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ORIGINAL RESEARCH

Association of Red Cell Index and Hospital Mortality in Chronic Obstructive Pulmonary Disease Patients Admitted to the Intensive Care Unit: A Retrospective Cohort Study

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Purpose: This study aims to explore the association between red cell index (RCI) and hospital mortality in Chronic Obstructive Pulmonary Disease (COPD) patients in the intensive care unit.

Patients and Methods: This was a retrospective cohort research. The study included 821 COPD patients. Clinical data from the Medical Information Mart for Intensive Care IV (MIMIC-IV) database was conducted. Multivariate logistic regression analysis was used to assess the correlation between RCI and in-hospital mortality. Age, SOFA score, diabetes mellitus, cerebrovascular disease, congestive heart failure and mechanical ventilation were considered for subgroup analysis.

Results: This study comprised 821 patients, of which 16.5% (124/821) suffered hospital mortality. In the multivariate logistic regression model, RCI was positively associated with hospital mortality, each unit increase in RCI was associated with a 3% increase in hospital mortality (odds ratio [OR] =1.03; 95% confidence interval [95CI%] =1.01–1.06). Meanwhile, compare with the lowest RCI group, the highest RCI groups tended to have higher risks of hospital mortality (OR [95% CI] 2.33 [1.27–4.27]). Additionally, subgroup analysis result was persistent among all the groups.

Conclusion: Higher RCI was positively associated with a higher risk of mortality in critically ill patients with COPD. Further investigation is necessary to confirm these findings.

Keywords: red cell index, chronic obstructive pulmonary disease, hospital mortality, retrospective cohort study, MIMIC-IV

Introduction

Chronic Obstructive Pulmonary Disease (COPD), characterized by persistent respiratory symptoms and progressive airflow limitations, is a significant cause of morbidity, mortality, and healthcare utilization worldwide.[1,2] Patients with COPD often require hospitalization or ICU admission for acute exacerbations.[3] Consequently, COPD has a significant impact on patients' quality of life, healthcare expenditures, and clinical and economic burden.[4] Furthermore, in critically ill patients, the risk-adjusted mortality of patients with COPD was higher than in patients without COPD. The presence of COPD was an independent risk factor for increased mortality and was associated with prolonged mechanical ventilation and prolonged weaning.[5] Therefore, identifying easily accessible and technically undemanding markers during hospitalization for COPD patients that are associated with hospital mortality becomes essential for reducing the disease burden and mortality rates.

There is a new indicator red cell index (RCI) that obtained from complete blood count measurements. RCI is related to red blood cell (RBC) count (10^12/L), hemoglobin (Hb) level (g/L), lymphocytes (Lym) count (10^9/L), and platelets

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(PLT) count (10^9/L), calculation formulas of RCI is (RBC × Hb)/(Lym × PLT).[6] RCI has been shown to be associated with decreased lung function and severity of disease, higher RCI level is associated with lower FEV1/FVC and higher PCO2.[7] Previous studies have also confirmed that RCI level was an effective biomarker to predict 3-month mortality in acute ischemic stroke (AIS) patients or pulmonary embolism (PE) patients.[8,9] RCI is positively correlated with adverse hospitalization outcomes in patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD).[10]

Nevertheless, the association between RCI level and hospital mortality in critically ill COPD patients is unclear. Therefore, we aimed to investigate the association between RCI and hospital mortality with COPD patients in the ICU.

Materials and Methods

Database introduction

The data were obtained from the open-source clinical database, Medical Information Mart for Intensive Care IV (MIMIC IV), an update to MIMIC-III, which covered over 50,000 patients admitted to the intensive care unit (ICU) at Beth Israel Deaconess Medical Center during the years from 2008 to 2019.[11] The first author, Yushan Shi, has gained access to the database (Certification No: 54017638) after passing the online exams and signing a data use agreement. The institutional review boards of both Beth Israel Deaconess Medical Center and MIT Affiliates have approved the establishment of the MIMIC-IV database. As database is anonymous, so informed consent was not applicable. The Ethics Committee of Affiliated Hospital of Shandong University of Traditional Chinese Medicine has granted an exemption from review for this particular study, ethics number was 2023–0020.

