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Usefulness of RBC distribution width and C-reactive protein to predict mortality in pediatric non-cardiac critical illness

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ABSTRACT

Introduction: We aimed to assess the performance of red blood cell distribution width (RDW), C-reactive protein (CRP) or the combination of both to predict clinical outcomes in pediatric non-cardiovascular critical illness.
Materials and methods: We analyzed 404 pediatric non-cardiovascular critically ill patients admitted to pediatric intensive care unit (PICU). Potential predictors were identified using multivariable logistic regression. We also calculated the power of RDW and CRP additive to pediatric critical illness score (PCIS) to predict mortality with calculation of C-index value, integrated discrimination improvement (IDI) and net reclassification improvement (NRI) indices.
Results: RDW and CRP independently predicted PICU mortality. The C-index value of PCIS with respect to prediction of PICU mortality was greater than that of RDW and CRP. The combination of RDW or CRP or both with PCIS did significantly increase C-index value for predicting mortality (all p<0.01). Addition of RDW or CRP or their combination to PCIS provided IDI of 7%, 1.1% and 9.4% (p=0.009, 0.01 and 0.003) and NRI of 15.9%, 13.1% and 19.6% (p=0.002, 0.043 and 0.002), respectively.
Conclusions: In pediatric non-cardiovascular critically ill patients, RDW and CRP could serve as independent predictors of PICU mortality and addition of RDW or CRP or both to PCIS significantly improves the ability to predict PICU mortality.

1. Introduction

Red cell distribution width (RDW), routinely measures variability in red blood cell size, which is a simple, inexpensive and widely available measure reported as part of the automated complete blood count in clinical practice. Traditionally, the clinical significance of RDW is mainly considered as an indicator of anemia caused by iron, cobalamin, or folate deficiency. Recently, it has been reported that elevated RDW was an independent predictor of mortality in adult patients with acute or chronic disease, critical illness [1-5], cardiovascular diseases [6-9], pneumonia [10,11] and sepsis [12,13]. Similarly, recent limited investigations also found that a high RDW value was associated with worse outcomes in unselected pediatric critical patients [14,15]. Nevertheless, the important value of prognosis has been neglected by the reporters in non-cardiovascular critical illness. There are few studies examining RDW as an important indicator in the prediction of mortality during pre-, and postoperative period of the pediatric congenital heart disease surgery [16,17].

C-reactive protein (CRP) is regarded as an extremely sensitive biomarker of inflammation reaction, tissue damage, tissue necrosis and infection. It has the ability to give reliable predictive value for outcomes in adult critical patients [18,19]. Although CRP had a poor prediction of mortality compared with other biomarkers in pediatric infective or non-infective population and critical illness [20-23], the sample of these study were rather small and confounded by some factors. In addition, another study revealed that CRP has been associated with long-term mortality in children undergoing allogeneic stem cell transplantation [24]. More and more studies highlighted that RDW could reflect the degree of in inflammation, and is closely correlated with CRP levels [25]. However, the predictive value of the combination of both RDW and CRP for outcomes has not been investigated in pediatric non-cardiovascular critical illness.

Abbreviations: RDW, red cell distribution width; CRP, C-reactive protein; PCIS, pediatric critical illness score; IDI, discrimination improvement; NRI, net reclassification improvement; APACHE-II, acute physiology and chronic health evaluation II; PIM-2, second generation pediatric index of mortality; ROC, receiver operating characteristic; AUC, area under the curve; OR, odds ratio; PPV, positive predictive value; NPV, negative predictive value.

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Clinical data showed that RDW could improve the prognostic scores of acute physiology and chronic health evaluation II (APACHE-II), one of the most common models used to evaluate ICU adult patients' condition and predict their outcomes in clinical practice [26]. In pediatric population, many clinical studies have confirmed that second-generation pediatric index of mortality (PIM-2) was a common indicator to assess the severity and predict the mortality in critical illness for children [27], while RDW did not significantly increase area under the curve (AUC) of PIM-2 for predicting mortality [14,28]. The reason may be that they used insensitive C-statistic method [29]. Fortunately, the new methods have being increasingly used to evaluate and compare predictive risk models such as integrated discrimination improvement (IDI) and net reclassification improvement (NRI) [30,31]. Pediatric critical illness score (PCIS) is commonly used in Chinese children [32-34], which contains patients' heart rate, blood pressure, respiratory rate, arterial oxygen pressure, potential of hydrogen, Sodium ion, Potassium ion, Serum creatinine, and Hemoglobin, and is inversely linked to the severity of disease. We hypothesized that higher RDW and CRP would be independently correlated with converse outcomes in pediatric non-cardiovascular critical illness. We, therefore, undertook a prospective, observational investigation to evaluate the prognosis for RDW, CRP or their combination in moderately large population in pediatric non-cardiovascular critical illness. We also assessed the ability of RDW and CRP additive to PCIS to predict mortality with calculation of C-statistic value, IDI and NRI indices.

