

Association of red cell distribution width with mortality in cardiac arrest patients: a retrospective analysis based on the MIMIC-IV database

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Abstract

Background There is a scarcity of studies that covers the relationship between the red cell distribution width (RDW) and the prognosis of cardiac arrest (CA) patients. Moreover, the prognostic value of the changes in RDW during intensive care unit (ICU) hospitalization for CA patients is not investigated. This study focuses on the correlation between RDW measures at ICU admission and RDW changes during ICU hospitalization and the prognosis of CA patients. **Methods** A retrospective cohort study is used to collect clinical characteristics of CA patients (>18years) that are on their first admission to ICU with RDW data measured from the Medical Information Mart for Intensive Care-IV database. The primary outcomes are 30- and 90-day all-cause mortality. A multivariate Cox regression model is applied to test whether the RDW represents an independent risk factor that affects the all-cause mortality of these patients. Meanwhile, the dose-response relationship between the RDW and the mortality is described by the restricted cubic spline (RCS). **Results** A total of 1138 adult CA patients are included in this study. Compared to the survivor group, non-survivors show higher level of RDW. The Kaplan-Meier survival curve indicates that the cumulative survival rate of CA patients at 30 and 90 days decreases gradually as the RDW on ICU admission increases (log-rank test, $\chi^2 = 46.460$, $\chi^2 = 47.210$, both p -values < 0.001), and rising RDW during ICU hospitalization (Δ RDW $\geq 0.4\%$) is associated with decreased the 30 and 90 days cumulative survival rates ($\chi^2 = 23.700$, $\chi^2 = 25.390$, both p -values < 0.001). The multivariate Cox regression analysis shows that increasing RDW at ICU admission ($\geq 13.89\%$) and rising RDW during ICU hospitalization (Δ RDW $\geq 0.4\%$) are independent risk factors for death at 30- and 90-day on CA patients. RCS illustrates that there is a non-linear relationship between the RDW on ICU admission and the increased risk of mortality of CA patients at 30 ($\chi^2 = 11.990$, p -value = 0.007) and 90 days ($\chi^2 = 12.340$, p -value = 0.006). **Conclusions** Elevated RDW levels on ICU admission and rising RDW during ICU hospitalization are powerful predictors of all-cause mortality for CA patients at 30 and 90 days, and they can be used as potential clinical biomarkers to predict the bad prognosis of these patients.

Background

Cardiac arrest (CA) is still a globally important public health concern, as it has a very high incidence and mortality rate [1, 2]. Although over time, there has been improvement in the caring of patients during and after CA, the general prognosis of these patients is still not ideal, especially their neurological outcome [2, 3]. A recent large study from two nationwide, prospective registries in Denmark [4] showed that out-of-hospital CA (OHCA) patients (26.84%) have a significantly lower rate to show the return of spontaneous circulation (ROSC) compared to in-hospital CA (IHCA) patients (48.50%), and the overall survival rate over 1 year for both the OHCA or IHCA patients are only 12.62% and 18.45%, respectively.

As we are all aware, the early evaluation of prognosis is a crucial part of caring for CA patients, and it helps medical staff to make clinical decisions [5]. In the past few decades, researchers have developed dozens of predictive tools or scoring systems for predicting the mortality or neurological outcome of CA patients [6]. However, these predictive tools or scoring systems are not widely applied clinically. Thus, it is necessary to find a convenient, economical, effective, and practice biomarker for a more accurate prognosis prediction of CA patients.

Red cell distribution width (RDW) is a parameter that measures the volume heterogeneity of peripheral red blood cells, and it is often used for the identification of the causes of anemia [7]. Apart from that, RDW is recently more frequently regarded as a new predictive factor for potential poor prognosis for a large variety of diseases, and many studies have already illustrated the correlation between the RDW value and poor prognosis of sepsis [8], acute kidney injury (AKI) [9], and COVID-19 [10]. Significantly, RDW, as a dynamic variable, might change rapidly throughout hospitalization [11]. Furthermore, prior studies have also suggested that RDW changes during hospitalization are associated with poor

prognosis of several diseases [11, 12]. However, based on our knowledge, the prognostic value of RDW changes during hospitalization for CA patients is not investigated. Thus, in this article, we aim to study the effect of the CA patient's RDW level measured when they are admitted into the ICU and RDW changes throughout ICU hospitalization on their all-cause mortality.

Methods

Data source

The data were acquired from the openly available Medical Information Mart for Intensive Care IV (MIMIC-IV) database ver. 1.0. The database consisted of comprehensive clinical information of inpatients at the Beth Israel Deaconess Medical Center (BIDMC), Boston, Massachusetts, from 2008 to 2019. To access the dataset, one individual completed the National Institutes of Health Web-based training course and the Protecting Human Research Participants examination (authorization code: 36142713). Information for all participants in this database was de-identified, thus no ethical approval and patient consent were required.

