cardiovascular diseases. Yet despite differences noted between the populations, the number of published studies investigating OHCA still far outweigh those exploring IHCA. Moreover, the studies that have examined IHCA have mainly focused on a limited number of pre-arrest patient characteristics (e.g., demographics,

number and types of comorbidities). Few [6,7] have examined pre-arrest changes in clinical variables (e.g., laboratory results). The lack of longitudinal data in public cardiac arrest registries that would enable determination of the prognostic and predictive value of pre-arrest clinical variables is a major reason, our understanding of the pathophysiological mechanisms of IHCA in patients with multimorbidity [8] remains limited.

The most common initial rhythms of IHCA (≥70 %) are non-shockable rhythms which include pulseless electrical activity and asystole [9,10]. These initial rhythms are associated with significantly higher in-hospital mortality rates (~80 %) compared with shockable rhythms (i.e., pulseless ventricular tachycardias and ventricular fibrillation; ~45 % mortality rate) [2,9,10]. Patients with hypoxia, acidosis, or high lactate levels are more likely to experience non-shockable than shockable rhythms in both IHCA and OHCA [11,12].

Arterial blood gas (ABG) analysis is one the most common diagnostic tests utilized in assessing and managing critically or acutely ill hospitalized patients because it reflects pathophysiological changes that may lead to adverse events or complications including IHCA (e.g., metabolic acidosis, tissue hypoxia). While studies have identified that the majority of patients who experience IHCA have a history of cardiopulmonary disease, no study has identified the co-existence of particular types of cardiovascular and pulmonary diseases (e.g., heart failure and chronic obstructive pulmonary disease) prior to IHCA. These patients can develop hypoxemia as the end result of poor gas exchange (e.g., decreased arterial oxygen pressure) accompanied by structural (e.g., air flow limitations particularly among chronic obstructive pulmonary patients patients) and hemodynamic changes (e.g., changes in blood pressure in heart failure patients) that can lead to mortality. Recent studies have reported the association between hypocapnia and an increased mortality among heart failure (HF) patients triggered by hypoxia, and compensated for by metabolic acidosis and elevated lactate level [13–17]. Moreover, some predictive tools of mortality have incorporated the values of some ABG parameters (e.g., APACHE II) [18] however, no study has investigated the temporal sequence or variations of ABG parameters before IHCA. Yet, despite the fact that respiratory distress (e.g., acute hypoxemia defined by SpO_2<90 %) is both a trigger for activation of hospital rapid response team [19,20] and a recognized cause of IHCA [2], the patterns of pre-arrest ABG parameters have not been fully investigated. Instead, studies of the prognostic value of ABG results in IHCA have typically examined either intra- or post-cardiac arrest values in relation to survival and neurological status or to determine the optimal time for tracheal intubation [21,22]. The limited number of studies that have investigated the association between pre-IHCA ABG results and survival have used either a single parameter (e.g., bicarbonate) at one time point or the mean and standard deviations of selected ABG parameters (e.g., HCO_3^-) 24 h after admission to the intensive care unit (ICU) [23,24]. In one of these studies [24] authors indicated that pre-arrest ABG results were not routinely available in the hospital from which they collected data. To our knowledge, no previous study has retrospectively investigated the predictive or prognostic value of the temporal characteristics of pre-IHCA ABG parameters. Understanding these pre-arrest signs should improve our ability to accurately assess risk for IHCA and identify its causes, leading to increased success of intra-arrest treatment [2].

In the present study, we used data from electronic health records (EHRs) to retrospectively identify temporal patterns of pre-arrest ABG parameters in the 72 h prior to IHCA. Specifically, we aimed to determine the predictive value of the temporal patterns of ABG results for the co-primary outcomes of initial rhythm of cardiac arrest and return of spontaneous circulation (ROSC) among patients with a history of cardiopulmonary diseases. Clustering time-series ABG results for a cohort of patients with similar clinical conditions should enable phenotyping that supports prediction of an adverse event with greater sensitivity compared to studying ABG parameters at a single point in time (e.g., admission) in a heterogeneous IHCA population [25]. Ultimately, identifying predictive and prognostic patterns of physiological measures for a relatively homogenous cohort of patients should improve clinicians' ability to develop personalized care plans to minimize the risk of IHCA in high-risk patients and respond in a more timely and effective manner when IHCA does occur.