2. Material and methods

2.1. Patients

We performed a prospective, observational trial of non-cardiac critically ill children admitted between January 4, 2015, and March 31, 2018 to the pediatric intensive care unit (PICU) at the Affiliated Hospital of Southwest Medical University and Chengdu Women's & Children's Central Hospital. All patients were eligible for enrollment if they needed to transfer to PICU from emergency department or department of pediatrics. Exclusion criteria were as follows: 1) their ages were <1month or >168months; 2) the following International Classification of Diseases, 9th Edition, admission diagnoses: malignancy, epilepsy or seizures; 3) history of RBC transfusion within 14days prior to PICU admission; 4) patients died within 5h of admission or were discharged from PICU because it was difficult to collect data for those patients; 5) patients from pediatric surgery; 6) patient had primary cardiac disease, but did not contain a secondary cardiac disease; 7) the patients with more than one PICU admission during the period of hospitalization, only the initial encounter was contained and any readmission were excluded. This study was approved by the ethics committee of Affiliated Hospital of Southwest Medical University and that of Chengdu Women's & Children's Central Hospital and was in accordance with the Declaration of Helsinki and its later amendments.

2.2. Laboratory methods

The RDW, platelet, white blood cell and hemoglobin level were measured using the Beckman Coulter LH-750 Hematology Analyzer (Beckman Coulter, Inc., Fullerton, California), as one part of a complete blood cell count. Normal RDW was defined as 11.5% 14.5% in the laboratory of our hospital. Serum CRP levels were examined with Quick Read CRP test kit (Orion Corporation, Orion Diagnostica, Espoo, Finland). The BNP level was determined using the Elecsys Electro-chemo luminescent assay (Cobas e411 analyzer; Roche Diagnostics; Mannheim, Germany). Blood samples were collected from the children in the first 24h of PICU admission.

2.3. Study outcomes

At baseline, demographic and clinical characteristics, including the PCIS (which can range from 0 to 110, with lower scores indicating more severe illness), were collected. The primary outcome was death in the PICU from any cause.

2.4. Statistical analysis

Data analysis was conducted with SPSS 13.0 software. Categorical variables and continuous variable were presented as mean standard deviation, median with interquartile range or %, where appropriate. But age, white blood cell, weight, CRP, BNP were logarithmically normalized (presented as log-age, log-white blood cell, log-weight, log-CRP and log-BNP, respectively) for statistical calculations. Unpaired Student's *t*-test or Mann-Whitney test was used to compare continuous variable and Chi-square or Fisher exact tests for categorical variable. Univariate logistic regression was performed to calculate odds ratio (OR) for mortality associated with each risk factor. A forward stepwise multivariate logistic regression was utilized to determine the independent predictors of mortality in non-cardiac critically ill children. A criterion of $p<$ 0.05 for entry and a p0.1 for removal was enforced in this procedure. Spearman correlation was used to assess the relationships among RDW, PCR and PCIS. In order to assess the goodness of fit of the model, Cox & Snell R Square and Nagelkerke R Square were calculated [35]. The receiver operating characteristic (ROC) was constructed for variables associated with the death. The area under the curve (AUC) was also calculated with 95% confidence intervals (CI). The differences between AUC were compared using the method of Hanley and McNeil [36]. In addition, the IDI and NRI were used to further check model discrimination. A p-value of <0.05 was considered statistically significant.

3. Results

3.1. Baseline characteristics of the patient population

A total of 1562 PICU admissions over the study period were screened; of these, 404 subjects including 38.9% female, with a median age of 12months (interquartile range: 4 to 60months) and a median weight of 10kg (interquartile range: 6 to 17 kg), met study criteria and were analyzed. The flow sheet research selection was shown in Fig. 1. Baseline clinical and laboratory characteristics of the patients were presented in Table 1. The primary reason for PICU admission was pulmonary disease. A total of 20.0% and 26.2% of the patients had sepsis and neurologic disease, respectively. For the full population, the mean heart rate, respiratory rate, hemoglobin, RDW, platelet and PCIS were 139.036.7 bpm, 39.216.0 breaths/min, 109.224.2g/L, 15.22.7%, 320.3175.5æ 10^9/L, 79.913.4, respectively. The median levels of white blood cell, CRP, BNP on admission was 11.7 (8.216.6)æ10^9/L, 4.09 (0.68316.3) mg/L and 52.4 (12.4147.0) pg/mL. There were 99 dead children during the PICU hospitalization. The leading cause for children death was pulmonary disease. Compared with survivors, non-survivors were younger and in a more severe condition as reflected by the higher heart rate, respiratory rate, white blood cell, RDW, CRP, BNP and had lower PCIS, platelet and weight. There were no difference in sex, Systolic pressure and Diastolic pressure between survivors group and non-survivors group.