Study population

All study populations are from the MIMIC-IV database, and we use the International Classification of Diseases (ICD)-9 and ICD -10 codes for identifying CA patients. The specific inclusion and exclusion criteria are the following: Inclusion :1. The patient's age is ≥ 18 years old; 2. The patient is admitted to ICU for the first time 3. The ICU stay for the patients is ≥ 24 hours. Exclusion: 1. The patient is not admitted to ICU 2. The patient dies within the first 24 hour of ICU stay 3. Important data for the patient is missing or unable to collect the outcome parameter.

Data extraction

We use PostgreSQL (version 10.13) and structure query language (SQL) to extract all data required for the study from the MIMIC-IV database, and the main variable extracted are listed in Table.1. Based on the follow-up survival conditions of the patients at 90 days, the student population is divided into a survivor group (n=648) and a non-survivor group (n=490). Based on the measured RDW value at ICU admission (normal range: 10.50-15.50%), a third quantile method is applied to divide the patients into three groups, which includes groups with RDW $<13.89\%$ (n=404), 13.89-15.39% (n=361), and $\geq 15.39\%$ (n=373). Based on the previous literature [12], all participants are divided into 3 groups ($\Delta\text{RDW} = \text{RDW on ICU discharge} - \text{RDW on ICU admission}$): group A ($-0.4\% < \Delta\text{RDW} < 0.4\%$ n=511), group B ($\Delta\text{RDW} \leq -0.4\%$ n=110) and group C ($\Delta\text{RDW} \geq 0.4\%$ n=517). The main outcome for this study is defined as the all-cause mortality rate of CA patients 30 and 90 days starting from their ICU admission.

Statistical analysis

During the data cleaning process, we deleted extreme values, which are very infrequent, based on clinical practice. When less than 5% of the values for one parameter are missing values, we replace them with either the mean value (i.e., white blood cells, hemoglobin, platelet, glucose, potassium, phosphorus, chlorine, total calcium, prothrombin time, and temperate) or median (i.e., creatinine, Glasgow coma scale) based on whether the values follow a normal distribution or not. When missing values account for $< 10\%$ of total values for one parameter, we replace the missing values with the back-to-fill method (i.e., lactate, PO_2).

For continuous variables that follow normal distributions, the values are represented as mean \pm standard deviation, and t-test is used to compare the two groups, and ANOVA is used to compared multiple groups. For continuous variables that do not follow a normal distribution, the values are represented as median (interquartile range) (M(QL,

QU)), and Mann-Whitney test, rank-sum test, or Kruskal-Wallis test are used to compare the different groups based on specific conditions. Discrete variables are represented by percentages (%), and χ^2 tests are used. The changes in the cumulative survival rate of patients from different groups is analyzed by the Kaplan-Meier survival curve, and the result is analyzed by a follow-up log-rank test. In this study, we include variables with p-values < 0.10 in single variable analysis in multivariable Cox regression analysis. The multivariate Cox regression model can be used to test whether RDW or Δ RDW is an independent risk factor for 30- and 90- day all-cause mortality of CA patients, and the corresponding hazard ratio (HR) and 95% confidence interval (CI) are calculated. Meanwhile, the restricted cubic spline (RCS) is utilized to portray the dose-response relationship between the RDW on ICU admission and the mortality rate, and the same relationship is measured again after we apply gender stratification to the data. We use Stata 14.0 and R language to perform data analysis. All statistical tests are two-sided tests, and a p-value < 0.05 is regarded as statistically significant.

Results

Subject characteristics

A flow of the test population selection is included in Figure 1, and based on our inclusion and exclusion criteria, a total of 1138 CA patients are included in present study. Compared with survivors, non-survivors have a higher SOFA score, RDW, anion gap, lactate, creatinine, prothrombin time, glucose, sodium, and phosphate values, and higher incidence rates of chronic obstructive pulmonary disease, cerebral infarction, and AKI. However, non-survivors also have lower temperatures, partial pressure of arterial oxygen, and hemoglobin values, and they have worse Glasgow coma scale and shorter hospital length of stay (all p-values < 0.05, Table 1). As shown in the table 2, the mortalities at 30-day and 90-day in group C (48.94%,51.45%) were much higher than those in groups A(34.83%, 36.79%) and B (30.91%, 32.73%), with a statistical significance (all p-values <0.001). Moreover, the characteristics of the study patients according to RDW levels and Δ RDW are illustrated in additional file 1.

Kaplan-Meier survival curve analysis

The Kaplan-Meier survival curve is shown in Figure 2, and it suggests that as the RDW value measured at the ICU admission increases, the cumulative survival rate at 30 and 90 days of CA patients gradually decreases, and the difference is statistically significant (log-rank test, $c_1^2=46.460, c_2^2=47.210$, both p-values <0.001). The result of Kaplan-Meier survival analysis shows that the group C (Δ RDW $\geq 0.4\%$) is associated with decreased the 30 and 90 days cumulative survival rates compared to the group A and group B (log-rank test, $c_1^2=23.700, c_2^2=25.390$, both p-values <0.001, Additional file 2).

Cox regression analysis

Considering the all-cause mortality rate at 30 days after ICU admission, the medium and higher RDW value groups have 1.745 (1.376-2.235) and 2.198 (1.742-2.733) HR (95%CI) respectively compared to the low RDW value group if the parameters are not adjusted. In model 1 and model 2, after the relevant mixed factors are adjusted, the multivariate Cox regression analysis should still recognize increased RDW ($\geq 13.89\%$) at ICU admission as an independent risk factor for 30-day all-cause mortality for CA patients (Table 3).

