Factors Predicting Cardiac Arrest in the Intensive Care Unit: A Matched Case-Control Study

Wentao Sang

Department of Emergency Medicine, Qilu Hospital, Shandong University

Yuhui Pan

Department of Emergency Medicine, Qilu Hospital, Shandong University

Xue Zhao

Department of Emergency Medicine, Qilu Hospital, Shandong University

Shuo Wu

Department of Emergency Medicine, Qilu Hospital, Shandong University

Wen Zheng

Department of Emergency Medicine, Qilu Hospital, Shandong University

Chang Pan

Department of Emergency Medicine, Qilu Hospital, Shandong University

Jiaqi Zheng

Department of Emergency Medicine, Qilu Hospital, Shandong University

Shuxing Wei

Department of Emergency Medicine, Qilu Hospital, Shandong University

Yongsheng Zhang

Department of Emergency Medicine, Qilu Hospital, Shandong University

Jian Zhang

Department of Emergency Medicine, Qilu Hospital, Shandong University

Jingjing Ma

Department of Emergency Medicine, Qilu Hospital, Shandong University

Yuguo Chen

Department of Emergency Medicine, Qilu Hospital, Shandong University

Feng Xu (✉ xufengsdu@126.com)

Department of Emergency Medicine, Qilu Hospital, Shandong University

Research Article

Keywords: Intensive care unit, Cardiac arrest, Predictive factors, Laboratory indicator, Vital sign

Posted Date: December 16th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-1169878/v1>

License: This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background: Early detection and intervention of disease deterioration are the keys to reducing the incidence of preventable intensive care unit cardiac arrest (ICU-CA). We aimed to investigate the ICU-CA predictive factors, including vital signs and laboratory indicators, and to analyze the performance of trends value of those factors on predicting ICU-CA.

Methods: We conducted a matched case-control study at Qilu Hospital of Shandong University. Data on adult patients in ICU who suffered a cardiac arrest (CA) were retrospectively collected from 2016 to 2019, including vital signs and laboratory indicators at 48, 36, 24, 12, and 8 hours before ICU-CA. These cases were matched (ward, sex, and admission data) with controls (no ICU-CA) at a 1:2 ratio. Univariable logistic regression was used for statistical comparisons between cases and controls, and multivariate logistic regression was used to investigate the independent associations of indicators and their tendency with ICU-CA at given time points. The area under receiver operating characteristic (AUROC) was used to evaluate the predictive performance on ICU-CA.

Results: Of 6164 ICU patients, 1042 patients suffered an ICU-CA during the 3 years. After careful screening, a total of 427 patients were included as the cases in the study, and 790 patients were included as controls. The vital signs and laboratory indicators at 8h before cardiac arrest, such as heart rate (HR), respiratory rate (RR), systolic blood pressure (SBP), oxygen saturation (SaO₂), hemoglobin (HGB), potassium (K⁺), sodium (Na⁺), lactic acid (Lac), and pH all can predict the ICU-CA. The mean value, maximum value, minimum value, and range of these indicators were related to the occurrence of ICU-CA, and the trend values were more accurate than the current value for the variability in laboratory indicators.

Conclusions: The ability of trends value of laboratory indicators for predicting ICU-CA was more accurate than the value at given time points for the variability in laboratory indicators. Adding trends of laboratory indicators may increase the accuracy of models designed to detect critical illness in ICU.

Trial registration: ClinicalTrials.gov Identifier: NCT04670458.

Background

Early detection and intervention of disease deterioration are the keys to reducing the incidence of preventable in-hospital cardiac arrest (IHCA)[1]. Vital signs have been shown to be accurate predictors of clinical deterioration[2-6]. However, the usefulness of vital signs is affected by the quality of the process of measurement[7, 8]. Due to the results of laboratory tests being subject to strict quality control and having independently been identified as risk factors for poor patient outcome[9-11], the laboratory indicators were used to be the predictors of IHCA[8, 9, 12, 13]. Compared to vital signs alone, laboratory indicators increase the ability to identify patients at risk of deterioration[14]. In spite of that, the difficulty in obtaining laboratory indicators limits the application of the prediction[15].

The patients in the intensive care unit (ICU) have differences with the general ward, which of the severity of illness, comorbidities, and the incidence of cardiac arrest[16-18]. With continuous vital signs monitoring, frequent laboratory tests, more medical care, and supportive therapies, in intensive care unit cardiac arrest (ICU-CA), where early detection and early intervention was more critical and necessary, it should be separated from the IHCA and form its own entity[16, 17]. Laboratory tests are common in ICU, such as arterial blood gas (ABG) analysis[19], which reduces the limitation of laboratory indicators in predicting cardiac arrest.

The previous study showed that the trends of these variables significantly improved the accuracy of detecting clinical deterioration compared to the vital sign values at a given time alone[1]. Same as the vital signs, simply including the laboratory indicator since the last collection may not adequately capture a patient's true physiologic trajectory[20]. Additional methods, such as including laboratory indicator variability (the mean and the range values), the most deranged previous values (the maximum and the minimum), may be more accurate[1]. However, it has not been confirmed that the trends of laboratory indicators are more accurate than laboratory indicators at a single time point in predicting ICU-CA.