3.2. Risk factors for predicting PICU mortality

On univariate logistic regression, we found higher RDW, CRP, BNP and lower PCIS and platelet were correlated to PICU mortality

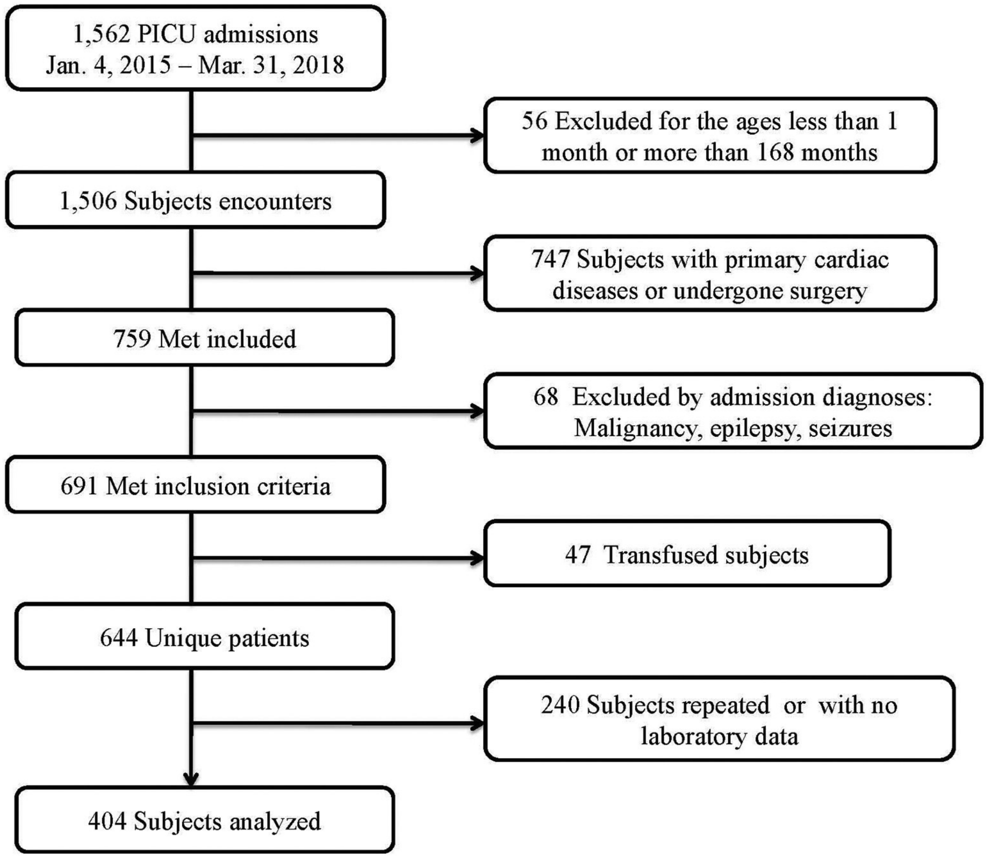

Fig. 1. Study flow diagram.

Table 1
Baseline clinical and laboratory characteristic of subjects.

	ALL	Survivors	Non-survivors	*p*-Value
Patients, no.	404	305	99	/
Female (%)	38.9	39	38.3	0.93
Age (months)	12 (460)	12 (3.566.5)	11 (660.0)	0.04
Weight (kg)	10 (617)	10 (618)	9.1 (617)	0.001
Main diagnosis leading to PICU admission (n, %)				
Pulmonary	176 (43.6)	144 (47.2)	32 (32.2)	
Neurologic	106 (26.2)	83 (27.2)	23 (23.2)	
Digestive	16 (4.0)	11 (3.6)	5 (5.1)	
Sepsis	81 (20.0)	50 (16.4)	31 (31.3)	
Other	25 (6.2)	17 (5.6)	8 (8.1)	
Systolic pressure (mmHg)	93.116.2	94.215.6	90.017.8	0.08
Diastolic pressure (mmHg)	56.613.1	57.012.0	55.716.5	0.73
Heart rate (bpm)	139.036.7	134.934.2	151.941.1	0.00
Respiratory rate (breaths/min)	39.216.0	38.315.1	4218.1	0.044
White blood cell (10^9/L)	11.7 (8.216.6)	11.2 (7.715.8)	14.9 (10.119.8)	0.005
Hemoglobin (g/L)	109.224.2	110.522.9	105.37.6	0.041
RDW (%)	15.22.7	14.92.5	16.23.3	0.00
PLT (10^9/L)	320.3175.5	336.4171	270.7180.9	0.004
CRP (mg/L)	4.09 (0.68316.3)	3.5 (0.66513.6)	8.0 (0.9520)	0.017
BNP (pg/mL)	52.4 (12.4147.0)	44.4 (9.38100)	100.9 (38.9375.4)	0.000
PCIS	79.913.4	84.29.4	66.615.1	0.000