For 90-day all-cause mortality, the medium and higher RDW value groups also express HR (95%CI) of 1.709(1.351-2.161) and 2.161(1.725-2.706) respectively relative to the low RDW value group with RDW <13.89 using unadjusted parameters. Even with parameters adjusted for certain mixed factors, the increased RDW ($\geq 13.89\%$) at ICU admission in patients is also regarded as an independent risk factor leading to a higher death rate in CA patients by the

multivariate Cox regression analysis (Table 3). Additionally, results of analysis concerning the relationship between RDW changes during ICU hospitalization and 30- and 90-day all-cause mortality of CA patients yielded similar positive findings as the aforementioned analyses, and reveal that the group C ($\Delta\text{RDW} \geq 0.4\%$) is an independent risk factor for all-cause death at 30 and 90 days on these patients (Additional file 2).

The dose-response relationship between the RDW measured at ICU admission and the all-cause mortality rate of CA patients

As shown in Figure 3, the RCS indicates that there exists a non-linear relationship between the RDW measured at ICU admission and the increased risk of mortality rate of CA patients at both 30 ($c_1^2=11.990$, p-value = 0.007) and 90 days ($c_2^2=12.340$, p-value = 0.006) after ICU admission. For the mortality rate at 30 days after admission, the HR is around 1 when RDW is 14.49%, and for the mortality rate at 90 days, the corresponding RDW giving an HR around 1 is 14.54%. Overall, as RDW value increased, CA patients have an increased risk of all-cause mortality. Also, as shown by Figure 4, female CA patients have an increased risk of death at both 30 and 90 days compared with male CA patients with the same RDW measured at ICU admission.

Discussion

In this study, we demonstrate that non-survivors have a higher RDW compared with survivors, and the association of increasing RDW at ICU admission and rising RDW during ICU hospitalization and the all-cause mortality in CA patients. The Kaplan-Meier survival curve indicates that the cumulative survival rate of CA patients at 30 and 90 days decreases gradually as the RDW on ICU admission increases, and group C ($\Delta\text{RDW} \geq 0.4\%$) is associated with decreased the 30 and 90 days cumulative survival rates. Moreover, the multivariate Cox regression analysis shows that increasing RDW at ICU admission ($\geq 13.89\%$) and rising RDW during ICU hospitalization ($\Delta\text{RDW} \geq 0.4\%$) are independent risk factors for all-cause death at 30 and 90 days on CA patients. Non-linear relationships are found by RCS between the RDW at ICU admission and the increased risk of mortality rate of CA patients at both 30 and 90 days. Our result, in line with some of existing meta-analyses [13, 14], illustrates that female CA patients have a higher risk of death compared to male patients.

Recently, more studies have shown that the RDW value can be useful in predicting the poor prognosis in patients with cardiovascular diseases including atrial fibrillation [15], heart failure [16], and cardiogenic shock, etc.[17]. Up to now, there are three studies about the influence of RDW on the prognosis of CA patients. In 2012, Kim et.al in Korea published a retrospective analysis on data from 219 OHCA patients undergoing ROSC shows a mortality rate of 73.52% after 30 days of admission, and the multivariable Cox regression analysis indicates the high RDW ($>15.5\%$) at emergency department (ED) admission is an independent risk factor for mortality at 30 days [18]. In 2018, a multivariable Cox regression analysis from a retrospective study in Belgium including 390 non-traumatic CA comatose patients (normal RDW range 10.90%-13.40%) with a 56.41% mortality rate and 64.36% poor neurological outcome at 90 days indicates that high RDW level on admission ($>13.40\%$) is an independent risk factor for the in-hospital mortality and the poor neurological outcome at 90 days [19]. In 2020, another study from Korea based on 1008 non-traumatic OHCA patients with ROSC shows a mortality rate of 54.56% within 30 days of admission, and 70.63% of patients have poor neurological outcomes when discharged. For this study, a high RDW ($>15\%$) at ED admission is regarded as an independent risk factor for both the death within 30 days and the poor neurological outcome [20]. Unlike those studies, we show a high RDW measured at ICU admission is an independent risk factor for mortality of CA patients after 30 or 90 days of ICU admission.

Currently, the mechanisms leading to the correlation between high RDW and poor prognosis of CA patients are still not clear. The hypoxic-ischemic brain injury (HIBI) after CA is the main reason that causes the death and long-term nerve dysfunction in survivors patients. A two-hit model, which means the primary ischemic injury and the secondary injury after ROSC, is the important pathophysiological mechanism for HIBI development [21]. Particularly, the primary ischemic injury leads to interrupted blood supply during CA, and the drastic drop of oxygen supply leads to the death of the neurons and glial cells. Within a few minutes, hours, and days of ROSC in CA patients, the unbalanced oxygen supply and demand in the brain tissues is the main mechanism for the secondary brain injury after ROSC, and the ischemic-refusion injury caused by oxidative stress also plays an important role in that [22, 23]. It is worth noting that the secondary injury after ROSC is much more harmful than the primary ischemic injury [24]. Besides, systematic inflammation is crucial in the development of post-CA syndrome [25]. Several previous reports have shown that increased RDW level relates to a lot of misregulations including senescence, oxidative stress, systemic inflammation, malnutrition, and impaired kidney function [26, 27]. Because of that, we hypothesize that increased RDW can potentially reflect a poor prognosis on CA patients through misregulations like oxidative stress and systemic inflammation, etc. More basic research is certainly required for a better understanding of the potential mechanisms included.