In this study, we aimed to investigate the ICU-CA predictive factors, including vital signs and laboratory indicators, and to analyze the predictive ability of trends of vital signs and laboratory indicators on ICU-CA.

Methods

Study design

This study was conducted as a matched case-control study at the Intensive Care Unit of Qilu Hospital of Shandong University in Jinan, China. The ICU of the Hospital comprises 7 ICUs (including general ICU, Cardiac Care Unit, Respiratory Intensive Care Unit, Gastroenterology Intensive Care Unit, Emergency Intensive Care Unit, Neurosurgical Intensive Care Unit, Cardiac Surgical Intensive Care Unit), with a total capacity of 162 ICU beds, approximately 2000 patients are treated annually.

Patient recruitment and eligibility

We included adult patients (>14) with a cardiac arrest event during their ICU stays as the cases from December 1st, 2016 to November 30th, 2019. We excluded patients with do not attempt resuscitation (DNAR), suffered cardiac arrest prior to ICU admission, had a length of stay (HLOS) less than 48 hours, or had cardiac arrest during surgery. Controls were the patients without cardiac arrest events during their ICU stays, and selected at 1:2 ratio, after being matched to cases by ward, sex, and admission data (around 1 month).

Data collection

Data were collected using an electronic case report form from the medical records, including age, sex, comorbidities at ICU admission, admission diagnosis, vital signs, laboratory indicators, the prognosis of

ICU-CA, and discharge information. Vital signs and laboratory indicators were collected at 48, 36, 24, 12, and 8 hours before the cardiac arrest onset in the case group and before a randomly selected time point during ICU stay in the control group. Vital signs comprised body temperature (T), heart rate (HR), respiratory rate (RR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and oxygen saturation (SaO₂); Laboratory indicators contained hemoglobin (HGB), potassium (K⁺), sodium (Na⁺), calcium (Ca²⁺), lactic acid (Lac) and pH. Pulse pressure index (PPI) was calculated using the following formula: $PPI = (SBP - DBP) / SBP$.

Definitions

ICU-CA was defined as the absence of circulatory signs in patients who had a pulse and circulation that requires chest compressions and/or electrical defibrillation during ICU stay [21]. The sustained return of spontaneous circulation (ROSC) was defined as stable circulation for at least 20 minutes. Neurological outcomes were assessed by physicians on-site using cerebral performance categories (CPC) within routine clinical care. A CPC score of 1-2 was defined as a favorable neurological outcome, whereas 3-5 was unfavorable. We set the time point when ICU-CA occurred to be T₀, and the time point at 48h before T₀ was -48h.

In our study, the trend of vital signs and laboratory indicators was defined as the mean, maximum, minimum and range values of variables[1]. The mean value was the average value of 5 time points (-48h, -36h, -24h, -12h, and -8h), the maximum value was the largest value of 5 time points, the minimum value was the smallest value of 5 time points, the range value was calculated using the following formula: range value= maximum value - minimum value.

Statistical analysis

Categorical variables were presented as percentages, and continuous variables as medians (Q1, Q3). Missing data were filled with data from the nearest time point. Considering the data distribution of SaO₂ and Lac, the SaO₂ was modified as a dichotomous variable with the cut-off of 95%, the value of Lac was natural log-transformed; considering the magnitude of the change in pH is small, the value of pH was multiplied by 100.

Univariable logistic regression was used for statistical comparisons between cases and controls, and the odds ratio (OR) with a 95% confidence interval (CI) was reported. The area under receiver operating characteristic (AUROC) was used to indicate the predictive power of the laboratory indicators and their trends for ICU-CA. To investigate the independent associations of ICU-CA, vital signs or laboratory indicators at given time points was evaluated by multivariate logistic regression model of stepwise selection, and the trends indicators across all indicators at given time points of no selection. Furthermore, as the nature of the data follows a hierarchy, the association of vital signs or laboratory indicators with the outcome was evaluated by the multilevel multivariate logistic regression model, and clinically relevant and significant variables in the univariable multilevel analysis were included.

Tests were two-sided. $P < 0.05$ was considered significant. All analysis was conducted using IBM SPSS Statistics Version 25.0 (IBM Corp., Armonk, NY), all of which were conducted in collaboration with a statistician.

Results

Study population

During the study period (December 1st, 2016 to November 31st, 2019), a total of 6164 patients were treated in ICU in Qilu Hospital of Shandong University. 1042 patients with ICU-CA were retrospectively identified. Patients younger than 14 years old (18 patients), with DNAR (386 patients), with cardiac arrest prior to ICU admission (104 patients) or cardiac arrest during surgery (21 patients), with HLOS less than 48 hours (137 patients) were excluded, and a total of 427 patients were enrolled as the cases in this study. There were 790 controls selected at a 1:2 ratio, after being matched to cases by ward, sex, and admission data (Figure.1).