PCIS, pediatric critical illness score; CRP, C-reactive protein; RDW, red cell distribution width; PLT, platelet; BNP, brain natriuretic peptide.

(Fig. 2) (because heart rate, respiratory rate, blood pressure and hemoglobin levels had been included in PCIS, they did not enter into the analysis). As shown in Fig. 3, a forward stepwise multivariate logistic regression analysis demonstrated that RDW, CRP and PCIS remained independently predicting mortality in non-cardiac critically ill children (p=0.001; p=0.012; p=0.000, respectively).

3.3. Correlation of RDW and CRP with PCIS

As shown in Fig. 4, RDW was negatively correlated with PCIS (r= 0.289, p=0.000; Fig. 4A); CRP was negatively correlated with PCIS (r =0.118, p=0.017; Fig. 4B); and RDW showed a distinctly positive correlation with CRP (r=0.157, p=0.002; Fig. 4C). The results indi-

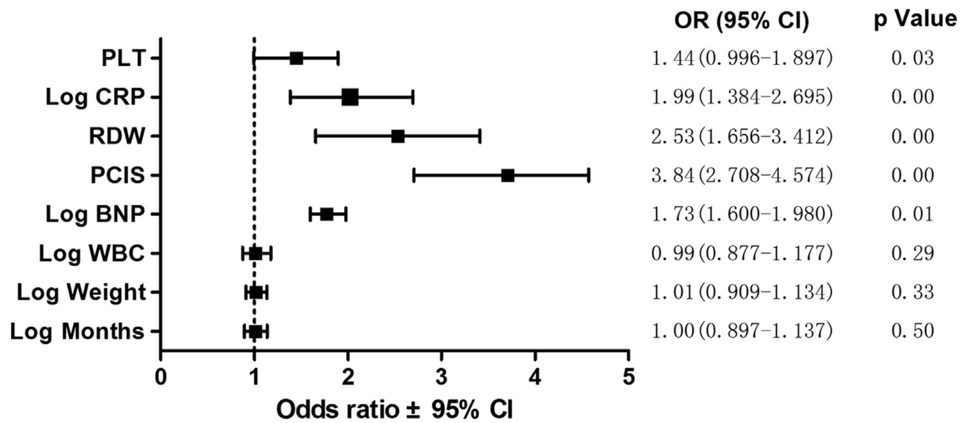

Fig. 2. Univariate logistic regression model predicting the mortality in non-cardiac critically ill children. Log-variable is the logarithm of the variable.

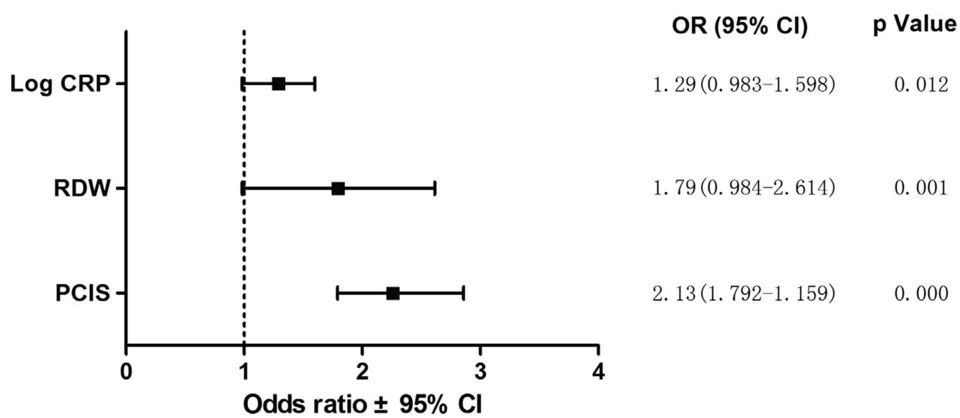

Fig. 3. Multivariate logistic regression analysis for the mortality in non-cardiac critically ill children. Log-variable is the logarithm of the variable.

cated that the higher RDW and CRP were correlated with disease severity.