Compared with some previous studies, our research has the following advantages. First, to the best of our current knowledge, this might be the first study to investigate the relationship between the RDW changes during ICU hospitalization and the all-cause mortality of CA patients, which suggests a dynamic change of RDW on mortality. Second, our study is a large sample analysis based on the real data from patients, and it contains data from the largest sample population (1138 CA patients) for the longest period of follow up (90 days), which reveals the correlation between the RDW and the long term clinical outcomes. Finally, the RCS diagrams in our study illustrate the relationship between RDW and the all-cause mortality rate in CA patients at 30 and 90 days after admission in a relatively visually intuitive way.

There are also drop-backs in our study. First, it is a single-center retrospective observational study, which means selection bias is inevitable. Second, the time span of the data used in this study is 12 years, and some parameters (such as BNP and troponin) are largely missing in the database, which means it is hard to have a comprehensive analysis of the data. Finally, the current version of MIMIC-IV database (v1.0) does not include the brain function outcome of patients (eg. the cerebral performance category scale), thus it is hard for us to investigate the relationship between RDW and neurological outcome in the CA patients in this study.

Conclusions

In conclusion, elevated RDW levels on ICU admission ($\geq 13.89\%$), as well as rising RDW during ICU hospitalization ($\Delta RDW \geq 0.4\%$), were powerful predictors of all-cause mortality for CA patients at 30 and 90 days. It can be an easy to get, low cost, and high adaptive blood marker for a relatively accurate prediction on the poor prognosis of CA patients. However, we need more forward-looking, large sample-sized, and even multi-centered studies to confirm our conclusion.

Abbreviations

AKI: acute kidney injury; CA: cardiac arrest; CI: confidence interval; ED: emergency department; HLOS: hospital length of stay; ICU: intensive care unit; ICULOS: ICU length of stay; IHCA: in-hospital cardiac arrest; MIMIC-IV: Medical Information Mart for Intensive Care IV; OHCA: out-of-hospital cardiac arrest; PaO₂: partial pressure of arterial oxygen;

RCS: restricted cubic spine; RDW: Red cell distribution width; ROSC: return of spontaneous circulation; RR: relative risk; SOFA: sequential organ failure assessment.

Declarations

Acknowledgements

None.

Authors' contributions

YXH, XB, ZL and JYY conceived the idea. ZL and WHL extracted the data, performed the analysis and interpreted the results. ZL and JYY were the major contributors in writing the manuscript. JXW and WHL participate in creating of this manuscript. YXH and XB read and then revised this manuscript from a professional standpoint. All authors read and approved the final manuscript.

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Availability of data and materials

The data are available in the physionet (<https://physionet.org/content/mimiciv/1.0/>).

Ethics approval and consent to participate

The database was approved by the institutional review boards of the BIDMC and the Massachusetts Institute of Technology.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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References

1. Wang H, Tang L, Zhang L, Zhang ZL, Pei HH: **Development a clinical prediction model of the neurological outcome for patients with coma and survived 24 hours after cardiopulmonary resuscitation.** *Clinical cardiology*2020, **43**(9):1024-1031.
2. Gill R, Teitcher M, Ruland S: **Neurologic complications of cardiac arrest.** *Handbook of clinical neurology*2021, **177**:193-209.
3. Hayashida K, Miyara SJ, Shinozaki K, Takegawa R, Yin T, Rolston DM, Choudhary RC, Guevara S, Molmenti EP, Becker LB: **Inhaled Gases as Therapies for Post-Cardiac Arrest Syndrome: A Narrative Review of Recent Developments.** *Frontiers in medicine*2020, **7**:586229.
4. Hoybye M, Stankovic N, Holmberg M, Christensen HC, Granfeldt A, Andersen LW: **In-Hospital vs. Out-of-Hospital Cardiac Arrest: Patient Characteristics and Survival.** *Resuscitation*2021, **158**:157-165.
5. Dumas F, Bougouin W, Cariou A: **Cardiac arrest: prediction models in the early phase of hospitalization.** *Current opinion in critical care*2019, **25**(3):204-210.
6. Gue YX, Adatia K, Kanji R, Potpara T, Lip GYH, Gorog DA: **Out-of-hospital cardiac arrest: A systematic review of current risk scores to predict survival.** *American heart journal*2021, **234**:31-41.
7. Akpınar CK, Gurkas E, Aykac O, Uysal Z, Ozdemir AO: **Elevated Red Blood Cell Distribution Width May Be a Novel Independent Predictor of Poor Functional Outcome in Patients Treated with Mechanical Thrombectomy.** *Neurointervention*2021, **16**(1):34-38.
8. Krishna V, Pillai G, Velickakathu Sukumaran S: **Red Cell Distribution Width As a Predictor of Mortality in Patients With Sepsis.** *Cureus*2021, **13**(1):e12912.
9. Jia L, Cui S, Yang J, Jia Q, Hao L, Jia R, Zhang H: **Red blood cell distribution width predicts long-term mortality in critically ill patients with acute kidney injury: a retrospective database study.** *Scientific reports*2020, **10**(1):4563.
10. Lorente L, Martin MM, Argueso M, Sole-Violan J, Perez A, Marcos YRJA, Ramos-Gomez L, Lopez S, Franco A, Gonzalez-Rivero AF *et al.*: **Association between red blood cell distribution width and mortality of COVID-19 patients.** *Anaesthesia, critical care & pain medicine*2021, **40**(1):100777.
11. Gorelik O, Izhakian S, Barchel D, Almozni-Sarafian D, Tzur I, Swarka M, Beberashvili I, Feldman L, Cohen N, Shteinshnaider M: **Changes in Red Cell Distribution Width During Hospitalization for Community-Acquired Pneumonia: Clinical Characteristics and Prognostic Significance.** *Lung*2016, **194**(6):985-995.
12. Shteinshnaider M, Barchel D, Almozni-Sarafian D, Tzur I, Tsatsanashvili N, Swarka M, Cohen N, Gorelik O: **Prognostic significance of changes in red cell distribution width in an internal medicine ward.** *European journal of internal medicine*2015, **26**(8):616-622.