Selection of Study Population

The total number of patients in MIMIC IV database was 73.181 and 50,920 of them first admitted to the ICU. This study was based on the real-world study concept and included all COPD patients from the MIMIC-IV database. Our inclusion criteria were as follows: (1) Patients were older than 18 years and stayed in the ICU for more than 24 hours;[12–14] (2) Patients were diagnosed as COPD by ICD-9 codes (code = 49120, 49121, 49122) and ICD-10 codes (code = J44, J440, J441 and J442). Patients whose red cell, platelets, lymphocyte, hemoglobin levels were unavailable during the first day of ICU admission were excluded, as well as, the length of hospital time and ICU stay time was less than 24h. For patients with multiple ICU admissions, we only included data from patients with their first hospital and first ICU admission.[15]

Variable Extraction and Outcome

Data were extracted using PostgreSQL (version 13.9). Data included demographic information, vital signs, laboratory tests, comorbidities, intervention and critical score. The baseline data were obtained within the first 24 hour after ICU admission. The initial value was considered for a variable that was measured multiple times within 24 hour after ICU admission.

Demographic information: age, gender, race and insurance status, length of hospital stays, and hospital death sign.

Vital signs: heart rate (HR), systolic blood pressure (SBP); diastolic blood pressure (DBP), mean blood pressure (MBP), respiratory rate (RR), and oxygen saturation (SpO2).

Laboratory data: routine blood tests included red blood cell (RBC) count, hemoglobin (Hb) level, lymphocytes (Lym) count, and platelets (PLT) count, glucose, serum sodium, serum potassium, serum chloride, creatinine, blood urea nitrogen (BUN), serum alanine transaminases (ALT), serum aspartate aminotransferase (AST) and bicarbonate, anion gap.

Comorbidities: cerebrovascular disease, congestive heart failure, peripheral vascular disease, diabetes, mild liver disease, moderate or severe liver disease, myocardial infarct, malignant cancer, and renal disease. It was identified by the ninth or tenth revision of the International Classification of Diseases (ICD-9 or ICD-10), chronic hepatitis or cirrhosis without or with portal hypertension was considered as mild or moderately to severe liver disease, respectively.[16]

Critical score: simplified acute physiology II score (SAPS II), oxford acute severity of illness score (OASIS) sequential organ failure assessment score (SOFA)

The RCI was estimated using the following equation: RCI = (RBC × Hb)/(Lym × PLT), In accordance with RCI at 24 hour, all patients were divided into tertiles.

The outcome of this study was hospital mortality.

Statistical Analysis

Participants were divided into tertiles based on RCI levels (RCI <1.18; 1.18 ≤ RCI<2.62; RCI ≥2.62).

Categorical variables are expressed as proportions (%) and tested with Chi-square or Fisher exact test. Continuous variables are expressed as mean ± standard deviation (SD) and tested with *T*-test or one-way ANOVA (normally distributed), non-normally distributed are expressed as median and interquartile range (IQR) and tested with Kruskal–Wallis *H*-test.

A univariate model was used to evaluate whether the RCI and other biochemical variables were associated with hospital mortality. Multivariate logistic regression models were used to examine whether RCI had an independent effect on hospital mortality. Variables, which differed significantly with p values of <0.05 in univariate logistic regression analysis, were acknowledged as covariates for multivariate logistic regression analysis. RCI was analyzed as continuous and categorical variables in regression analyses, respectively. Values of the variation inflation factor (VIF) were used to assess multicollinearity. More than 10 VIFs showed multicollinearity. We constructed five models: crude model, unadjusted; model 1, adjusted for age, sex, and race; model 2, adjusted for model 1 and additionally for HR, RR, SBP, SpO2, cerebrovascular disease, liver disease, congestive heart failure, and diabetes; model 3, adjusted for model 2 and additionally for anion gap, chloride, bicarbonate, BUN, serum creatinine, ALT, and AST; model 4, adjusted for model 3 and additionally for SAPSII, OASIS, SOFA, and mechanical ventilation.

To further explore the stability of results, we conducted interaction and subgroup analyses based on age (<65 years and ≥65 years), congestive heart failure, diabetes, ventilation, and SOFA score (<4 and ≥4). Each stratification was adjusted for factors in multivariate logistic regression analysis model 4, except for the stratification factor itself. Interaction across subgroups was tested using the likelihood ratio test.

Percentage of covariates with missing data is about 40%, Missing values of covariates were imputed via multiple imputations.[17] Specifically, we imputed five sets of missing values and then selected one set for logistic regression analysis and subgroup analysis. We also performed sensitivity analysis with variable deletion for missing values and then conducted multivariate analysis using only the non-missing population. The results of this analysis can be found in Table S1.

We performed all analyses using the statistical software packages R 3.3 and Free Statistics software versions 1.7.[15] All statistical tests were two-tailed, and $p < 0.05$ was considered significant.

