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The Association Between Mean Corpuscular Hemoglobin Concentration and Prognosis in Patients with Acute Pulmonary Embolism: A Retrospective Cohort Study

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Abstract

Introduction: Acute pulmonary embolism (APE) is a typical cardiovascular emergency worldwide. Mean hemoglobin concentration (MCHC) is a standard indicator of anemia. Studies on the association between MCHC and APE are scarce. We aimed to investigate the relationship between MCHC and APE.

Methods: Clinical data were extracted from the Medical Information Bank for Intensive Care (MIMIC)-III. Adult (≥18 years) patients with APE admitted for the first time were included in this study. An analysis was conducted to evaluate the association between MCHC and the prognosis of patients by the Cox regression analysis, generalized additives models and Kaplan–Meier survival curves. The primary outcome was 30-day mortality, and the secondary outcomes were 1-year and 3-year mortality.

Results: A total of 813 patients who met the selection criteria were enrolled, of whom 130 (16.0%) died within 30 days of admission. Univariate Cox regression indicated that MCHC was significantly associated with mortality (30-day: HR = 0.74, 95% CI = 0.66–0.82, $P < 0.001$; 1-year: HR = 0.80, 95% CI = 0.74–0.86, $P < 0.001$; 3-year: HR = 0.82, 95% CI = 0.77–0.88, $P < 0.001$). MCHC remains stable after adjusting multiple models. Kaplan-Meier survival curves showed that patients with lower MCHC had a poorer 30-day prognosis.

Conclusions: Lower MCHC is an independent risk factor for increased mortality in patients with APE. As an inexpensive biomarker, MCHC should receive more attention.

Keywords

acute pulmonary embolism, mean corpuscular hemoglobin concentration, hematological parameter, prognosis

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Introduction

Acute pulmonary embolism (APE) has become a common cardiovascular emergency worldwide.[1] The 30-day mortality ranged from 7.7% to 20.9% for APE patients.[2–5] It is a severe disease, and the prognosis is closely related to hemodynamic stability. Hypotension and right ventricular insufficiency are critical factors in short-term mortality in patients with APE.[6] Many biomarkers have been proposed to predict the onset, progression, and short-term mortality of pulmonary embolism.[7] However, studies on the long-term prognosis of patients with APE are also lacking.[7–9] In addition, the biomarkers such as troponin I, troponin T, and brain natriuretic peptide (BNP) were susceptible to the effects of previous physical activity.[10] It is still necessary to find new stable markers for the prognosis of APE.

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Increased vascular resistance due to abnormal pulmonary vasoconstriction in patients with APE is the leading cause of death.[11] Such vasoconstriction abnormalities are thought to be APE-derived factors, such as hypoxia or decreased nitric oxide (NO) levels.[12–14] Reduced NO is an important pathological mechanism in APE, and studies have found that mean hemoglobin concentration (MCHC, hemoglobin to hematocrit ratio) is closely related to NO diffusion.[14,15] We hypothesized that MCHC might be used as an indicator of prognosis in patients with APE. MCHC, a common indicator of anemia, has been shown to correlate with the prognosis of myocardial infarction, congestive heart failure (CHF), acute coronary syndrome, and atherosclerosis severity.[16–19] However, as a common cardiovascular disease, few studies on the association between MCHC and APE. Therefore, we plan to conduct a study to investigate the relationship between MCHC and prognosis in patients with APE.

Methods

Study Design and Data Source

This study used a retrospective cohort study. Clinical data were extracted from the Medical Information Bank for Intensive Care (MIMIC)-III (v 1.4). MIMIC-III covered 53423 adult patients hospitalized at the Beth Israel Deaconess Medical Center in Boston from June 2001 to October 2012.[20] One author Zhishen Ruan gained access to the database by completing the online course and passing the National Institutes of "Protecting Human Research Participants Exam" (certification number 43453324). The Institutional Review Board of Beth Israel Deaconess Medical Center and MIT affiliates approved the database.[21] Our findings were reported following the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.[22]

Inclusion and Exclusion Criteria

Based on SQL language, the clinical data of eligible patients are extracted from the MIMIC-III database. The inclusion criteria: (1) patients diagnosed with APE, which the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes were 41511, 41512, 41519; (2) patients with APE older than 18 years; and (3) Patients with APE who received routine blood tests within 24 h of admission. Indicators include MCHC, red blood cell distribution width (RDW), peripheral white blood cell count (WBC), platelet, creatinine, blood urea nitrogen (BUN), hematocrit, hemoglobin, serum sodium, and serum potassium. The exclusion criteria: (1) APE patients with a hospital stay $\leq$ 24 h; and (2) patients with diseases involving altered MCHC levels (anemia, ICD-9-CM codes were 28xx, 28521, 28522, 28529).