13. Parikh PB, Hassan L, Qadeer A, Patel JK: **Association between sex and mortality in adults with in-hospital and out-of-hospital cardiac arrest: A systematic review and meta-analysis.** *Resuscitation*2020, **155**:119-124.
14. Lei H, Hu J, Liu L, Xu D: **Sex differences in survival after out-of-hospital cardiac arrest: a meta-analysis.** *Critical care*2020, **24**(1):613.
15. Zeng H, Tao T, Ma Z, Wang M, Lu X, Zhao Y, Shen Z: **Predictive value of red blood cell distribution width in critically ill patients with atrial fibrillation: a retrospective cohort study.** *Annals of palliative medicine*2021, **10**(3):2469-2480.
16. Yamada S, Yoshihisa A, Kaneshiro T, Amami K, Hijioka N, Oikawa M, Takeishi Y: **The relationship between red cell distribution width and cardiac autonomic function in heart failure.** *Journal of arrhythmia*2020, **36**(6):1076-1082.
17. Wang B, Aihemaiti G, Cheng B, Li X: **Red Blood Cell Distribution Width Is Associated with All-Cause Mortality in Critically Ill Patients with Cardiogenic Shock.** *Medical science monitor : international medical journal of experimental and clinical research*2019, **25**:7005-7015.
18. Kim J, Kim K, Lee JH, Jo YH, Rhee JE, Kim TY, Kang KW, Kim YJ, Hwang SS, Jang HY: **Red blood cell distribution width as an independent predictor of all-cause mortality in out of hospital cardiac arrest.** *Resuscitation*2012, **83**(10):1248-1252.
19. Fontana V, Spadaro S, Villois P, Righy Shinotsuka C, Fogagnolo A, Nobile L, Vincent JL, Creteur J, Taccone FS: **Can red blood cell distribution width predict outcome after cardiac arrest?** *Minerva anesthesiologica*2018, **84**(6):693-702.
20. Woo SH, Lee WJ, Kim DH, Cho Y, Cho GC: **Initial red cell distribution width as a predictor of poor neurological outcomes in out-of-hospital cardiac arrest survivors in a prospective, multicenter observational study (the KoCARC study).** *Scientific reports*2020, **10**(1):17549.
21. Sekhon MS, Ainslie PN, Griesdale DE: **Clinical pathophysiology of hypoxic ischemic brain injury after cardiac arrest: a "two-hit" model.** *Critical care*2017, **21**(1):90.
22. Richter J, Sklienka P, Setra AE, Zahorec R, Das S, Chatterjee N: **Is jugular bulb oximetry monitoring associated with outcome in out of hospital cardiac arrest patients?** *Journal of clinical monitoring and computing*2021, **35**(4):741-748.
23. Yamamoto R, Yoshizawa J: **Oxygen administration in patients recovering from cardiac arrest: a narrative review.** *Journal of intensive care*2020, **8**:60.
24. Katz A, Brosnahan SB, Papadopoulos J, Parnia S, Lam JQ: **Pharmacologic neuroprotection in ischemic brain injury after cardiac arrest.** *Annals of the New York Academy of Sciences*2021.
25. Meyer MAS, Wiberg S, Grand J, Meyer ASP, Obling LER, Frydland M, Thomsen JH, Josiassen J, Moller JE, Kjaergaard J *et al.* **Treatment Effects of Interleukin-6 Receptor Antibodies for Modulating the Systemic Inflammatory Response After Out-of-Hospital Cardiac Arrest (The IMICA Trial): A Double-Blinded, Placebo-Controlled, Single-Center, Randomized, Clinical Trial.** *Circulation*2021, **143**(19):1841-1851.
26. Zerbo S, Perrone G, Bilotta C, Adelfio V, Malta G, Di Pasquale P, Maresi E, Argo A: **Cardiovascular Implantable Electronic Device Infection and New Insights About Correlation Between Pro-inflammatory Markers and Heart Failure: A Systematic Literature Review and Meta-Analysis.** *Frontiers in cardiovascular medicine*2021, **8**:602275.
27. Lippi G, Turcato G, Cervellin G, Sanchis-Gomar F: **Red blood cell distribution width in heart failure: A narrative review.** *World journal of cardiology*2018, **10**(2):6-14.