Results

Population of the Study

Based on the above inclusion and exclusion criteria, 821 patients were identified in the final cohort, including 697 survivors and 124 non-survivors. The flow chart of the study patients is presented in Figure 1.

Baseline Characteristics of the Study Subjects

The baseline characteristics of patients are presented in Table 1. The overall rate of hospital mortality was 15.1% (124/821). The patient age was 71.1 ± 10.6 years, and approximately 56.3% (462/821) patients were men, most of whom were white. According to RCI values at first 24 hour, patients were divided into tertiles (RCI <1.18; 1.18 ≤ RCI<2.62; RCI ≥2.62).

RCI <1.18 was considered as the lower group,1.18 ≤ RCI<2.62 was considered as the middle group, and ≥2.62 was considered as the higher group. Among three groups, no significant correlation was found in terms of bicarbonate, glucose, sodium, ALT, AST, serum creatinine, SOFA score, and length of hospital stay history of congestive heart failure, peripheral vascular disease, cerebrovascular disease, renal disease. Patients in the higher red cell index (RCI) group were more likely to develop liver disease, malignant cancer and were less likely to develop diabetes than patients in the lower group (all $P < 0.05$). As the red cell index (RCI) increased, age, respiratory rate, MBP, RBC and

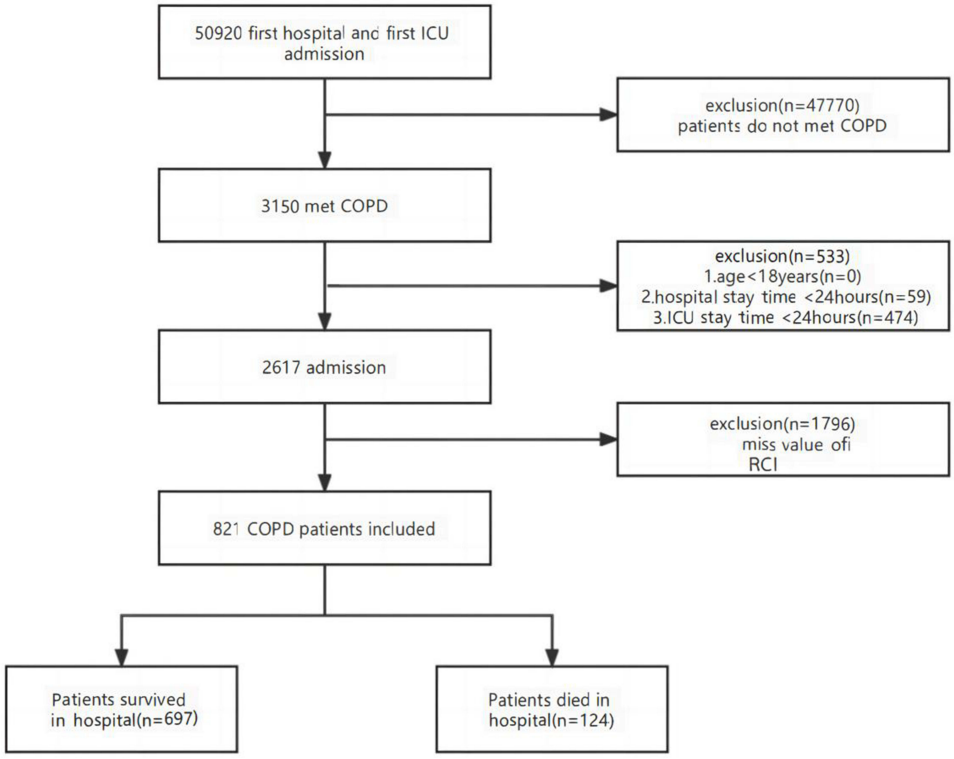

Figure 1 Flowchart of participant selection.
Abbreviations: ICU, intensive care unit; COPD, chronic obstructive pulmonary disease; RCI, red cell index.

Hb, anion gap, creatinine level, BUN, increased, whereas PLT, Lym, SpO2 and serum potassium, chloride levels decreased.

Results of Logistic Regression Analysis

Univariate regression analyses were performed to identify factors associated with hospital mortality (Table 2), it indicated that age, race, RCI, HR, RR, BUN, ALT, AST, liver disease, SOFA score, mechanical ventilation were risk factors for in-hospital mortality (all P<0.05,).