Baseline characteristics before cardiac arrest

Patients were predominantly male (70.1%, $n=853$) and the median age was 63 (50,73) years. Comorbidities in our study were frequent, with leading comorbidities as hypertension (50.5%, $n=614$), coronary artery disease (CAD; 35.3%, $n=429$), diabetes mellitus (22.6 %, $n=275$), and stroke (21.0%, $n=255$). Other common comorbidities were malignancy (tumor) (10.8%, $n=131$) and chronic obstructive pulmonary disease (6.7%, $n=81$). There were no significant differences in other characteristics, except age (64 vs. 62, $P=0.045$) and CAD (39.8% vs. 32.8%, $P=0.014$). The main reasons for ICU admission were respiratory diseases in 21.6% of patients ($n=263$, pulmonary infections were counted as respiratory diseases), cardiovascular diseases in 18.7% of patients ($n=228$), trauma in 7.1% of patients ($n=87$), and cerebrovascular diseases in 6.5% of patients ($n=79$). Table 1 shows the baseline characteristics of the cases and controls.

Characters during ICU-CA and Outcome after ICU-CA

Of the 427 cases, all patients (100%) were witnessed when cardiac arrest occurred. The initial rhythms of 62 cases (14.5%) were ventricular fibrillation (VF) or ventricular tachycardia (VT). 121 cases (28.3%) had ROSC, 51 cases (11.9%) survived to hospital discharge, and 9 cases (2.1%) had good neurological function ($CPC \leq 2$). Table 2 reported the characteristics of ICU-CA and the outcome after ICU-CA.

Factors associated with ICU-CA

Patients in the ICU-CA group were older (64 vs. 62, $P=0.045$) and had more CAD (39.8% vs. 32.8%, $P=0.014$) (Table 1). Age and CAD were used as the concomitant variable in multivariable logistic regression analysis.

After univariable logistic regression analysis, both vital signs and laboratory indicators were correlated with ICU-CA. Then we conducted multivariable logistic regression analysis adjusted age and CAD. HR, SaO₂, Na⁺, and Lac at five time points, SBP and K⁺ at four time points, HGB and pH at three time points, T, DBP, and PPI at one time point were all associated with the occurrence of ICU-CA. However, the laboratory indicator of Ca²⁺ at any time point was not associated with ICU-CA. Table 3 shows the relationship between ICU-CA and the vital signs or laboratory indicators at different time points.

In the multilevel analysis, clinically relevant and significant variables in the univariable analysis were included. Finally, the HR, RR, SBP, SaO₂, HGB, K⁺, Na⁺, and Lac were related to the ICU-CA, as shown in Table 4.

Trends of vital signs

Then we analyzed the relationships between the mean value, maximum value, minimum value and range of vital signs or laboratory indicators and ICU-CA, with the results shown in Table 5. The mean value ($P<0.001$), maximum value ($P<0.001$), minimum value ($P<0.001$) and range ($P<0.001$) of HR; the mean value ($P<0.001$), maximum value ($P=0.002$), and minimum value ($P<0.001$) of RR; the mean value ($P<0.001$), maximum value ($P<0.001$), and minimum value ($P<0.001$) of SBP were related to the occurrence of ICU-CA.

Trends of laboratory indicators

The minimum value ($P=0.001$) of HGB; the mean value ($P=0.011$), maximum value ($P<0.001$), and range ($P<0.001$) of K⁺; the mean value ($P<0.001$), maximum value ($P<0.001$), and minimum value ($P=0.001$) of Na⁺; the mean value ($P<0.001$), maximum value ($P<0.001$), and range ($P<0.001$) of Lac; and the mean value ($P=0.027$), minimum value ($P<0.001$), and range ($P<0.001$) of pH were related to the occurrence of ICU-CA (Table 5).

During univariable analysis, Lac was the most accurate laboratory indicator when using the current value at -8h time point (AUROC: 0.769), and the trend values were more accurate than the current value for the variability in Lac (AUROC: 0.770 for maximum value). Rang of pH (AUROC: 0.740 vs. 0.672 for the current value), rang of K⁺ (AUROC: 0.712 vs. 0.620 for the current value), rang of Ca²⁺ (AUROC: 0.695 vs. 0.601 for the current value), maximum value of Na⁺ (AUROC: 0.683 vs. 0.677 for the current value), and the minimum value of HGB (AUROC: 0.627 vs. 0.621 for the current value). The results are shown in Figure 2.

Discussion

In our study, for the first time, we analyzed the ability of trends value of laboratory indicator for predicting ICU-CA. We found that the trend values of laboratory indicators were more accurate than the value at given time points for the variability in laboratory indicators. Overall, the range of laboratory indicators performed well in predicting ICU-CA, especially pH, K⁺, and Ca²⁺, as shown in Figure 2. This may be

related to the patient's physiological state, a large change in a short period often means a deterioration of patients. The maximum value of Lac, the maximum value of Na^+ , and the minimum value of HGB were also more accurate than the current value.

Ryo Ueno et al. proposed that the addition of laboratory indicators to vital signs did not significantly improve the overall performance of the machine learning model in predicting IHCA[15]. It seems to contradict our conclusion, but we should be aware that the laboratory indicators they used were only two sets from the last seven days. The abnormal laboratory indicators could not reflect physiological deterioration, due to the intervention by doctors and nurses. As a result, such deterioration might not result in IHCA[21]. In ICU, where laboratory tests are frequent, especially for AGB, we can obtain more timely laboratory test results that may better reflect the patient's physiological deterioration. Using laboratory indicators to predict the outcomes of patients, such as cardiac arrest, seems more feasible in ICU than in the general wards.