Tables

Table 1 Baseline characteristics of the study population according to the main outcomes of 90-day all-cause mortality

Variables	All (n=1138)	Survivors (n=648)	Non-survivors (n=490)	t/z/χ ²	P value
Age(years)	64.92±16.55	64.12±16.52	65.97±16.54	-1.869	0.062
Female (n%)	435(38.22)	232(35.80)	203(41.43)	3.740	0.053
SOFA score	8.45±4.44	7.67±4.35	9.49±4.34	-7.003	<0.001
GCS	12.00(5.00-15.00)	13.00(8.00-15.00)	9.00(3.00-15.00)	6.189	<0.001
Temperature (°C)	36.43±1.16	36.55±1.03	36.28±1.30	3.935	<0.001
RDW(%)	14.94±2.10	14.57±1.95	15.44±2.19	-7.094	<0.001
Anion gap (mmol/L)	16.82±5.10	16.10±4.75	17.77±5.40	-5.535	<0.001
Lactate (mmol/L)	2.60(1.70,4.50)	2.4(1.6,3.8)	3.00(1.80,5.30)	-5.495	<0.001
PaO ₂ (mmHg)	128.00(68.00,218.00)	148.00(76.00,244.50)	109.00(62.00,199.04)	3.923	<0.001
WBC ×10 ⁹ /L	14.33±8.75	13.89±9.42	14.91±7.75	-1.963	0.050
Hemoglobin (g/L)	113.92±26.44	115.39±26.14	111.97±26.73	2.169	0.030
Platelet ×10 ⁹ /L	207.73±94.01	204.36±86.07	212.18±103.49	-1.391	0.165
Creatinine (umol/L)	106.08(79.56-159.12)	97.24(70.72,141.44)	114.92(79.56,185.64)	-4.505	<0.001
PT (s)	17.06±11.01	15.99±8.95	18.47±13.14	-3.730	<0.001
Glucose (mmol/L)	10.29±5.29	9.90±4.75	10.80±5.90	-2.854	0.004
Potassium (mmol/L)	4.33±0.94	4.34±0.96	4.31±0.90	0.587	0.557
Sodium (mmol/L)	138.11±5.31	137.69±4.96	138.67±5.69	-3.102	<0.001
Total calcium (mmol/L)	2.07±0.26	2.06±0.26	2.08±0.27	1.191	0.234
Phosphate (mmol/L)	1.38±0.58	1.32±0.54	1.46±0.61	-4.095	<0.001
Chloride (mmol/L)	103.87±6.38	103.58±6.00	104.24±6.84	-1.728	0.084
Comorbidities (n%)					
Hypertension	482(42.36)	272(41.98)	210(42.86)	0.089	0.766
Diabetes	382(33.57)	208(32.10)	174(35.51)	1.456	0.228
Atrial fibrillation	401(35.24)	222(34.26)	179(36.53)	0.631	0.427
Cirrhosis	52(4.57)	25(3.86)	27(5.51)	1.747	0.186
COPD	149(13.09)	65(10.03)	84(17.14)	12.403	<0.001
Cerebral infarction	183(16.08)	89(13.73)	94(19.18)	6.139	0.013
AMI	202(17.75)	121(18.67)	81(16.53)	0.877	0.349
	573(50.35)	282(43.52)	291(59.39)	28.108	<0.001

AKI					
LOS ICU (days)	4.31(2.39,8.46)	4.20(2.27,8.80)	4.36(2.52,7.93)	-0.099	0.921
LOS Hospital (days)	9.17(4.96,17.88)	11.83(7.08,21.85)	6.58(3.21,12.25)	11.005	<0.001

SOFA sequential organ failure assessment, GCS Glasgow Coma Scale, RDW red cell distribution width, PaO2 partial pressure of arterial oxygen, WBC white blood cell, PT prothrombin time, CHD coronary heart disease, COPD chronic obstructive pulmonary disease, AMI acute myocardial infarction, AKI acute kidney injury, ICU intensive care unit, LOS ICU length of ICU stay, LOS Hospital length of hospital stay

Table 2 Comparison of all-cause mortalities among groups A, B and C

Group	30-day		90-day	
	Survivors (n=673)	Non-survivors (n=465)	Survivors (n=648)	Non-survivors (n=490)
Group A (n=511)	333(65.17)	178(34.83)	323(63.21)	188(36.79)
Group B (n=110)	76(69.09)	34(30.91)	74(67.27)	36(32.73)
Group C (n=517)	264(51.06)	253(48.94)	251(48.55)	266(51.45)
χ^2	26.142		27.828	
p value	<0.001		<0.001	