Table 1 Baseline and Clinical Characteristics of the Study Population

Variables	Total (n = 821)	RCI<1.18 (n = 274)	1.18≤RCI<2.62 (n = 273)	RCI≥2.62 (n = 274)	*p*
Male, n (%)	462 (56.3)	133 (48.5)	158 (57.9)	171 (62.4)	0.004
Age, year	71.1 ± 10.6	69.9 ± 10.2	70.9 ± 10.6	72.4 ± 11.0	0.024
Medicare	469 (57.1)	150 (54.7)	149 (54.6)	170 (62)	0.39
White, n (%)	570 (69.4)	199 (72.6)	188 (68.9)	183 (66.8)	0.258
HR, bpm	85.9 ± 15.1	85.1 ± 13.9	83.0 ± 14.0	89.6 ± 16.6	<0.001
RR, bpm	19.8 ± 3.8	19.0 ± 3.3	19.5 ± 3.6	20.9 ± 4.2	< 0.001
SBP, mmHg	114.2 ± 14.0	112.6 ± 12.1	113.9 ± 13.1	116.0±16.3	0.018
DBP, mmHg	61.1 ± 10.3	58.3 ± 8.4	61.0 ± 10.9	64.1 ± 10.8	< 0.001
MBP, mmHg,	76.7 ± 9.6	74.4 ± 7.7	76.9 ± 10.0	78.7 ± 10.4	< 0.001
SpO2, %	96.3 ± 2.5	96.8 ± 2.0	96.5 ± 2.6	95.5 ± 2.6	< 0.001
Hematocrit, %	29.2 ± 6.5	26.7 ± 4.7	29.4 ± 6.2	31.6 ± 7.4	< 0.001
Anion gap, mmol/L	13.0 ± 3.9	12.5 ± 3.7	12.7 ± 3.9	13.7 ± 4.0	< 0.001
RBC,10^12/L	3.4 ± 0.7	3.2 ± 0.5	3.5 ± 0.6	3.6 ± 0.8	< 0.001
Hb, g/L	10.2 ± 1.9	9.5 ± 1.4	10.2 ± 1.8	10.7 ± 2.2	< 0.001
PLT, 10^9/L	178.2 ± 85.5	215.9 ± 95.1	176.2 ± 70.4	142.7 ± 72.5	< 0.001

(*Continued*)

Table 1 (Continued).

Variables	Total (n = 821)	RCI<1.18 (n = 274)	1.18≤RCI<2.62 (n = 273)	RCI≥2.62 (n = 274)	*p*
Lym, 10^9/L	1.7 ± 8.4	3.3 ± 14.3	1.3 ± 0.6	0.6 ± 0.4	< 0.001
Bicarbonate, mmol/L	21.8 ± 5.0	21.5 ± 4.4	22.0 ± 4.7	21.8 ± 5.7	0.518
Chloride, mmol/L	100.5 ± 6.2	101.3 ± 5.4	101.0 ± 6.0	99.2 ± 6.9	< 0.001
Glucose, mg/dL	121.1 ± 42.5	119.6 ± 37.5	120.9 ± 40.7	122.6 ± 48.6	0.714
Sodium, mmol/L	136.8 ± 4.9	136.9 ± 4.2	136.9 ± 4.5	136.6 ± 5.9	0.672
Potassium, mmol/L	4.1 ± 0.6	4.2 ± 0.6	4.1 ± 0.6	3.9 ± 0.6	< 0.001
ALT, IU/L	24.5 (14.0, 55.8)	22.0 (14.0, 42.0)	26.0 (14.0, 56.0)	27.0 (15.0, 77.5)	0.216
AST, IU/L	35.0 (22.0, 77.5)	35.0 (19.0, 57.5)	37.0 (24.0, 87.2)	35.5 (22.0, 90.2)	0.373
BUN, mg/dL	19.0 (13.0, 30.0)	17.0 (12.0, 28.0)	18.0 (13.0, 27.0)	24.0 (15.0, 36.0)	< 0.001
Scr, mg/dL	0.9 (0.7, 1.4)	0.9 (0.7, 1.4)	0.9 (0.7, 1.3)	1.0 (0.7, 1.5)	0.182
Myocardial infarct, n (%)	241 (29.4)	84 (30.7)	97 (35.5)	60 (21.9)	0.002
Congestive heart failure, n (%)	374 (45.6)	130 (47.4)	117 (42.9)	127 (46.4)	0.531
Peripheral vascular disease, n (%)	146 (17.8)	44 (16.1)	60 (22)	42 (15.3)	0.083
Cerebrovascular disease, n (%)	115 (14.0)	47 (17.2)	33 (12.1)	35 (12.8)	0.18
Mild liver disease, n (%)	67 (8.2)	20 (7.3)	11 (4)	36 (13.1)	< 0.001
Severe liver disease, n (%)	34 (4.1)	3 (1.1)	5 (1.8)	26 (9.5)	< 0.001
Diabetes, n (%)	304 (37.0)	122 (44.5)	101 (37)	81 (29.6)	0.001
Renal disease, n (%)	220 (26.8)	73 (26.6)	75 (27.5)	72 (26.3)	0.949
Malignant cancer, n (%)	105 (12.8)	26 (9.5)	20 (7.3)	59 (21.5)	< 0.001
SAPSII	41.8 ± 13.4	41.4 ± 13.2	39.7 ± 12.1	44.3 ± 14.5	< 0.001
OASIS	35.5 ± 8.8	34.7 ± 8.8	34.2 ± 7.9	37.5 ± 9.2	< 0.001
SOFA	4.3 ± 2.5	4.2 ± 2.2	4.1 ± 2.2	4.5 ± 2.8	0.347
Mechanical ventilation, n (%)	467 (60.2)	170 (64.9)	158 (61.5)	139 (54.1)	0.037
Length of hospital stay	8.9 (5.8, 15.4)	9.0 (5.9, 14.0)	8.7 (5.6, 15.7)	9.8 (5.9, 16.0)	0.494
Hospital mortality, n (%)	124 (15.1)	25 (9.1)	29 (10.6)	70 (25.5)	< 0.001