3.4. Prognostic value of RDW and CRP

According to receiving operating characteristic analysis, the AUC for PCIS, RDW and CRP to predict mortality was 0.841 (95% CI, 0.802 to 0.875) (p<0.01), 0.729 (95% CI, 0.683 to 0.772) (p< 0.01) and 0.58 (95% CI, 0.828 to 0.897) (p<0.01), respectively. The AUC of PCIS was significantly higher than that of both RDW and CRP (all p<0.01), while there was no difference between RDW and CRP in the AUC (p>0.05). The optimal cutoff value of PCIS for predicting mortality was 71, which yielded sensitivity 75.76% (95% CI, 66.1 to 83.8), specificity 85.25% (95% CI, 80.8 to 89.0), positive predictive value (PPV) of 62.5%(95% CI, 53.2 to71.2) and negative predictive value (NPV) 91.5% (95% CI, 87.794.5), and of RDW (15.52%) gave sensitivity 75.76% (95% CI, 66.1 to 83.8), specificity 63.61% (95% CI, 57.9 to 69.0), PPV 40.4% (95% CI, 33.247.7) and NPV 89.0% (95% CI, 84.192.8). The optimal cutoff value of CRP (34 mg/L) provided sensitivity 40.4% (95% CI, 30.7 to 50.7), specificity of (95% CI, 72.3 to 82.0), PPV 36.7% (95% CI, 27.6 to 46.5) and NPV 80.0% (95% CI, 75.084.4) (Fig. 5 and Table 2).

3.5. Combination of CRP or RDW or both with PCIS for predicting PICU mortality

To further evaluate whether RDW or CRP or their combination improve the prognostic performance of PCIS, we combined one or two biomarkers with the PCIS to construct new ROC curves (Fig. 6). Compared with the PCIS, combination of CRP [AUC 0.858 (95% CI, 0.820.891)] or RDW [AUC 0.866 (95% CI, 0.828 to 0.897)] or both [AUC 0.874(95% CI, 0.8380.905)] did not only significantly increase AUC for the prognostic performance of mortality (p=0.0046, 0.0019 and 0.0004), but also slightly improved sensitivity and NPV, respectively (Table 2). There were not significantly different in AUC for predicting PICU mortality between combination of CRP or RDW with PCIS (p=0.373). The AUC of both with PCIS was significantly superior to the combination of CRP and PCIS for predicting PICU mortality (p=0.018), while it was not superior to the addition of RDW to PCIS (p=0.06). The combination of CRP and RDW [AUC 0.737 (95% CI, 0.6920.78)] was significantly inferior to PCIS to predict PICU mortality (p=0.0006) (Table 2). Additionally, the forward stepwise multivariate logistic regression analysis indicated that the addition of RDW or both biomarkers to PCIS improved the model discrimination for slightly increased the Cox & Snell R Square and Nagelkerke R Square (Table 3). Furthermore, when using more sensitive statistical analysis, we found that the combination of RDW or CRP or both with PCIS significantly improved the ability to predict the outcomes (Table 4). The combination of RDW with PCIS provided an IDI of 7% (95% CI, 4.2 to 9.8) (p=0.009) and NRI of 15.9% (95% CI, 7.5 to 24.8) (p=0.002). CRP plus PCIS yielded an IDI of 1.1% (95% CI, 0.3 to 1.9) (p=0.01) and NRI of 13.1% ((95% CI, 2.5 to 23.7) (p=0.043). The addition of both biomarkers to the PCIS gave an IDI of 9.4% (95% CI, 7.1 to 11.6) (p=0.003) and NRI of 19.6% (95% CI, 8.630.5) (p=0.002).