2. Methods

We conducted an exploratory retrospective cohort study using a database of patients who had experienced IHCA in 2014–2016 at a medical center with > 800 beds. This pilot study had a relatively small sample size and was designed to generate effect size and odds ratio estimates for calculation of sample size, and power for a future larger study. In order to create a relatively homogenous sample, we limited the study to patients with a history of cardiopulmonary diseases. Prior research has shown that the majority of patients who experience IHCA have a history of these diseases [2,26]. The study was qualified for expedited review and approved by the Institutional Review Board (IRB) of data collection site.

Records of patients who experienced IHCA and underwent cardiopulmonary resuscitation (CPR) for 1 min or more were extracted from the EHRs and screened for study eligibility. Patients were eligible if they had a documented history of any of the following: structural heart diseases, including coronary artery disease, myocardial infarction (MI), percutaneous coronary intervention or coronary artery bypass graft surgery (CABG), cardiomyopathy, or valvular disease; heart failure, with signs and symptoms confirmed by physician documentation during the hospitalization in which the IHCA occurred and by echocardiogram showing left ventricular systolic dysfunction (ejection fraction [EF] <50 %); pulmonary disease, including chronic obstructive pulmonary disease. Patients with a history of cardiopulmonary diseases who experienced stroke or complications after CABG (e.g., sternal bleeding after cardiac surgery) were eligible. We selected only the first episode of IHCA for any period of hospitalization. Exclusion criteria included IHCA due to trauma, drug overdose, hypothermia, drowning, chronic terminal illness such as cancer (Stage IV and/or active treatments including radiation therapy and chemotherapy) or human immunodeficiency virus (HIV), or bleeding not caused by hemorrhage in the brain (e.g., stroke) or heart (e.g., bleeding after cardiac surgery). We excluded patients with cancer or HIV because the effects of these diseases on the development of cardiovascular diseases is not fully understood and the underlying mechanism(s) may differ from the traditional pathway(s) of developing or progressing heart disease [27,28]. Also excluded were patients who were comatose (not related to administered sedatives), received resuscitation therapy

as the result of error (i.e., “Do Not Resuscitate” documentation was found in the medical charts), or had incomplete digital code blue sheets in the EHR (i.e., missing time, date, or initial rhythms).

We collected ABG test results for the 72 h prior to the first episode of IHCA for any single period of hospitalization. We selected this time period because of the high probability that it would capture at least one set of lab values. Additionally, it has been reported that 1–2 days is the median time from admission to IHCA [2]. The ABG tests were standardized and measured using the Siemens Rapidlab 1265 system. ABG parameters included pH, partial pressure of oxygen (PaO_2), partial pressure of carbon dioxide ($PaCO_2$), bicarbonate (HCO_3^-), and lactate from whole arterial blood (WB). We also collected dates, times, and causes of mechanical intubation prior to IHCA and extracted causes of mortality from the standardized mortality form signed by a physician. The co-primary outcomes were initial rhythms of IHCA and ROSC. The initial rhythms of cardiac arrest were classified as the presence of non-shockable or shockable rhythms [29]. ROSC was defined as the cessation of CPR therapy in the presence of pulse or circulation [29].

Descriptive statistics including mean and standard deviation (SD) or median and interquartile range for continuous variables and frequency and percent for categorical variables were reported. We used clinical values for each ABG parameter collected during the 72 h prior to IHCA. Day 0 was defined as 0–23 h prior to IHCA, Day −1 as 24–47 h prior to IHCA, and Day −2 as 48–72 h prior to IHCA. To characterize differences in ABG parameters among study days, we calculated coefficients of variation (CVs) by dividing the mean by the SD and then comparing the CVs using the modified likelihood ratio test (MLRT) [30] using the worst value of ABG parameters. Linear regression models were run for the continuous ABG parameters and logistic regression models for the dichotomous primary variables. Overall model effect and least squares means, SDs, mean differences within and between days (with 95 % confidence intervals [CIs]), *p*-values and effect sizes are reported for continuous variables. For categorical variables, estimates and standard errors, 95 % CIs, Wald X^2 values and *p*-values were presented. Results with a *p*-value <.05 were considered statistically significant. Statistical analyses were performed using SAS version 9.4 (SAS Institute, Inc., Cary, NC) and R version 4.3.1 (https://www.Rproject.org/).