Notes: Continuous variables are presented as mean ± SD or median (quartile), while categorical variables are presented as absolute numbers (percentages).
Abbreviations: RCI, red cell index; HR, heart rate; RR, respiratory rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; SpO2, pulse oximetry derived oxygen saturation; RBC, red blood cell; Hb hemoglobin; Lym, Lymphocytes, PLT, platelets; ALT, alanine transaminase; AST, aspartate transferase; BUN, blood urea nitrogen; Scr, serum creatinine; SAPS II, simplified acute physiology score II; OASIS, oxford acute severity of illness score; SOFA, sequential organ failure assessment.

Table 2 Univariate Analysis of Risk Factor Associated with Hospital Mortality in Patients with COPD

Variable	OR (95% CI)	*P*
Gender (Male vs female)	0.64 (0.43–0.94)	0.021
Age, year	1.04 (1.02–1.06)	<0.001
Race		
Non-white	Ref	
Other	3.1 (1.43–6.73)	0.004
White	1.4 (0.67–2.9)	0.369
RCI	1.05 (1.02–1.07)	<0.001
HR	1.03 (1.02–1.05)	<0.001
RR	1.14 (1.08–1.19)	<0.001
SBP	0.98 (0.96–0.99)	0.008
DBP	0.99 (0.98–1.01)	0.552
MBP	0.99 (0.97–1.01)	0.199
Hematocrit	0.97 (0.95–1)	0.098
SpO2	0.86 (0.8–0.93)	<0.001

(*Continued*)

Table 2 (Continued).

Variable	OR (95% CI)	*P*
Anion gap	1.14 (1.09–1.2)	<0.001
Bicarbonate	0.92 (0.89–0.96)	<0.001
Glucose	1 (0.99–1)	0.387
BUN	1.02 (1.01–1.03)	<0.001
Scr	1.28 (1.12–1.48)	<0.001
Sodium	0.98 (0.95–1.02)	0.431
Potassium	0.74 (0.54–1.02)	0.063
Chloride	0.95 (0.93–0.98)	0.002
ALT	1 (1–1)	0.003
AST	1 (1–1)	0.001
Myocardial infarction (Yes vs No)	1.12 (0.74–1.7)	0.578
Congestive heart failure (Yes vs No)	1.55 (1.06–2.28)	0.025
Cerebrovascular disease (Yes vs No)	2.3 (1.44–3.67)	0.001
Peripheral vascular disease (Yes vs No)	1.06 (0.65–1.74)	0.809
Renal disease (Yes vs No)	1.31 (0.86–1.98)	0.205
Liver disease (Yes vs No)	2.48 (1.43–4.28)	0.001
Diabetes (Yes vs No)	0.49 (0.32–0.76)	0.002
Malignant cancer (Yes vs No)	1.49 (0.88–2.51)	0.136
SAPSII	1.06 (1.05–1.08)	<0.001
OASIS	1.11 (1.08–1.13)	<0.001
SOFA	1.18 (1.09–1.27)	<0.001
Mechanical ventilation (Yes vs No)	1.56 (1.04–2.35)	0.032

Abbreviations: OR, odds ratio; CI, confidence interval; Ref, reference; RCI, red cell index; COPD, chronic obstructive pulmonary disease; HR, heart rate; RR, respiratory rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; SpO2, pulse oximetry derived oxygen saturation; ALT, alanine transaminase; AST, aspartate transferase; BUN, blood urea nitrogen; Scr, serum creatinine; SAPS II, simplified acute physiology score II; OASIS, oxford acute severity of illness score; SOFA, sequential organ failure assessment.