RDW red cell distribution width, Group A $-0.4\% < \Delta \text{RDW} < 0.4\%$, Group B $\Delta \text{RDW} \leq -0.4\%$, Group C $\Delta \text{RDW} \geq 0.4\%$

Table 3 Association of red cell distribution width at ICU admission with clinical outcomes

RDW(%)	Non-adjusted		Model 1		Model 2	
	HR(95% CI)	p value	HR (95% CI)	p value	HR (95% CI)	p value
30-day all-cause mortality						
<13.89(n=404)	1		1		1	
13.89–15.39(n=361)	1.754(1.376-2.235)	<0.001	1.925(1.502-2.468)	<0.001	1.859(1.438-2.403)	<0.001
≥ 15.39 (n=373)	2.198(1.742-2.773)	<0.001	2.484(1.931-3.195)	<0.001	2.157(1.628-2.858)	<0.001
90-day all-cause mortality						
<13.89(n=404)	1	<0.001	1	<0.001	1	<0.001
13.89–15.39(n=361)	1.709(1.351-2.161)	<0.001	1.806(1.420-2.296)	<0.001	1.735(1.355-2.222)	<0.001
≥ 15.39 (n=373)	2.161(1.725-2.706)		2.307(1.813-2.936)		2.031(1.552-2.657)	

Model 1 was adjusted for age, gender, sofa, GCS, temperature, chronic obstructive pulmonary disease, cerebral infarction, acute kidney injury and hospital length of hospital stay; Model 2 adjusted for model 1 plus anion gap,

lactate, white blood cell, chloride, glucose, hemoglobin, sodium, phosphate, partial pressure of arterial oxygen, prothrombin time and creatinine.

Figures

A total of 523,740 admission records in MIMIC IV database

Figure 1

The flowchart of the included population. MIMIC Medical Information Mart for Intensive Care, LOS ICU length of ICU stay, RDW red cell distribution width, ICU intensive care unit

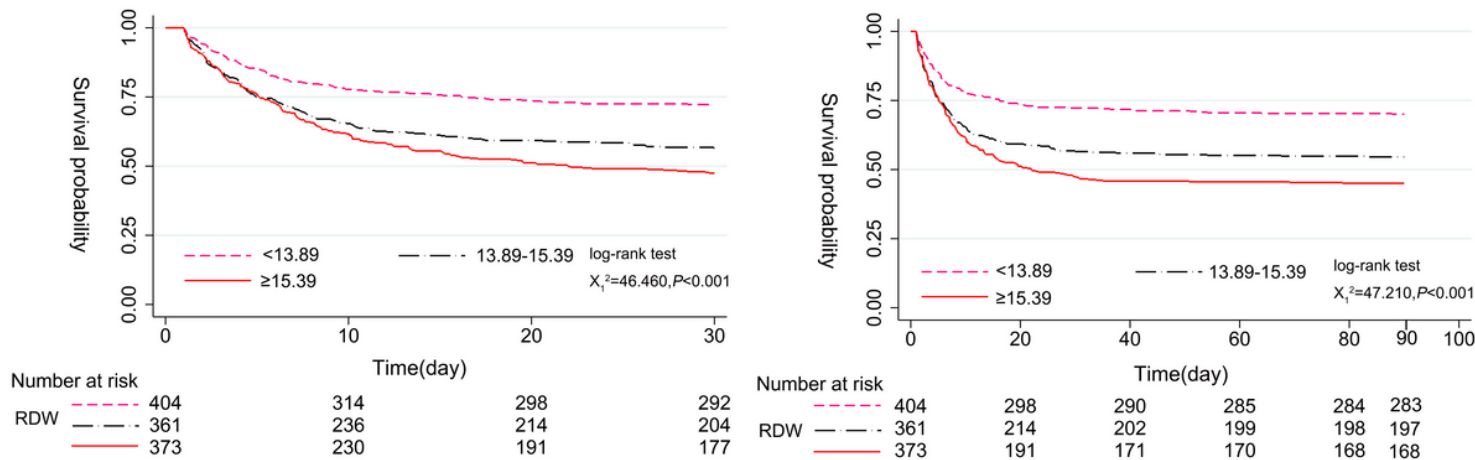


Figure 2

Kaplan–Meier curve of 30- and 90-day survival in CA patients based on RDW at ICU admission. RDW red cell distribution width, CA cardiac arrest, ICU intensive care unit