3. Results

Of the 100 patients records that remained after eligibility screening, two were excluded due to patient refusal of treatment or unavailability of lab results. Of the remaining 98 records, 44 had ABG results (Fig. 1), and were included in our analyses. Clinical characteristics of these patients are reported in Table 1.

A total of 26 patients were intubated. Causes of intubation prior to IHCA are described in Appendix Table A.1. The median time between intubation and IHCA was 2 days (range 0.2–5 days). None of the intubations were intermittent. Of these 26 patients, 10 were intubated in the 24 h prior to IHCA with specific timing ranging from 17 min to 16 h and 34 min prior to IHCA. Among these 10 patients, the time between the last set of ABG results and IHCA ranged from 6 min to 21 h and 35 min.

The number of ABG tests was greatest on Day 0 ($n = 33$) compared to Day −1 ($n = 20$) and Day −2 ($n = 19$). ABG test results were available for 11 (25 %) patients for all 3 days, 5 (11 %) patients for 2 days, and 28 (64 %) patients for 1 day. The majority of patients had multiple ABG tests on Day 0, ranging from 1 to 11 tests.

The CVs for pH, $PaCO_2$, and HCO_3^- differed significantly between study days (using MLRT; $p < .05$; Table 2). While CVs for lactate-WB did not differ significantly by day, they reached maximum CV (100.07 %) on Day −1. The least square means for both pH and lactate-WB differ significantly by day (Table 3). Lactate-WB was the only parameter that predicted both co-primary outcomes of initial rhythm of IHCA (shockable versus non-shockable) and ROSC (Table 4). pH and HCO_3^- only predicted ROSC.

4. Discussion

In this pilot study, we retrospectively examined ABG parameters across the 3 days prior to IHCA to identify significant temporal variability and ability to predict the co-primary outcomes of initial rhythm of cardiac arrest and ROSC. Our results demonstrate, for the first time, the presence of significant variability in ABG parameters across the 3 days prior to IHCA. Specifically, the CVs for pH, $PaCO_2$, and HCO_3^- varied significantly across study days, though mean values for HCO_3^- remained in the normal range. These results may reflect the heterogenous progression of organ dysfunction in the presence of multimorbidity in hospitalized patients with a history of cardiopulmonary diseases. In fact, the variability of physiological parameters (e.g., kidney function parameters) is an important independent biomarker for mortality among hypertensive patients [31] and patients diagnosed with HF with preserved EF [32].

Our results also demonstrated significant changes in lactate-WB and pH in the 72 h prior to IHCA, which may indicate that these parameters are potential predictors of IHCA. In a recent analysis of data from national registries in Denmark (n=9268 cases with IHCA, n=92395 controls without IHCA), investigators reported a significantly higher level of lactate 24 h prior to IHCA compared to levels for matched controls [6]. Lactate values were only available for 1/3 of the cases and were presented as mean (SD) and median (IQR) at a single point in time, while the difference between groups was presented as absolute mean differences (95 % CI) [6]. Both venous and arterial blood was used to measure lactate, while we only used arterial blood gas for lactate measurements. It has been shown that arterial and venous lactate correlated strongly in certain systematic diseases such as sepsis and septic shock, however, trends should be reported rather than absolute values of lactate [33]. Nevertheless, combined with findings from the present study, these findings suggest that lactate holds promise as an IHCA biomarker.

The present study is the first to examine the predictive potential of pre-arrest ABG test results for the IHCA co-primary outcomes of initial rhythms of cardiac arrest and ROSC. We found that lactate-WB was predictive for both outcomes while pH and HCO_3^- were predictive for ROSC. Two studies of OHCA [34,35] examined the prognostic value of post-arrest ABG results. In the first, pH < 7.0 and lactate ≥ 5.0 mmol/L obtained within 1 h after hospital admission were the measures most strongly associated with mortality in the first 5 days

after resuscitation [34]. The second reported that pH and lactate measured at admission for OHCA were predictors of mortality in the emergency department (ED) for both patients with ROSC or with ongoing CPR [35]. Though neither of these studies examined temporal patterns of pre-arrest ABGs, findings support our hypothesis that ABG measures have prognostic value for the outcome of IHCA.