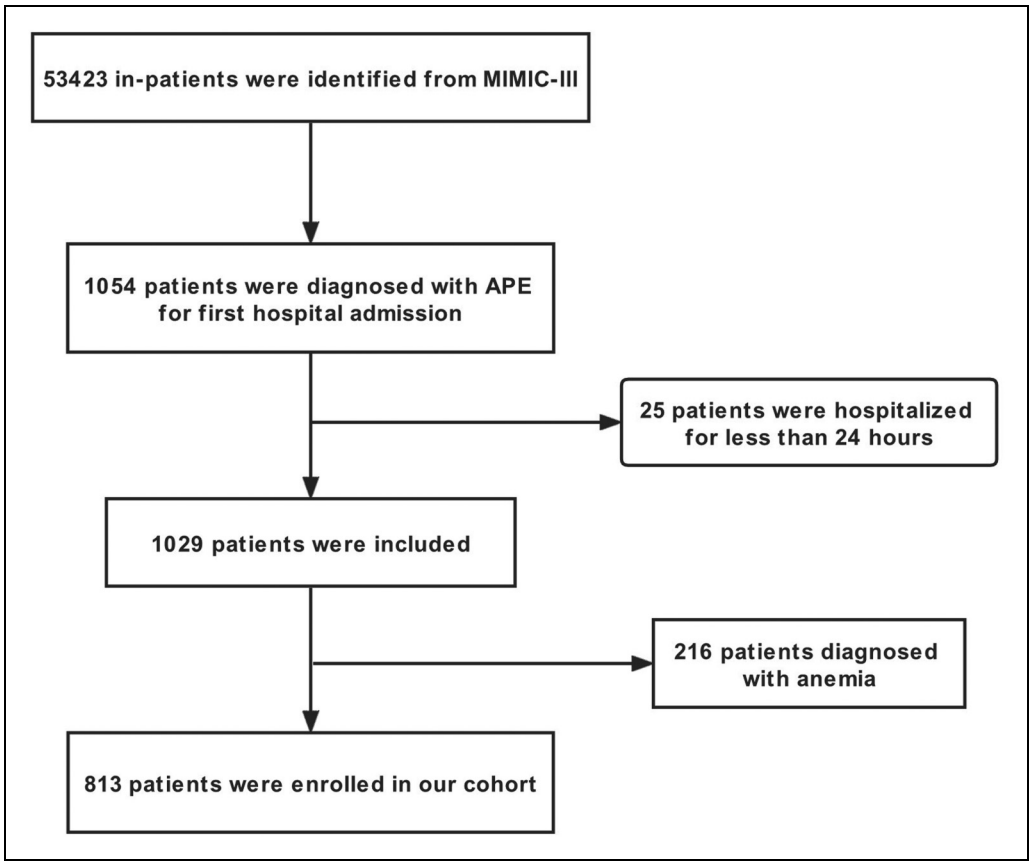

Figure 1. Flow chart of the study participants. Abbreviations: APE, acute pulmonary embolism.

Demographic Characteristics

We extracted the following outcome variables: age, gender, ethnicity, vital signs [heart rate, respiratory rate, systolic blood pressure (SBP), percutaneous oxygen saturation (SpO_2)], scores [Acute Physiology Score (APS) III, Oxford acute severity of illness score (OASIS), quick sequential organ failure assessment score (qSOFA), simplified acute physiology II (SAPSII)], comorbidities [diabetes, hypertension, chronic obstructive pulmonary disease (COPD), coronary artery disease (CAD), CHF, renal failure, liver disease, malignancy, obesity, weight loss), laboratory parameters(MCHC initial, MCHC max, MCHC min, hematocrit, hemoglobin, RDW, WBC, platelet, creatinine, BUN, sodium, potassium), vasopressor use, and mechanical ventilation.