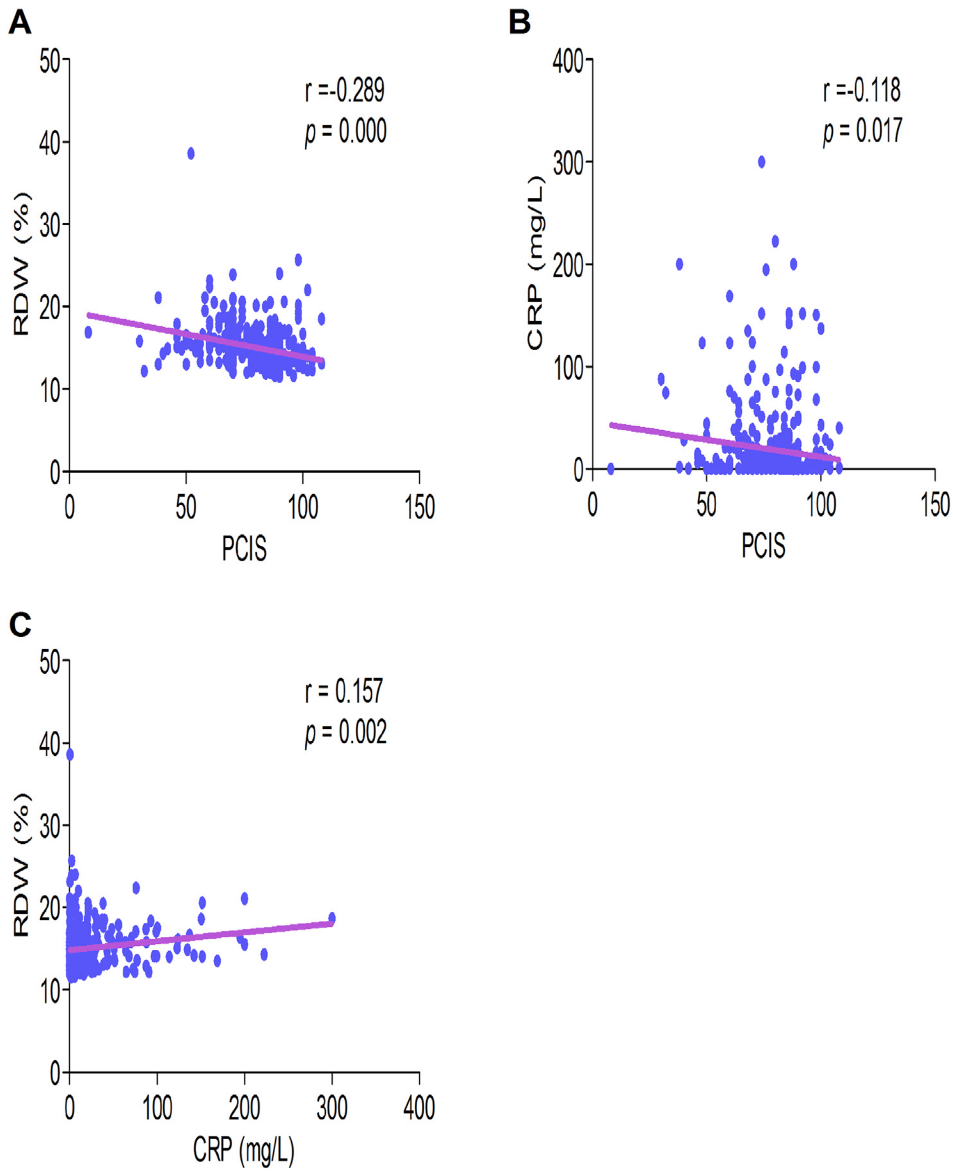

Fig. 4. Correlation analysis: RDW and CRP with PCIS in all non-cardiac critically ill children. RDW and CRP were negatively correlated with PCIS (A and B). (C) There was a positive relationship between RDW and CRP.

4. Discussion

With over 400 pediatric non-cardiovascular critically ill patients, we found that RDW and CRP independently predicted PICU mortality and multiple potential confounders including platelet and BNP. RDW and CRP were negatively correlated with PCIS, and there was a positive relationship between RDW and CRP. Although the predictive power of RDW and CRP was lower as compared with the PCIS, the addition of RDW or CRP or both to PCIS can significantly improve the ability to predict PICU mortality, as demonstrated by C-index value, NRI and IDI indices. To our best knowledge, this is the first investigation to explore the power of RDW and CRP added to the PCIS to predict mortality in pediatric non-cardiac critical illness, especially using the new statistic method, that is, the NRI and IDI indices.

Traditionally, as a simple and low cost parameter, RDW is utilized in laboratory hematology for differential diagnosis of anemia. Nonetheless, evidences have suggested that RDW was the most promising biomarker to predict disease severity and clinical outcomes in adult various cardiovascular conditions [37,38], including coronary heart disease, pulmonary hypertension, acute heart failure, stroke and pulmonary embolism. In addition, recent studies found that RDW was associated with mortality in adult non-cardiovascular diseases, especially unselected critically ill or acutely patients [39-41], such as pneumonia and sepsis. In accordance with these studies, our data showed that increased RDW was closely correlated with PCIS respecting disease severity and had strong power to independently predict mortality in pediatric non-cardiac critical illness. There are several reports supporting our results in unselected pediatric critical illness [14], respiratory failure [42], neonatal sepsis [43], and pediatric congenital heart disease surgery [16,17]. Previous studies attested that the adding of RDW to established prediction models such as APACHE-II, Simplified Acute Physiology Score (SAPS) II and the Initial Sequential Organ Failure Assessment (SOFA) Score significantly improved the discriminative power in adult critical illness with the common method of C statistic [26,44-47]. Similarly, the addition of RDW to PCIS did improve the ability of PCIS for predicting mortality in