While respiratory distress or failure is often considered one of the primary causes of IHCA [2], only 39 % of the patients in our sample had a history of pulmonary disease. Furthermore, the majority of deaths in our sample were attributed to either cardiac dysfunction or causes other than cardiac or respiratory dysfunction and intubations were not strictly related to respiratory insufficiency or distress. It is important to note, however, that we did not assess the association between the cause of intubation requirement and outcomes including IHCA nor did we have access to autopsy reports to confirm cause of death. Nonetheless, our findings imply that, while ABG parameters may warn clinicians about impending adverse events, merely correcting the ABG abnormalities might not be adequate to prevent IHCA. For example, 30 % of patients in the present study had sepsis, some of whom were intubated due to acidosis or respiratory failure caused by sepsis. Sepsis has been identified as the leading cause of mortality among critically ill patients [36]. One study [37] found that the proportion of IHCA patients with sepsis ranged from 13 % to 27 %, and that outcomes for these patients are worse than for IHCA patients without sepsis. It is associated with acidemia due to different factors (e.g., tissue hypoxia, respiratory failure) including organ dysfunction (e.g., chronic renal insufficiency, diabetic ketoacidosis) which may cause electrolyte imbalances including hyperkalemia [31,32]. Any factor (e.g., lack of insulin) that decreases the activity of sodium-potassium pump located in the outer plasma membrane of the cell (Na-K-ATPase) causes an increase in serum potassium leading to hyperkalemia [38]. The inability of Na-K-ATPase to pump 3 sodium ions out of the cell and 2 potassium ions into the cell cause an accumulation of potassium extracellularly (e.g., hyperkalemia). Sepsis is also associated with hyperchloremic [39,40] metabolic acidosis which promotes inflammatory responses including proinflammatory cytokines (e.g., interleukin-6, nitric oxide). These abnormalities ultimately depress myocardial function (e.g., electrical disturbances, contractility) leading to cardiac arrhythmias and potentially to cardiac arrest [36,37].

4.1. Implications and recommendations for research and clinical practice

Our findings in this pilot study of significant temporal variation in pre-arrest ABG parameters as well as associations between ABG parameters and the initial rhythms of cardiac arrest and ROSC suggest that further research is warranted. In particular, future studies using machine learning to predict IHCA and outcomes among a large sample should include longitudinal pre-arrest ABG parameters. To date, such studies have either not included pre-arrest ABG parameters, [7,41] or have not examined the temporal characteristics of test results in relation to IHCA or identified whether lactate was measured in arterial or venous blood [42]. Furthermore, our findings suggest that phenotyping pre-arrest ABG parameters for patient subpopulations may provide better insight into the complex pathophysiology of IHCA than studying these parameters across patients with varied comorbidities. Such data could provide diagnostic clues to underlying

mechanism(s) of IHCA, thus improving clinicians' decision-making process and leading to more personalized treatment plan to prevent adverse events or minimize the severity of post-IHCA complications. Finally, our finding of high lactate-WB levels 72 h prior to IHCA suggests that patterns of laboratory values, including ABG parameters, should be investigated for a longer pre-arrest period than has been typical in IHCA studies. In future studies, we will collect ABG parameters and other laboratory results over at least 1 week prior to IHCA. We will also include time series data on electrolyte levels prior to IHCA. This data would imporve our knowledge of predictive value of changes in Lab's parameters and may improve our ability to identify and respond to the onset of instability. If these findings are validated in larger studies, clinicians will be able to use the temporal patterns of ABG values to monitor at-risk patients more effectively.

4.2. Strengths and limitations

The primary limitations of the present study are its retrospective design and small sample size. Results need to be validated with a larger sample size before they can be generalized to cardiopulmonary patient population. Despite its small sample size, however, findings add to the scant literature on pre-arrest clinical characteristics in patients with IHCA. Other limitations are that we only included patients who underwent 1 min or more of CPR which excluded more patients relative to other resuscitation studies. We also did not examine the effect of intubation on outcomes and did not address sex as a biological variable [43] due to our small sample size.