For MCHC initial, MCHC max, and MCHC min, the initial level represented the initial level measurement after admission, the max level represented the maximum level measured during hospitalization, and the level min represented the minimum level measured during hospitalization.[23] Given that all variables were missing by less than 0.5%, we directly ignored these data in the further study.

Outcome Variables

The primary outcome was 30-day mortality after admission, and secondary outcomes were 1-year mortality and 3-year mortality. Because the MIMIC III database was linked to the social

Table 1. Comparison of Baseline Characteristics Between the Survivors and Non-Survivors.

Variables	Survivors (n = 683)	Non-survivors (n = 130)	*p*
Age, (years)	60.7 ± 16.9	70.3 ± 14.8	< 0.001
Female, n (%)	291 (42.6)	71 (54.6)	0.015
No-white, n (%)	160 (23.4)	42 (32.3)	0.042
Vital signs			
Heart rate, (beats/min)	90.0 ± 19.6	96.4 ± 23.2	< 0.001
SBP, (mm Hg)	124.6 ± 22.1	117.2 ± 23.6	< 0.001
Respiratory Rate, (beats/min)	19.6 ± 5.9	21.6 ± 6.5	< 0.001
SpO_2, (%)	97.0 ± 3.4	96.3 ± 6.1	0.055
Scores			
APSIII	40.6 ± 17.7	60.9 ± 29.0	< 0.001
OASIS	30.6 ± 8.5	38.3 ± 9.4	< 0.001
qSOFA	1.7 ± 0.7	2.0 ± 0.7	< 0.001
SAPSII	31.8 ± 12.4	49.4 ± 17.7	< 0.001
Comorbidities			
Hypertension n (%)	339 (49.6)	48 (36.9)	0.01
Diabetes, n (%)	132 (19.3)	25 (19.2)	1
COPD, n (%)	70 (10.2)	21 (16.2)	0.071
CAD, n (%)	95 (13.9)	11 (8.5)	0.121
CHF, n (%)	95 (13.9)	22 (16.9)	0.447
Renal failure, n (%)	41 (6.0)	14 (10.8)	0.073
Liver disease, n (%)	32 (4.7)	7 (5.4)	0.906
Malignancy, n (%)	105 (15.4)	51 (39.2)	< 0.001
obesity, n (%)	49 (7.2)	6 (4.6)	0.382
Weight loss, n (%)	33 (4.8)	9 (6.9)	0.441
Laboratory parameters			
MCHC initial, (g/dL)	33.8 ± 1.5	33.0 ± 1.6	< 0.001
MCHC max, (g/dL)	35.0 ± 1.4	34.3 ± 1.7	< 0.001
MCHC min, (g/dL)	32.5 ± 1.4	31.8 ± 1.4	< 0.001
Hematocrit, (%)	35.1 ± 6.5	33.8 ± 6.4	0.004
Hemoglobin (g/dL)	11.8 ± 2.3	11.2 ± 2.1	0.039
RDW, (%)	14.9 ± 2.1	15.7 ± 2.2	< 0.001
WBC, (10^{12}/L)	12.8 ± 13.4	15.9 ± 18.3	0.027
Platelet, (10^9/L)	253.3 ± 140.7	253.7 ± 158.5	0.975
Creatinine, (mg/dL)	1.1 ± 0.8	1.3 ± 1.0	0.002
BUN, (mg/dL)	20.8 ± 14.8	30.4 ± 20.8	< 0.001
Serum sodium, (mmol/L)	138.0 ± 4.5	137.5 ± 5.3	0.239
Serum potassium, (mmol/L)	4.2 ± 0.7	4.4 ± 0.8	0.003
Vasopressor use, n (%)	171 (25)	68 (52.3)	< 0.001
Mechanical ventilation, n (%)	218 (31.9)	64 (49.2)	< 0.001

Abbreviations: SBP, systolic blood pressure; SpO2, pulse oxygen saturation; APS III, Acute Physiology Score III; OASIS, Oxford acute severity of illness score; qSOFA, quick sequential organ failure assessment score; SAPSII, simplified acute physiology II; COPD, chronic obstructive pulmonary disease; CAD, Coronary artery disease; CHF, Congestive heart failure; MCHC, mean corpuscular hemoglobin concentration; RDW, red cell distribution width BUN, blood urea nitrogen; WBC, white blood cell.

security database, all patients were followed up for three years and were not missed. Since a patient might be admitted multiple times, only the first admission was selected.