After over three years of retrospective data gathering, a total of 6164 patients were treated in ICU and 1042 ICU-CA patients were identified. The incidence was about 169 cases per 1000 admissions, which was higher than other studies[6, 8, 17]. The higher incidence may be related to the more severe conditions of the patients in ICU[22] and to the transferring potential of IHCA events to ICU by Hospital-wide rapid response teams[16].

The demographics of ICU-CA patients and the initial rhythm in our study were consistent with previous studies[17]. The median age was 63 years old and 70.1% were male. 85.5% of the initial rhythms were unshockable rhythm. However, outcomes after the ICU-CA, such as ROSC, survival to Hospital discharged, and the good neurological function at discharge was slightly worse than previous studies[16, 17], especially the rate of good neurological function. In our study, the rate of CPC<2 at discharge was only 2.1%, whereas Enohumah et al. reported up to 39% of patients with good neurological function[23].

Consistent with previous findings[4-6, 13, 21, 24, 25], IHCA can be predicted by vital signs and laboratory indicators. Previous studies have shown that abnormal vital signs and laboratory indicators could predict the occurrence of IHCA 48 hours in advance[6, 26-29], which was similar to our study and earlier than the commonly used early warning scores and other prediction models with only 24 hours in advance[30-34]. A recent study has shown that the trends of vital signs, such as mean, standard deviation, slope, maximum, minimum, are better predictors than current values of vital signs[1], the same conclusion was observed in our study.

It is confusing that in our study, the PPI was not associated with ICU-CA, which was inconsistent with previous researches[6, 27]. The inconsistent conclusions may be relevant to the enrolled population that patients enrolled in previous studies mostly came from general wards[6, 27], although a recent study has shown that there is no difference in PPI of patients in ICU from general wards[35].

Limitations

Firstly, this study was conducted in a single center in China, thus, our results must be generalised with caution. Secondly, the retrospective data collected in this study may be missing at some point. Although the data of the most recent moment have been used to fill in the gaps, there is still inevitably some information bias. Thirdly, despite the suitability of the study design (a matched case-control study with twice the controls), it is possible that some factors did not reach statistical significance due to the difference in the incidence of ICU-CA in reality compared with the ratio of ICU-CA in our study population. Next, studies will be designed for external validation to evaluate the performance of the trend of laboratory indicators.

Conclusions

The ability of trends value of laboratory indicators for predicting ICU-CA was more accurate than the value at given time points for the variability in laboratory indicators. Adding trends of laboratory indicators may increase the accuracy of models designed to detect critical illness in ICU.

List Of Abbreviations

ABG: arterial blood gas	IHCA: in-Hospital cardiac arrest
AUROC: area under receiver operating characteristic	K ⁺ : potassium
CAD: coronary artery disease	Lac: lactic acid
Ca ²⁺ : calcium	Na ⁺ : sodium
CPC: cerebral performance categories	OR: odds ratio
CI: confidence interval	PPI: pulse pressure index
DBP: diastolic blood pressure	ROSC: return of spontaneous circulation
DNAR: do not attempt resuscitation	RR: respiratory rate
HGB: hemoglobin	SaO ₂ : oxygen saturation
HLOS: Hospital length of stay	SBP: systolic blood pressure
HR: heart rate	T: body temperature
ICU: in intensive care unit	VF: ventricular fibrillation
ICU-CA: intensive care unit cardiac arrest	VT: ventricular tachycardia

Declarations

Ethics approval

The study protocol was approved by the Ethics Committee Scientific Research of Qilu Hospital of Shandong University (Approval No.: KYLL-202008-028). The requirement for informed patient consent was waived, because this was a retrospective observational study. ClinicalTrials.gov Identifier: NCT04670458.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

This work was supported by National S&T Fundamental Resources Investigation Project [2018FY100600, 2018FY100602], National Key R&D Program of China [2020YFC1512700, 2020YFC1512705, 2020YFC1512703], Taishan Young Scholar Program of Shandong Province [tsqn20161065, tsqn201812129], Taishan Pandeng Scholar Program of Shandong Province [tspd20181220], the Interdisciplinary Young Researcher Groups Program of Shandong University [2020QNQT004], Clinical Research Center of Shandong University [2020SDUCRCB003], the Clinical Research Center of Shandong University [2020SDUCRCC025], the National Natural Science Foundation of China [81873950, 82072144, 81772036, 81873953], the State Key Program of the National Natural Science Foundation of China [82030059], the Natural Science Foundation of Shandong Province [ZR2020QH163]. The funding organization had no involvement in any aspect of the study.

Authors' contributions

WTS, FX planned and established the project, including the procedures for data collection, drafted the manuscript, and performed data analysis. SW performed detailed statistical analysis of the data. CP, JQZ, WZ, and YSZ drafted the manuscript, and performed data collection and data analysis. YHP, XZ, SXW, JZ, and JJM performed data collection. FX and YGC reviewed critical revisions to the manuscript. All authors took part in rewriting and approved the final manuscript.