5. Conclusions

To our knowledge, this study is the first to describe longitudinal patterns of ABG lab results across the 72 h prior to IHCA. While the small sample size means that results cannot be applied to clinical practice without validation in a larger sample, the study confirms the feasibility of exploring temporal patterns in pre-arrest ABG data from the EHRs and makes a valuable contribution to the literature in this area. Future studies with larger sample sizes of relatively homogeneous patients, including at least 1 week of pre-arrest ABG parameters, will enable determination of the sensitivity and specificity of pre-arrest ABG parameters for predicting initial rhythms and outcomes of IHCA. Such studies should also include sex [43] as a biological variable and look at prediction of specific types of initial rhythms (e.g., pulseless electrical activity) rather than the larger categories of shockable versus non-shockable. Findings of larger studies on the predictive and prognostic value of patterns of ABG parameters and other pre-arrest laboratory values may be used to design models that better predict risk for impending adverse events and guide patient care in the pre-, intra-, and post-arrest periods.

Acknowledgments

Funding Acknowledgement

Dr. Lin's research was supported by the NIH R61 MH120236-01A1, NIH/NIMHD UG3 MD018353, and NIH/NHLBI R01HL158538. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Appendix

Table A1

Causes of intubation prior to in-hospital cardiac arrest (n=26)

Reasons for Intubation	*n*
Cardiac (n=10)	
Procedure or Surgery[a]	5
Cardiac Complications (e.g., MI)	5
Respiratory Diseases (n=5)	
Aspiration pneumonia	2
Pulmonary disease (Pneumonia)	1
Respiratory distress	1
Respiratory failure (Sepsis)	1
Others (n=11)	
Medications	1
Stroke	1
Metabolic disorders (i.e., acidosis, seizure after hyperglycemia)	3
Procedure or surgery (i.e., abdominal and craniectomy; airway protection)	4
Hemodynamic instability (airway protection)	2

Note. MI = myocardial infarction

[a]Procedures or surgery included Transesophageal echocardiogram; Cardiac Surgeries, Coronary artery bypass graft Surgery, aortic valve and aortic dissection surgeries.

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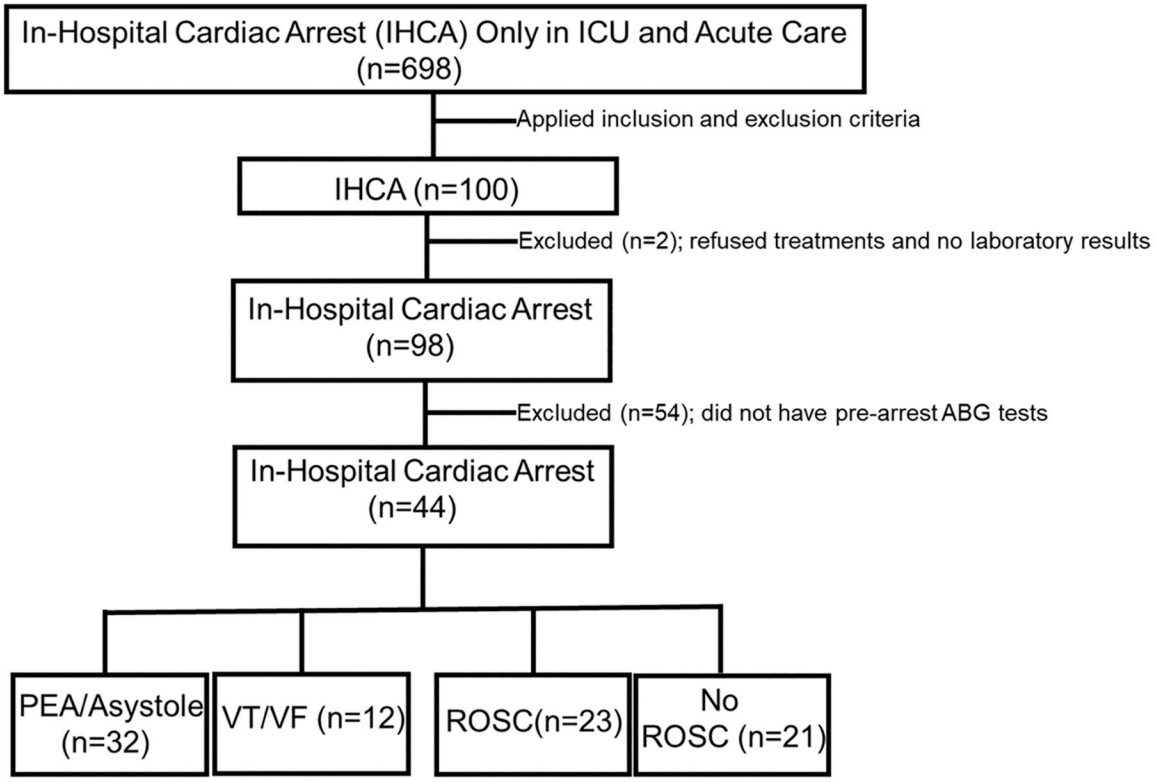