Statistical Analysis

Data were described as mean ± standard deviation, median (25th-75th percentile), or number (percentage), depending on the type and distribution of the variable. Kruskal Wallis and Chi-square (or Fisher's exact) tests compared the categorical covariates. Univariate Cox regression was used to analyze prognostic factors of mortality (30-day, 1-year, and 3-year mortality) for APE. Three multivariate Cox regression models were applied to adjust for potential confounders. Model 1 adjusted for age, sex, ethnicity, and vital signs. Model 2 was adjusted for age, gender, ethnicity, vital signs, scores, vasopressor use, and mechanical ventilation. Model 3 adjusted for comorbidities based on model 2. To further analyze the relationship between MCHC and prognosis, we analyzed the effects of MCHC initial, MCHC max, and MCHC min in generalized additives models. Kaplan-Meier survival curves were used to compare the short and long-term mortality of MCHC with different quartiles.

The analyses were performed with the statistical software packages R v3.3.2 (http://www.R-project.org, The R Foundation) and Free Statistics software versions (1.4).

Results

Characteristics of Patients

The flow chart is presented in Figure 1. A total of 813 APE patients was included in our study. 130 (16.0%) patients died within 30 days of admission, and 683 (84.6%) were survivors in the cohort. The baseline information for APE patients is briefly summarized in Table 1, including age, gender, ethnicity, vital signs, scores, comorbidities, and laboratory parameters. In terms of demographics, non-survivors are more likely to be female and older. Non-survivors had higher heart rates, respiratory rates, and criticality scores compared to survivors. In addition, non-survivors had much lower MCHC levels (initial: 33.0 vs 33.8, $P < 0.050$; max: 34.3 vs 35, $P = 0.001$; min: 31.8 vs32.5, $P < 0.001$) and SBP compared to survivors.

Factors Associated with Mortality

The results of univariate Cox regression analysis were shown in Table 2. Initial MCHC was obviously associated with 30-day (HR = 0.74, 95% CI = 0.66–0.82, $P < 0.001$), 1-year mortality (HR = 0.80, 95% CI = 0.74–0.86, $P < 0.001$), and 3-year mortality (HR =0.82, 95% CI = 0.77–0.88, $P < 0.001$), MCHC min and MCHC max also has similar results. In addition, age, sex, vital signs, scores, certain comorbidities (COPD, renal failure, malignancy), and laboratory parameters (hematocrit,

Table 2. Univariate Cox Regression Analyses for Prognosis in APE Patients.