Acknowledgements

Not applicable

References

1. Churpek MM, Adhikari R, Edelson DP: **The value of vital sign trends for detecting clinical deterioration on the wards.** *Resuscitation* 2016, **102**:1-5.
2. Kwon JM, Lee Y, Lee Y, Lee S, Park J: **An Algorithm Based on Deep Learning for Predicting In-Hospital Cardiac Arrest.** *Journal of the American Heart Association* 2018, **7**(13).
3. Srivilaithon W, Amnuaypattanapon K, Limjindaporn C, Imsuwan I, Daorattanachai K, Dasanadeba I, Siripakarn Y: **Predictors of in-Hospital cardiac arrest within 24 h after emergency department triage: A case-control study in urban Thailand.** *Emerg Med Australas* 2019, **31**(5):843-850.
4. Andersen LW, Kim WY, Chase M, Berg KM, Mortensen SJ, Moskowitz A, Novack V, Cocchi MN, Donnino MW: **The prevalence and significance of abnormal vital signs prior to in-Hospital cardiac arrest.** *Resuscitation* 2016, **98**:112-117.
5. Hong W, Earnest A, Sultana P, Koh Z, Shahidah N, Ong ME: **How accurate are vital signs in predicting clinical outcomes in critically ill emergency department patients.** *European journal of emergency medicine : official journal of the European Society for Emergency Medicine* 2013, **20**(1):27-32.
6. Churpek MM, Yuen TC, Huber MT, Park SY, Hall JB, Edelson DP: **Predicting cardiac arrest on the wards: a nested case-control study.** *Chest* 2012, **141**(5):1170-1176.
7. Skyttberg N, Chen R, Koch S: **Man vs machine in emergency medicine - a study on the effects of manual and automatic vital sign documentation on data quality and perceived workload, using observational paired sample data and questionnaires.** *BMC emergency medicine* 2018, **18**(1):54.
8. Jarvis SW, Kovacs C, Badriyah T, Briggs J, Mohammed MA, Meredith P, Schmidt PE, Featherstone PI, Prytherch DR, Smith GB: **Development and validation of a decision tree early warning score based on routine laboratory test results for the discrimination of Hospital mortality in emergency medical admissions.** *Resuscitation* 2013, **84**(11):1494-1499.
9. Blanco N, Leekha S, Magder L, Jackson SS, Tamma PD, Lemkin D, Harris AD: **Admission Laboratory Values Accurately Predict In-Hospital Mortality: a Retrospective Cohort Study.** *Journal of general internal medicine* 2020, **35**(3):719-723.
10. Bayat V, Phelps S, Ryono R, Lee C, Parekh H, Mewton J, Sedghi F, Etminani P, Holodniy M: **A Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Prediction Model From Standard Laboratory Tests.** *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* 2021, **73**(9):e2901-e2907.
11. Heikkilä E, Salminen M, Viljanen A, Katajamäki T, Koivula MK, Pulkki K, Isoaho R, Kivelä SL, Viitanen M, Löppönen M *et al*: **A practical laboratory index to predict institutionalization and mortality - an 18-year population-based follow-up study.** *BMC geriatrics* 2021, **21**(1):139.
12. Mohammed MA, Rudge G, Watson D, Wood G, Smith GB, Prytherch DR, Girling A, Stevens A: **Index blood tests and national early warning scores within 24 hours of emergency admission can predict the risk of in-Hospital mortality: a model development and validation study.** *PloS one* 2013, **8**(5):e64340.
13. Ratnayake H, Johnson D, Martensson J, Lam Q, Bellomo R: **Laboratory-derived early warning score for the prediction of in-Hospital mortality, intensive care unit admission, medical emergency team**