Fig. 1.
Flowchart. Patients included in the study for final analyses.

Table 1

Clinical characteristics of study subjects.

Characteristics	Descriptive Statistics
Age (years)	70±12
Sex (Female)	10 (23 %)
Location (ICU)	33 (75 %)
Body mass index (BMI)	31±7
Length of stay (days)	5 (2–8)
Initial rhythm of cardiac arrest (VT/VF)	12 (28 %)
ROSC	23 (52 %)
Survival to hospital discharge	8 (18 %)
Ejection Fraction	49±21 %
APACHE II scores	29.7±10
Day 0	43.9±25.9
Day –1	44.4±23.5
Day –2	45.5±23.9
History of cardiac disease	
Coronary artery diseases	29 (66 %)
Heart failure	28 (64 %)
Myocardial infarction (at either current or prior admissions)	13 (30 %)
Cardiomyopathy	12 (27 %)
Implanted heart devices (pacemaker, ICD)	7 (16 %)
Non-cardiac disease	
Dialysis	6 (14 %)
Pulmonary diseases (e.g., COPD)	17 (39 %)
Sepsis on admission or during hospitalization	13 (30 %)
Cause of mortality (n=36)	
Cardiac diseases	17 (38 %)
Acute respiratory distress/pneumonia	5 (11 %)
Others	12 (27 %)
No documentation	2 (4 %)

Note. Continuous variables are reported as mean ± SD or median (interquartile range); categorical variables are reported as n (%). ICU = intensive care unit; Day 0 = 0–23 h prior to cardiac arrest; Day −1 = 24–47 h prior to cardiac arrest; Day −2 = 48–72 h prior to cardiac arrest. BMI = Body mass index; COPD = Chronic obstructive pulmonary disease; eGFR = estimated glomerular filtration rate; ICD = Implantable cardioverter defibrillator; MI = Myocardial infarction; ROSC = Return of spontaneous circulation; VT/VF = Pulseless ventricular tachycardias/ventricular fibrillation

Table 2

Values of arterial blood gas parameters over the 3 days prior to in-hospital cardiac arrest (n=44).

	Day 0				Day –1				Day –2			
ABG Parameters	**N**	**Mean**	**SD**	**CV**	**N**	**Mean**	**SD**	**CV**	**N**	**Mean**	**SD**	**CV**
pH[a,b,c]	33	7.26	0.16	2.33 %	20	7.39	0.09	1.30 %	19	7.36	0.12	1.67 %
$PaCO_2$[a,b,c] (mm Hg)	33	41.69	18.50	44.37 %	20	34.15	8.53	24.97 %	19	36.68	11.47	29.72 %
PaO2 (mm Hg)	33	170.42	157.02	92.13 %	20	106.20	95.48	89.90 %	19	114	84.64	74.24 %
HCO_3^-[a,b,c,d](mm Hg)	33	20.27	9.77	48.19 %	20	21.40	5.94	27.75 %	19	23.05	5.69	24.68 %
Lactate-WB (mmol/L)	27	7.41	6.03	81.37 %	16	3.83	3.84	100.07 %	15	2.88	2.27	77.08 %

Note. Day 0 = 0–23 h prior to IHCA; Day −1 = 24–47 h prior to IHCA; Day −2 = 48–72 h prior to IHCA; N = Number; CV = Coefficient of variations; SD = Standard deviation $PaCO_2$ = Partial pressure of carbon dioxide; PaO_2 = Partial pressure of oxygen; HCO_3^- = Bicarbonate; lactate-WB = Lactate from whole arterial blood;

[a]Significant variations by modified likelihood ratio test (MLRT) at $p < .05$;

[b]Significant variations over the 3-day study period at $p < .05$;

[c]Significant variations from Day 0 to Day −1 (pH $p \leq 0.02$; $PaCO_2$ and HCO_3^- $p \leq 0.03$);

[d]Significant variations comparing Day −1 to day −2 ($HCO_3^- p \leq 0.02$)

Table 3

Changes in values of arterial blood gas parameters over 72 h prior to in-hospital cardiac arrest.