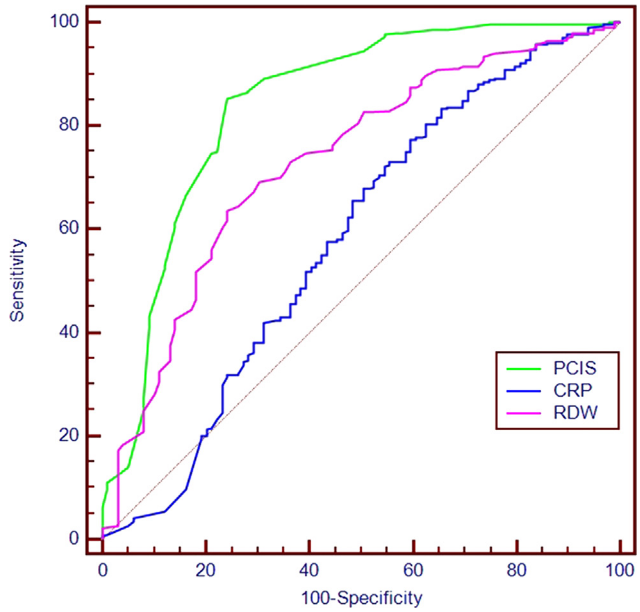

Fig. 5. Receiver operator characteristic (ROC) curves for mortality. ROC curves for mortality were calculated for PCIS, RDW and CRP. The area under the ROC curve of PCIS was larger than that of RDW or CRP (all $p<0.05$).

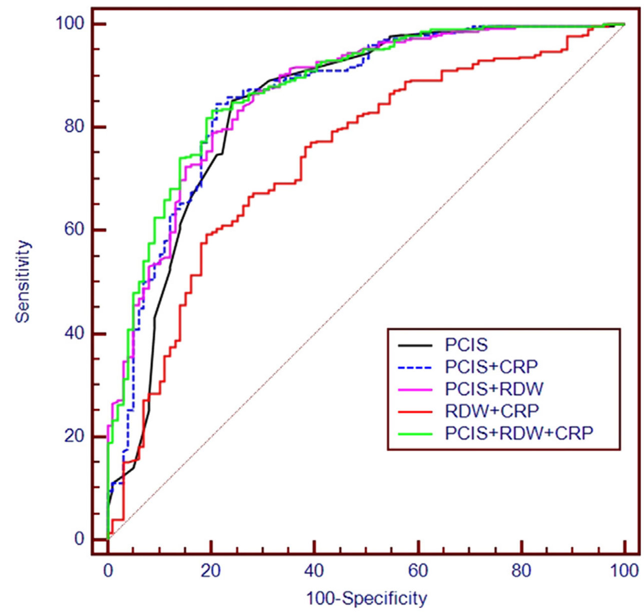

Fig. 6. Receiver operator characteristic (ROC) curves for combination of two or three variables among PCIS, RDW and CRP. Combination of RDW or CRP or both with PCIS significantly increased AUC in prediction of mortality (all $p<0.05$).

pediatric non-cardiac critical illness with AUC (0.866, p=0.0019), sensitivity (79.8%) and NPV (92.3%). Currently, some statisticians have raised many doubts about C statistic to evacuate predictors [48], so, we further used a more sensitive method of improvement in model discrimination to verify our results. We found that the addition of RDW to the PCIS also significantly increased the power to predict mortality in pediatric non-cardiac critical illness as demonstrated by the NRI (15.9%, p=0.002) and IDI (7%, p=0.009) indices.

CRP is an acute phase reactant, which has been shown to be a reliable marker of inflammation [49]. Usually, the more severe the inflammation, the more serious the disease is, especially the infectious disease. It was inversely related to PCIS in present study. Additionally, our data indicated that RDW was positively associated with CRP. A similar relationship has also been shown in a large cohort of unselected adult outpatients with cardiovascular disease [50]. These finding suggest that CRP may be an indicator of disease severity in pediatric non-cardiac critical illness. A finding indicated that increased CRP values correlated with non-relapse mortality in children undergoing allogeneic stem cell transplantation [24] and hematopoietic stem cell transplantation in adults [24]. Consistently, our study indicated that CRP was not only an independent predictor of mortality in pediatric non-cardiac critical illness, but also significantly improved discrimination of mortality in addition to PCIS as supported by AUC (0.858, p=0.0046), IDI (1.1%, p=0.01) and NRI (13.1%, p=0.043), compared with PCIS alone. It slightly improved sensitivity (78.79%) and NPV (92.5%) as well. In a report by Wang and co-workers, CRP was also an independent predictor of ICU mortality in unselected adult patients and non-cardiac adult patients, and the addition of CRP to APACHE-II score significantly improved the ability to predict ICU mortality [35]. Up to now, the complexity of interactions driving host immune response and genetic variation implies that multiple biomarkers could be increasingly more power for predicting outcomes in the pediatric population. Although the C-index value, specificity, PPV and NPV showed the predictive power of CRP plus RDW for mortality was inferior to PCIS in pediatric non-cardiac critical illness, the addition of CRP and RDW to PCIS significantly improved the predictive power as demonstrated by AUC (0.874, p=0.0004), IDI (9.4%, p=0.003) and NRI (19.6%, p= 0.002), and it also slightly improved the sensitivity (79.8%) and NPV (92.7%).