Multivariate logistic regression analysis was constructed in five different models, the odds ratios (OR) and 95% confidence interval (95% CI) are shown in Table 3. Crude model, unadjusted; model 1, adjusted for age, sex, and race; model 2, adjusted for model 1 and additionally for HR, RR, SBP, SpO2, cerebrovascular disease, liver disease, congestive heart failure, and diabetes; model 3, adjusted for model 2 and additionally for anion gap, chloride, bicarbonate, BUN, serum creatinine, ALT, and AST; model 4, adjusted for model 3 and additionally for SAPSII, OASIS, SOFA, and mechanical ventilation. When RCI level was used as a continuous variable, in the non-adjusted model, it was significantly associated with hospital mortality (OR=1.05, 95% CI: 1.02–1.07, p<0.001), as well as in the fully adjusted model 4 (OR=1.03, 95% CI: 1.01–1.06, p=0.012). When RCI was turned into

Table 3 Relationship Between Red Cell Index and Hospital Mortality in Different Models

Variable	Crude model		Model 1		Model 2		Model 3		Model 4	
	OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*
RCI continuous	1.05 (1.02–1.07)	<0.001	1.05 (1.02–1.07)	<0.001	1.04 (1.01–1.06)	0.006	1.03 (1.01–1.06)	0.006	1.03 (1.01–1.06)	0.012
RCI tertiles										
RCI<1.18	1(Ref)		1(Ref)		1(Ref)		1(Ref)		1(Ref)	
1.18≤RCI<2.62	1.18 (0.67–2.08)	0.557	1.15 (0.64–2.04)	0.642	1.23 (0.67–2.27)	0.509	1.21 (0.64–2.28)	0.55	1.4 (0.73–2.7)	0.31
RCI≥2.62	3.42 (2.09–5.59)	<0.001	3.37 (2.02–5.6)	<0.001	2.55 (1.45–4.49)	0.001	2.41 (1.35–4.3)	0.003	2.33 (1.27–4.27)	0.006
p for trend		<0.001		<0.001		0.001		0.002		0.005

Notes: Crude model was not adjusted. Model 1 was adjusted for gender+ age+ race. Model 2 was adjusted for model 1+ HR+ RR+ SBP+ SpO2 +cerebrovascular disease+ liver disease+ congestive heart failure+ diabetes. Model 3 was adjusted for model 2+ anion gap + chloride + bicarbonate + BUN+ Scr +ALT+AST. Model 4 was adjusted for model3 + SAPSII+OASIS+ SOFA+ mechanical ventilation.

Abbreviations: OR, odds ratio; CI, confidence interval; Ref, reference; RCI, red cell index; HR, heart rate; RR, respiratory rate; SBP, systolic blood pressure; SpO2, pulse oximetry derived oxygen saturation; ALT, alanine transaminase; AST, aspartate transferase; BUN, blood urea nitrogen;Scr, serum creatinine; SAPS II, simplified acute physiology score II; OASIS, oxford acute severity of illness score; SOFA, sequential organ failure assessment.

a categorical variable, comparison with the lower group, the fully adjusted model 4 OR were 1.4 (95% CI: 0.73–2.7, p=0.31) and 2.33 (95% CI: 1.27–4.27, p=0.006) in the second and third tertiles, respectively.

Subgroup Analyses and Sensitivity Analyses

To evaluate the underlying clinical heterogeneity, we used interaction and stratified analysis. We used subgroups and interactive analyses according to age (<65 and ≥65 years), sofa score (<4 and ≥4), diabetes mellitus (No and Yes), cerebrovascular disease (No and Yes), congestive heart failure (No and Yes), mechanical ventilation (No and Yes) (Figure 2). Effect size of RCI on the hospital mortality in subgroups were stable. No significant interactions were observed in the subgroups (all p for interaction > 0.05).