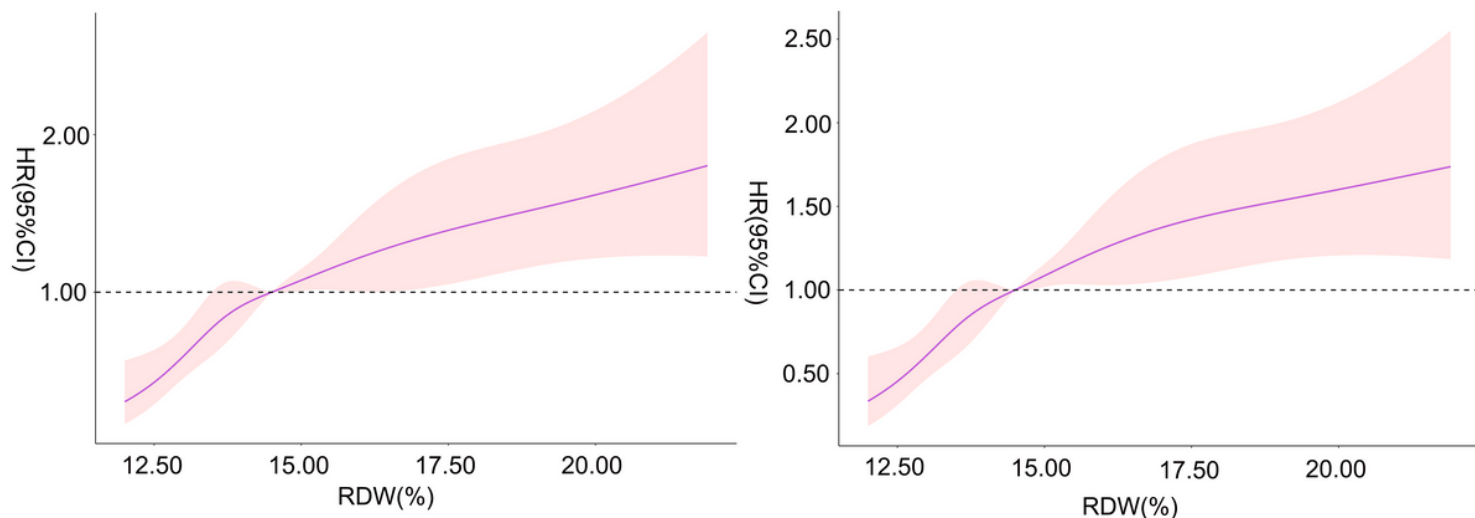


Figure 3

Association between RDW at ICU admission and 30-(left) and 90-day(right) all-cause mortality. RDW red cell distribution width, ICU intensive care unit

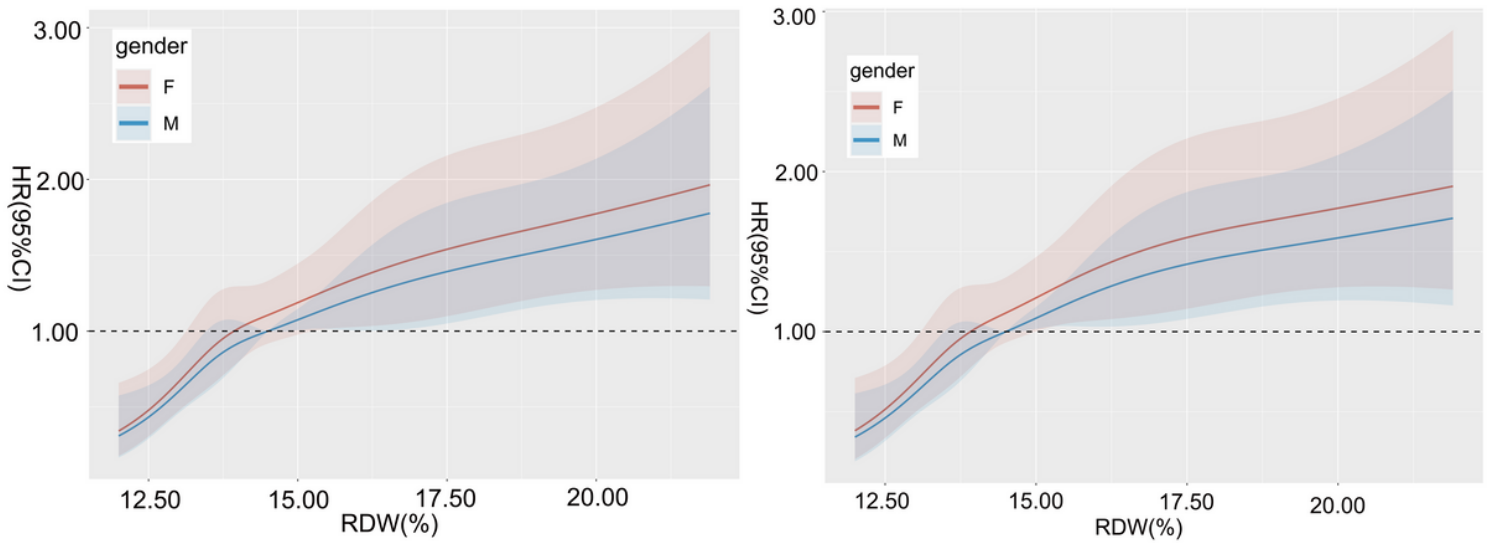


Figure 4

Association between RDW at ICU admission and 30-(left) and 90-day(right) all-cause mortality based by sex. RDW red cell distribution width, ICU intensive care unit HR hazard ratio, F female, M male.

Supplementary Files

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

- [Additionalfile1Baselinecharacteristics.docx](#)
- [Additionalfile2results.docx](#)