Several limitations of our investigation should be discussed. Firstly, even though our population came from two hospitals, the number of patients was relatively small; hence, our population may not reflect the whole cohort. Secondly, although we controlled several factors affecting RDW, it was possible that other residual confounding variables were not contained in the analysis, such as biomarker of nutritional status, iron deficiency and other markers of inflammation. Thirdly, since ours was not a randomized trial, the inherent bias was inevitable. Finally, we did not undertake more work to assess subgroup analysis to explore the

Table 2
Values of PCIS, RDW, CRP and their combinations on the basis of ROC curves.

Test	AUC	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	p value
PCIS	0.841 (0.8020.875)	75.76 (66.183.8)	85.25 (80.889.0)	62.5 (53.271.2)	91.5 (87.794.5)	<0.0001
RDW	0.729 (0.6830.772)	75.76 (66.183.8)	63.61 (57.969.0)	40.4 (33.247.7)	89.0 (84.192.8)	<0.0001
CRP	0.58 (0.530.629)	40.4 (30.750.7)	77.38 (72.382.0)	36.7 (27.646.5)	80.0 (75.084.4)	0.0178
PCIS+RDW	0.866 (0.8280.897)	79.8 (70.587.2)	79.02 (7483.4)	55.2 (46.763.6)	92.3 (88495.3)	<0.0001
PCIS+CRP	0.858 (0.820.891)	78.79 (69.486.4)	84.59 (80.088.5)	62.4 (53.370.9)	92.5 (88.795.3)	<0.0001
RDW+CRP	0.737 (0.6920.78)	80.81 (71.788.0)	59.34 (53.664.9)	39.2 (32.546.3)	90.5 (85.594.2)	<0.0001
PCIS+RDW+CRP	0.874 (0.8380.905)	79.8 (70.587.2)	83.28 (78.687.3)	60.8 (51.869.2)	92.7 (88.995.5)	<0.0001

PCIS, pediatric critical illness score; RDW, RBC distribution width; CRP, C-reactive protein; PPV, positive predictive value; NPV, negative predictive value.

Table 3
Independent predictors of death by multivariable logistic regression.

		OR	*p*	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
Model I	PCIS	1.140	0.000	310.42	0.292	0.435
Model II	RDW	0.798	0.001	298.545	0.312	0.465
	PCIS	1.125	0.000			
Model III	Log-CRP	0.991	0.017	292.609	0.323	0.48
	RDW	0.810	0.002			
	PCIS	1.126	0.000			

PCIS, pediatric critical illness score; RDW, RBC distribution width; CRP, C-reactive protein; OR, odds ratio.

Table 4
IDI and NRI for assessing improvement in model performance after adding biomarkers to PCIS.

	IDI (95% CI), %	*p* value	NRI (95% CI), %	*p* value
PCIS+RDW	7 (95% CI, 4.29.8)	0.009	15.9 (95% CI, 7.524.8)	0.002
PCIS+log-CRP	1.1 (95% CI, 0.31.9)	0.01	13.1 (95% CI, 2.523.7)	0.043
PCIS+RDW+log-CRP	9.4 (95% CI, 7.111.6)	0.003	19.6 (95% CI, 8.630.5)	0.002

IDI, integrated discrimination improvement; NRI, net reclassification improvement; PCIS, pediatric critical illness score; RDW, RBC distribution width; CRP, C-reactive protein; CI, confidence interval.

relationship between RDW or CRP and mortality in each kind of disease.

5. Conclusions

In this study of pediatric non-cardiac critically ill patients, we verified that RDW and CRP were independent predictors of PICU mortality. The predictive power of RDW and CRP were lower compared with the PCIS, while the addition of RDW or CRP or both the PCISC could significantly improve the ability to predict PICU mortality, as demonstrated by C-index value, IDI and NRI indices.

Declaration of interest

None.

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