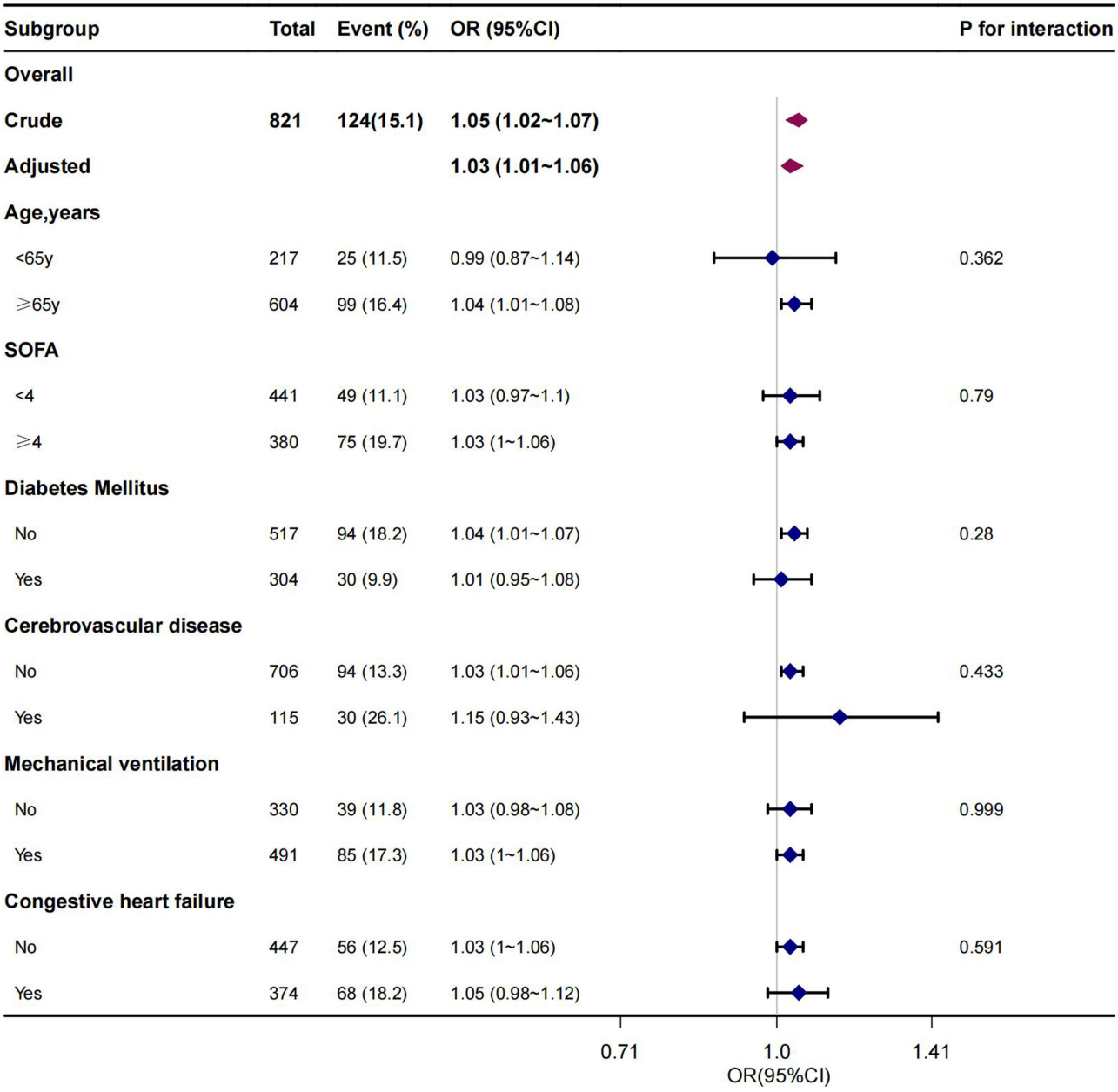

Figure 2 Forest plot of association between red cell index (RCI) and hospital mortality. Crude: unadjusted; Adjusted: adjusted for gender, age, race, HR, RR, SBP, SpO2, cerebrovascular disease, liver disease, congestive heart failure, diabetes, anion gap, chloride, bicarbonate, BUN, Scr, ALT, AST, APSII, OASIS, SOFA, mechanical ventilation. **Abbreviations**: OR, odds ratio; CI, confidence interval; HR, heart rate; RR, respiratory rate; SBP, systolic blood pressure; SpO2, pulse oximetry derived oxygen saturation; BUN, blood urea nitrogen; Scr, serum creatinine; ALT, alanine transaminase; AST, aspartate transferase; SAPS II, simplified acute physiology score II; OASIS, oxford acute severity of illness score; SOFA, sequential organ failure assessment.