- activation and cardiac arrest in general medical wards.** *Internal medicine journal* 2021, **51**(5):746-751.
14. Redfern OC, Pimentel MAF, Prytherch D, Meredith P, Clifton DA, Tarassenko L, Smith GB, Watkinson PJ: **Predicting in-Hospital mortality and unanticipated admissions to the intensive care unit using routinely collected blood tests and vital signs: Development and validation of a multivariable model.** *Resuscitation* 2018, **133**:75-81.
 15. Ueno R, Xu L, Uegami W, Matsui H, Okui J, Hayashi H, Miyajima T, Hayashi Y, Pilcher D, Jones D: **Value of laboratory results in addition to vital signs in a machine learning algorithm to predict in-Hospital cardiac arrest: A single-center retrospective cohort study.** *PloS one* 2020, **15**(7):e0235835.
 16. Efendijev I, Nurmi J, Castren M, Skrifvars MB: **Incidence and outcome from adult cardiac arrest occurring in the intensive care unit: a systematic review of the literature.** *Resuscitation* 2014, **85**(4):472-479.
 17. Armstrong RA, Kane C, Oglesby F, Barnard K, Soar J, Thomas M: **The incidence of cardiac arrest in the intensive care unit: A systematic review and meta-analysis.** *J Intensive Care Soc* 2019, **20**(2):144-154.
 18. Hyland SL, Faltys M, Hüser M, Lyu X, Gumbsch T, Esteban C, Bock C, Horn M, Moor M, Rieck B *et al*: **Early prediction of circulatory failure in the intensive care unit using machine learning.** *Nature medicine* 2020, **26**(3):364-373.
 19. Martínez-Balzano CD, Oliveira P, O'Rourke M, Hills L, Sosa AF: **An Educational Intervention Optimizes the Use of Arterial Blood Gas Determinations Across ICUs From Different Specialties: A Quality-Improvement Study.** *Chest* 2017, **151**(3):579-585.
 20. Hollander-Rodriguez JC, Calvert JF, Jr.: **Hyperkalemia.** *American family physician* 2006, **73**(2):283-290.
 21. Rozen TH, Mullane S, Kaufman M, Hsiao YF, Warrillow S, Bellomo R, Jones DA: **Antecedents to cardiac arrests in a teaching Hospital intensive care unit.** *Resuscitation* 2014, **85**(3):411-417.
 22. Roedl K, Jarczak D, Blohm R, Winterland S, Müller J, Fuhrmann V, Westermann D, Söffker G, Kluge S: **Epidemiology of intensive care unit cardiac arrest: Characteristics, comorbidities, and post-cardiac arrest organ failure - A prospective observational study.** *Resuscitation* 2020, **156**:92-98.
 23. Enohumah KO, Moerer O, Kirmse C, Bahr J, Neumann P, Quintel M: **Outcome of cardiopulmonary resuscitation in intensive care units in a university Hospital.** *Resuscitation* 2006, **71**(2):161-170.
 24. Ong ME, Lee Ng CH, Goh K, Liu N, Koh ZX, Shahidah N, Zhang TT, Fook-Chong S, Lin Z: **Prediction of cardiac arrest in critically ill patients presenting to the emergency department using a machine learning score incorporating heart rate variability compared with the modified early warning score.** *Critical care (London, England)* 2012, **16**(3):R108.
 25. Xu M, Tam B, Thabane L, Fox-Robichaud A: **A protocol for developing early warning score models from vital signs data in Hospitals using ensembles of decision trees.** *BMJ open* 2015, **5**(9):e008699.
 26. Roberts D, Patrick W, Mojica J, Ostryzniuk P, Patrick M, MacKnight C, Kraut A, Shafer LA: **The ALERT scale: an observational study of early prediction of adverse Hospital outcome for medical patients.**

BMJ open 2015, **5**(4):e005501.

27. Churpek MM, Yuen TC, Park SY, Meltzer DO, Hall JB, Edelson DP: **Derivation of a cardiac arrest prediction model using ward vital signs***. *Critical care medicine* 2012, **40**(7):2102-2108.
28. Churpek MM, Yuen TC, Park SY, Gibbons R, Edelson DP: **Using electronic health record data to develop and validate a prediction model for adverse outcomes in the wards***. *Critical care medicine* 2014, **42**(4):841-848.
29. Oh H, Lee K, Seo W: **Temporal patterns of change in vital signs and Cardiac Arrest Risk Triage scores over the 48 hours preceding fatal in-Hospital cardiac arrest**. *Journal of advanced nursing* 2016, **72**(5):1122-1133.
30. Prytherch DR, Smith GB, Schmidt PE, Featherstone PI: **ViEWS—Towards a national early warning score for detecting adult inpatient deterioration**. *Resuscitation* 2010, **81**(8):932-937.
31. Smith GB, Prytherch DR, Meredith P, Schmidt PE, Featherstone PI: **The ability of the National Early Warning Score (NEWS) to discriminate patients at risk of early cardiac arrest, unanticipated intensive care unit admission, and death**. *Resuscitation* 2013, **84**(4):465-470.
32. Srivilaithon W, Amnuaypattanapon K, Limjindaporn C, Imsuwan I, Daorattanachai K, Dasanadeba I, Siripakarn Y: **Predictors of in-Hospital cardiac arrest within 24 h after emergency department triage: A case-control study in urban Thailand**. *Emerg Med Australas* 2019, **31**(5):843-850.
33. Churpek MM, Yuen TC, Winslow C, Robicsek AA, Meltzer DO, Gibbons RD, Edelson DP: **Multicenter development and validation of a risk stratification tool for ward patients**. *American journal of respiratory and critical care medicine* 2014, **190**(6):649-655.
34. Tarassenko L, Clifton DA, Pinsky MR, Hravnak MT, Woods JR, Watkinson PJ: **Centile-based early warning scores derived from statistical distributions of vital signs**. *Resuscitation* 2011, **82**(8):1013-1018.
35. Rozemeijer S, Haitsma Mulier JLG, Röttgering JG, Elbers PWG, Spoelstra-de Man AME, Tuinman PR, de Waard MC, Oudemans-van Straaten HM: **Renal Resistive Index: Response to Shock and its Determinants in Critically Ill Patients**. *Shock (Augusta, Ga)* 2019, **52**(1):43-51.

Tables

Table 1. Baseline characteristics of the cases (ICU-CA, n=427) compared with controls (no ICU-CA, n=790).