Characteristic Observations (N=72)	Least Square Mean (SE)	Δ (95 % CI)[a]	*p*-Value[a]	Effect Size *f*
pH				
Day 0	7.26 (0.02)			
Day–1	7.40 (0.03)	**0.13 (0.05, 0.21)**	**<.01**	
Day –2	7.36 (0.03)	**0.09 (0.01, 0.17)**	**.01**	
Overall effect[b]		***F*=6.24**	**<.01**	**0.38**
$PaCO_2$mm Hg				
Day 0	41.70 (2.54)			
Day –1	34.15 (3.27)	−7.55 (−15.80, 0.71)	.07	
Day –2	38.68 (3.35)	−3.01 (−11.40, 5.38)	.48	
Overall effect[b]		*F*=1.66	.20	**1.79**
HCO_3^- mmol/L				
Day 0	20.27 (1.38)			
Day –1	21.40 (1.77)	1.12 (−3.34, 5.60)	.61	
Day –2	23.05 (1.81)	2.87 (−1.76, 7.32)	.22	
Overall effect[b]		*F*=0.75	.47	**0.88**
PaO_2mm Hg				
Day 0	170.42 (21.89)			
Day –1	106.20 (28.12)	−64.22 (−135.32, 6.87)	.08	
Day –2	114.00 (28.85)	−56.42 (−128.67, 15.83)	.12	
Overall effect[b]		*F*=2.08	.13	**5.89**
Lactate-WB (mmol/L)				
Day 0	7.41 (0.91)			
Day –1	3.84(1.19)	**−3.57 (−6.57, −0.58)**	**.02**	
Day –2	2.88(1.22)	**−4.53 (−7.59, −1.47)**	**<.01**	
Overall effect[b]		***F*=5.39**	**<.01**	**1.69**

Note. Day 0 = 0–23 h prior to IHCA; Day −1 = 24–47 h prior to IHCA; Day −2 = 48–72 h prior to IHCA;

$PaCO_2$ = Partial pressure of carbon dioxide; HCO_3^- = Bicarbonate; PaO_2 = Partial pressure of oxygen;

lactate-WB = Lactate from whole arterial blood;

[a]Effect size *f* values > .10 = small, > 0.25 = medium, and > 0.40 = large effect sizes.

[a]Change relative to Day 0 (0–23 hours=day of IHCA);

[b]Effect over all time points.

Table 4

Prediction of primary outcomes by ABG parameters.

	ROSC[a]				Initial Rhythms[b]			
Lab Parameter	**Estimate (SE)**	**95 % CI**	**Wald X^2**	***p*-Value**	**Estimate (SE)**	**95 % CI**	**Wald X^2**	***p*-Value**
pH	4.31 (1.93)	0.53, 8.08	4.99	**.03**	−1.34 (1.95)	−5.15, 2.48	0.47	.49
$PaCO_2$	0.03 (.02)	−0.004, 0.07	2.93	.09	0.02 (.02)	−0.02, 0.06	0.65	.42
HCO_3^-	0.08 (.03)	0.02, 0.15	5.95	**.01**	0.01 (.03)	−0.06, 0.08	0.08	.78
PaO_2	0.004 (.002)	−0.00002, 0.009	3.80	.05	0.001 (.002)	−0.003, 0.006	0.35	.55
Lactate-WB	−0.08 (.03)	−0.14, −0.02	6.08	**.01**	0.20 (.05)	0.10, 0.31	14.34	**.0002**

Note. Bold font indicates significance at $p < .05$

[a]ROSC = Return of spontaneous circulation; Reference group = Non-survivor;

[b]Initial Rhythms; Reference group = Pulseless Ventricular tachycardias/ventricular fibrillation (VT/VF)

J Med Surg Public Health. Author manuscript; available in PMC 2025 January 24.