Sensitivity analysis was further performed with variable deletion for missing values, and then multivariate analysis was performed with a non-missing population, and the results are in Table S1.

Discussion

For the first time, to our knowledge, this retrospective cohort study indicated that high levels of RCI were positively correlated with hospital mortality in severe COPD patients in the ICU. In fully adjusted model 4, the effect value was 1.03 (95% CI: 1.01–1.06), indicating that the risk of hospital mortality increases by 3% for per unit increase in RCI. When RCI was turned into categorical variable, the result was stable and reliable, while the results were stable in all subgroups without any interaction.

RCI is a relatively recent and complex marker that combines hemoglobin, platelet, lymphocyte, and RBC. Being calculated by trusted formulas, which are more stable and have more accurate prognostic results than a single blood parameter. RCI could provide researchers with a more accurate assessment of disease severity.[7] Hb is an iron-containing metalloprotein that transports oxygen, and red blood cells carry Hb and play an important role in delivering oxygen to tissues.[18] RBC and Hb levels compensate for low lung function and reflect sensitivity to hypoxia.[19] In cases of poor pulmonary function, increased RBC and Hb levels can act as compensatory mechanisms.[20] However, some studies have reported that anemia might be more common in COPD patients.[21,22] and anemia increased mortality in COPD.[23,24] Our current study observed that higher RBC and Hb levels in the higher RCI group. The reason could be due to severe COPD has associated with secondary polycythemia and which contributes to the development of pulmonary heart disease and pulmonary hypertension, linked to poor prognosis.[25,26]

Lymphopenia has been related to poor outcome in acute inflammatory diseases.[27] It has been shown that lymphocyte counts were lower in patients with COPD than healthy controls.[28] Furthermore, lymphocytopenia has been related to all-cause mortality in COPD patients.[29–31] In our study, we identified that lymphocyte count in the higher RCI group is lower in patients with severe COPD. Similar study found an association between a low relatively lymphocyte count and high mortality among elderly patients with COPD[32] An immune response characteristic of lymphocytes is likely to explain the lymphocyte's influence on COPD. Although platelet counts in COPD patients is unclear extensively, thrombocytopenia has been reported in COPD patients and has been associated with poor outcomes and increased mortality.[33] Consistent with these findings, we also found lower platelet counts in the higher RCI group. Since lymphocytes and platelets tend to be little affected by other factors, they are used as benchmarks for measuring the total permeability of a blood cell.

Previously, the RCI index was widely recognized as an effective measure for evaluating lung function and severity of COPD.[6,7] Other study demonstrated that RCI was significantly associated with 3-month mortality in among acute ischemic stroke (AIS) patients treated with recombinant tissue plasminogen activator (r-tPA).[9] This study is the first to explore the connection of RCI and hospital mortality in COPD patients being treated in ICU. RCI, which is based on the complete blood count parameter, is easier to obtain and identify critically ill patients early and thus to reduce the burden of disease and mortality. The data for the study come from large public databases, the sample size is large and the results will be compelling. Additionally, after multiple adjustment of covariates, the result was still stable and higher RCI levels are associated with mortality. Patients with chronic obstructive pulmonary disease (COPD) will have varying degrees of pulmonary dysfunction, especially critically ill patients admitted to the ICU, however, the use of RCI allows for the assessment of the patient's pulmonary functional status and prognosis.

However, our study also has some limitations. Firstly, it is impossible to account for all confounding variables in a retrospective cohort study. Despite attempts to adjust for known confounding factors, there may still be some unmeasured variables impacting the results. Furthermore, since not all variables are tracked in MIMIC-IV, certain indicators such as pulmonary function are missing which may have an impact on our results. Secondly, we excluded patients aged <18 years. Therefore, our findings cannot be generalized to these patients. Thirdly, the ALT, AST, and SOFA data for covariates were missing about 40% of the participants. However, we employed multiple interpolation to address the challenges presented by the missing data. What's more, we utilized multivariate regression analysis after removing the missing values, the obtained results remained robust. Finally, it is important to note that our study did not involve mechanistic studies, and future research must delve deeper into the underlying mechanisms to further elucidate the results.

Conclusion

RCI was positively correlated with hospital mortality. Higher RCI value was associated with higher risk of hospital mortality in COPD patients admitted to the ICU. Nevertheless, it is crucial to conduct rigorously planned, prospective, and multicenter studies to validate our results in the future.

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Disclosure

The authors report no conflicts of interest in this work.

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