	Overall n (%)	Cases n (%)	Controls n (%)	OR	95%CI	<i>P</i> - value
Age (median, Q1, Q3)	63(50,73)	64(52,74)	62(48,73)	1.007	1.000-1.014	0.045
Sex (male)	853(70.1)	294(68.9)	559(70.8)	0.913	0.707-1.180	0.488
CAD	429(35.3)	170(39.8)	259(32.8)	1.356	1.062-1.731	0.014
COPD	81(6.7)	31(7.3)	50(6.3)	1.159	0.728-1.843	0.534
DM	275(22.6)	109(25.5)	166(21)	1.288	0.977-1.699	0.073
Stroke	255(21)	84(19.7)	171(21.6)	0.887	0.662-1.188	0.420
Malignancy	131(10.8)	51(11.9)	80(10.1)	1.204	0.829-1.748	0.329
Hypertension	614(50.5)	204(47.8)	410(51.9)	0.848	0.670-1.073	0.170
Hyperlipidemia	156(12.8)	59(13.8)	97(12.3)	1.145	0.809-1.621	0.444
Smoking	508(41.7)	180(42.2)	328(41.5)	1.026	0.809-1.303	0.830
Drinking	523(43)	175(41)	348(44.1)	0.882	0.695-1.120	0.302
Hospital admission diagnosis						
Cardiovascular	228 (18.7)	93 (21.8)	135 (17.1)			
Respiratory	263 (21.6)	105 (24.6)	158 (20.0)			
Infection	45 (3.7)	15 (3.5)	30 (3.8)			
Cerebrovascular	79 (6.5)	20 (4.7)	59 (7.5)			
Malignancy	51 (4.2)	25 (5.9)	26 (3.3)			
gastrointestinal	41 (3.4)	10 (2.3)	31 (3.9)			
Trauma	87 (7.1)	38 (8.9)	49 (5.3)			
Hepatic	15 (1.2)	6 (1.4)	9 (1.1)			

Nephrology	20 (1.6)	2 (0.5)	18 (2.3)
Aortal	188 (15.4)	48 (11.2)	140 (17.7)
Other medical	90 (7.4)	13 (3.0)	77 (9.8)
Other surgical	110 (9.0)	52 (12.2)	58 (7.3)

ICU-CA, intensive care unit cardiac arrest; OR, odds ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CAD, coronary artery disease; DM, diabetes Mellitus

Table 2. The characteristics of ICU-CA in 427 cases.

	n (%)
Witnessed arrest	427 (100)
Initial rhythm	
VT/VF	62 (14.5)
PEA	4 (0.9)
Asystole	128 (30.0)
Bradycardia	233 (54.6)
ROSC	121 (28.3)
ROSC time>24h	74 (61.2)
Discharged alive	51 (11.9)
CPC≤2 at discharge	9 (2.1)
Hospital mortality	376 (88.1)

Data were presented as counts (percentage); ICU-CA, intensive care unit cardiac arrest; VT, ventricular tachycardia; VF, ventricular fibrillation; PEA, pulseless electrical activity; ROSC, restoration of spontaneous circulation; CPC, cerebral performance categories

Table 3. Multivariate logistic regression of the vital signs and laboratory indicators at different time points adjusted the age and CAD.

	-48h	-36h	-24h	-12h	-8h
T (°C)	-	-	-	0.782(0.647-0.946; 0.011)	-
HR (bpm)	1.022(1.015-1.029; <0.001)	1.023(1.015-1.031; <0.001)	1.029(1.021-1.037; <0.001)	1.031(1.022-1.04; <0.001)	1.024(1.015-1.034; <0.001)
RR (bpm)	-	1.043(1.013-1.074; 0.004)	-	1.062(1.029-1.097; <0.001)	1.082(1.046-1.118; <0.001)
SBP (mmHg)	0.985(0.979-0.991; <0.001)	0.978(0.972-0.985; <0.001)	-	0.981(0.974-0.988; <0.001)	0.972(0.965-0.980; <0.001)
DBP (mmHg)	-	-	0.959(0.947-0.971; <0.001)	-	-
PPI	-	-	0.023(0.004-0.127; <0.001)	-	-
SaO ₂ * (%)	0.378(0.25-0.571; <0.001)	0.374(0.241-0.58; <0.001)	0.489(0.322-0.744; <0.001)	0.397(0.256-0.616; <0.001)	0.453(0.284-0.720; <0.001)
HGB (g/L)	0.993(0.988-0.999; 0.013)	-	0.992(0.986-0.998; 0.01)	-	0.991(0.985-0.998; 0.009)
K ⁺ (mmol/L)	1.266(1.055-1.52; 0.011)	-	1.263(1.042-1.531; 0.017)	1.43(1.168-1.752; <0.001)	1.463(1.187-1.804; <0.001)
Na ⁺ (mmol/L)	1.029(1.016-1.042; <0.001)	1.032(1.019-1.045; <0.001)	1.031(1.017-1.044; <0.001)	1.027(1.012-1.042; <0.001)	1.030(1.014-1.045; <0.001)
Ca ²⁺ (mmol/L)	-	-	-	-	-
Lac [#] (Log mmol/L)	1.782(1.493-2.127; <0.001)	1.885(1.564-2.273; <0.001)	2.218(1.843-2.669; <0.001)	2.170(1.786-2.637; <0.001)	2.153(1.736-2.67; <0.001)
pH†	-	0.982(0.968-0.997; 0.021)	-	0.982(0.966-0.998; 0.024)	0.981(0.965-0.998; 0.025)

* The SaO₂ was modified as a dichotomous variable with the cut-off of 95%;

The value of Lac was natural log-transformed;;

†The value of pH was multiplied by 100.

Data were presented as Odds ratio (95% Confidence interval; *P*). T, body temperature; HR, heart rate; bpm, beats per minute; RR, respiratory rate; SBP, systolic blood pressure; DPB, diastolic blood pressure; PPI, pulse pressure index; SaO₂, oxygen saturation; HGB, hemoglobin; K⁺, potassium; Na⁺, sodium; Ca²⁺, calcium; Lac, lactic acid

Table 4. Multilevel multivariate logistic regression analysis of the vital signs and laboratory indicators.

Predictor	Coefficient	SE	OR(95%CI)	<i>P</i> -value
Intercept	0.987	7.458		0.895
HR(bpm)	0.027	0.005	1.028 (1.018-1.037)	<0.001
RR(bpm)	0.035	0.016	1.036 (1.004-1.069)	0.029
SBP(mmHg)	-0.022	0.004	0.978 (0.971-0.986)	<0.001
SaO ₂ *	-0.854	0.247	0.426 (0.262-0.691)	0.001
HGB(g/L)	-0.010	0.004	0.990 (0.983-0.998)	0.019
K ⁺ (mmol/L)	0.322	0.127	1.380 (1.077-1.769)	0.011
Na ⁺ (mmol/L)	0.047	0.010	1.049 (1.028-1.069)	<0.001
Lac [#] (Log mmol/L)	0.936	0.132	2.550 (1.969-3.302)	<0.001
pH†	-0.015	0.010	0.985 (0.966-1.004)	0.124
time	-0.125	0.054	0.883 (0.792-0.982)	0.022
age	0.016	0.007	1.016 (1.002-1.030)	0.023
CAD	0.582	0.246	1.790 (1.105-2.900)	0.018

*The SaO₂ was modified as a dichotomous variable with the cut-off of 95%;

[#] The value of Lac was natural log-transformed;;

†The value of PH was multiplied by 100.

SE, standard error; OR, odds ratio; CI, confidence interval; HR, heart rate; bpm, beats per minute; RR, respiratory rate; SBP, systolic blood pressure; SaO₂, oxygen saturation; HGB, hemoglobin; K⁺, potassium; Na⁺, sodium; Lac, lactic acid CAD, coronary artery disease

Table 5. Multivariable logistic regression analysis of the mean value, standard deviation, maximum value, minimum value and range of vital signs.

	Mean	Max	Min	Range
HR (bpm)	1.033(1.023-1.043; <0.001)	1.035(1.027-1.044; <0.001)	1.025(1.016-1.035; <0.001)	1.018(1.008-1.028; <0.001)
RR (bpm)	1.097(1.054-1.141; <0.001)	1.042(1.015-1.069; 0.002)	1.117(1.068-1.169; <0.001)	1.025(0.997-1.053; 0.08)
SBP (mmHg)	0.967(0.959-0.976; <0.001)	0.980(0.973-0.988; <0.001)	0.963(0.955-0.971; <0.001)	1.007(0.999-1.015; 0.076)
HGB (g/L)	0.995(0.989-1.001; 0.119)	0.997(0.991-1.003; 0.319)	0.990(0.984-0.996; 0.001)	0.989(0.977-1.000; 0.051)
K ⁺ (mmol/L)	1.349(1.070-1.701; 0.011)	1.705(1.392-2.088; <0.001)	0.882(0.708-1.099; 0.264)	1.718(1.349-2.187; <0.001)
Na ⁺ (mmol/L)	1.031(1.017-1.046; <0.001)	1.032(1.017-1.046; <0.001)	1.024(1.009-1.039; 0.001)	1.019(0.990-1.049; 0.194)
Lac [#] (Log mmol/L)	2.201(1.772-2.733; <0.001)	1.197(1.149-1.246; <0.001)	1.038(0.971-1.110; 0.271)	1.211(1.136-1.291; <0.001)
pH [†]	0.979(0.961-0.998; 0.027)	1.013(0.994-1.031; 0.175)	0.937(0.923-0.951; <0.001)	1.070(1.047-1.093; <0.001)

[#] The value of Lac was natural log-transformed;;

[†]The value of PH was multiplied by 100.

Data were presented as Odds ratio (95% Confidence interval; *P*). HR, heart rate; bpm, beats per minute; RR, respiratory rate; SBP, systolic blood pressure; Max, maximum value; Min, minimum value; HGB, hemoglobin; K⁺, potassium; Na⁺, sodium; Lac, lactic acid

Figures

Figure 1

Study flow chart. CA, cardiac arrest; ICU-CA, intensive care unit cardiac arrest; DNAR, do not attempt resuscitation; ICU, intensive care unit; HLOS, Hospital length of stay.

Figure 2

AUROC for the value of laboratory indicators at given time point and the trend models. (A): lactic acid; (B): pH; (C): potassium; (D): calcium; (E): sodium; (F): hemoglobin.