	30-day mortality		1-year mortality		3-year mortality	
Variable	HR (95%CI)	*P*	HR (95%CI)	*P*	HR (95%CI)	*P*
MCHC initial	0.74 (0.66–0.82)	< 0.001	0.80 (0.74–0.86)	< 0.001	0.82 (0.77–0.88)	< 0.001
MCHC max	0.74 (0.66–0.83)	< 0.001	0.81 (0.74–0.88)	< 0.001	0.83 (0.77–0.89)	< 0.001
MCHC min	0.74 (0.66–0.83)	< 0.001	0.81 (0.74–0.88)	< 0.001	0.81 (0.75–0.88)	< 0.001
Male	0.64 (0.45–0.90)	0.01	0.72 (0.56–0.91)	0.007	0.76 (0.62–0.95)	0.016
Age	1.04 (1.02–1.05)	< 0.001	1.03 (1.02–1.04)	< 0.001	1.03 (1.02–1.04)	< 0.001
Heart rate	1.01 (1.01–1.02)	< 0.001	1.01 (1.00–1.02)	0.003	1.00 (1.00–1.01)	0.163
SBP	0.99 (0.98–0.99)	< 0.001	0.99(0.99–1.00)	0.002	0.99 (0.99–1.00)	0.001
Respiratory rate	1.05 (1.02–1.08)	< 0.001	1.03 (1.01–1.05)	0.007	1.02 (1.00–1.04)	0.047
SpO_2	0.96 (0.93–1.00)	0.03	0.96 (0.94–0.99)	0.004	0.97 (0.95–1.00)	0.023
APSIII	1.03 (1.03–1.04)	< 0.001	1.03 (1.02–1.03)	< 0.001	1.02 (1.02–1.03)	< 0.001
OASIS	1.10 (1.07–1.12)	< 0.001	1.06 (1.05–1.08)	< 0.001	1.05 (1.04–1.07)	< 0.001
qSOFA	1.84 (1.42–2.39)	< 0.001	1.43 (1.19–1.71)	< 0.001	1.28 (1.09–1.50)	0.002
SAPSII	1.06 (1.05–1.07)	< 0.001	1.05 (1.04–1.06)	< 0.001	1.05 (1.04–1.05)	< 0.001
COPD	1.61 (1.01–2.57)	0.046	1.29 (0.90–1.84)	0.172	1.75 (1.30–2.34)	< 0.001
Renal failure:	1.79 (1.03–3.12)	0.039	1.82 (1.22–2.72)	0.003	1.85 (1.29–2.65)	< 0.001
Malignancy	3.00 (2.11–4.27)	< 0.001	4.30 (3.35–5.51)	< 0.001	3.93 (3.13–4.95)	< 0.001
Obesity:	0.63 (0.28–1.42)	0.265	0.50 (0.27–0.95)	0.033	0.46 (0.26–0.82)	0.009
Hematocrit	0.97 (0.95–1.00)	0.042	0.96 (0.94–0.98)	< 0.001	0.96 (0.94–0.97)	< 0.001
Hemoglobin	0.90 (0.83–0.97)	0.004	0.87 (0.83–0.92)	< 0.001	0.87 (0.83–0.91)	< 0.001
RDW	1.12 (1.06–1.19)	< 0.001	1.15 (1.11–1.20)	< 0.001	1.15 (1.11–1.19)	< 0.001
Creatinine	1.24 (1.09–1.41)	< 0.001	1.13 (1.01–1.26)	0.038	1.18 (1.08–1.29)	< 0.001
BUN	1.02 (1.01–1.03)	< 0.001	1.02 (1.01–1.02)	< 0.001	1.02 (1.01–1.02)	< 0.001

Abbreviations: SBP, systolic blood pressure; SpO2, pulse oxygen saturation; APS III, Acute Physiology Score III; OASIS, Oxford acute severity of illness score; qSOFA, quick sequential organ failure assessment score; SAPSII, simplified acute physiology II; COPD, chronic obstructive pulmonary disease; RDW, red cell distribution width BUN, blood urea nitrogen; HR, hazard ratio; CI, confidence interval.
Notes: For 1-year and 3-year mortality, only patients (581/813) in the Care Vue system with at least 3 years of follow-up were analyzed.

Table 3. Association Between MCHC With Prognosis of APE Patients.

Outcome		HR	95% CI	P
30-day mortality				
MCHC initial	Model 1	0.77	0.68~0.87	<0.001
	Model 2	0.79	0.70–0.89	<0.001
	Model 3	0.79	0.70–0.90	0.001
MCHC max	Model 1	0.78	0.69–0.89	<0.001
	Model 2	0.72	0.63–0.82	<0.001
	Model 3	0.69	0.61–0.80	<0.001
MCHC min	Model 1	0.76	0.67–0.87	<0.001
	Model 2	0.82	0.71–0.94	0.004
	Model 3	0.82	0.71–0.95	0.01
1-year mortality				
MCHC initial	Model 1	0.84	0.77–0.91	<0.001
	Model 2	0.85	0.78–0.92	<0.001
	Model 3	0.84	0.77–0.92	<0.001
MCHC max	Model 1	0.86	0.79–0.95	0.002
	Model 2	0.82	0.74–0.90	<0.001
	Model 3	0.78	0.71–0.86	<0.001
MCHC min	Model 1	0.83	0.76–0.92	<0.001
	Model 2	0.87	0.79–0.97	0.008
	Model 3	0.87	0.79–0.97	0.011
3-year mortality				
MCHC initial	Model 1	0.85	0.79–0.92	<0.001
	Model 2	0.86	0.80–0.93	<0.001
	Model 3	0.86	0.79–0.93	<0.001
MCHC max	Model 1	0.88	0.81–0.96	<0.001
	Model 2	0.84	0.77–0.91	<0.001
	Model 3	0.81	0.74–0.88	<0.001
MCHC min	Model 1	0.82	0.76–0.90	<0.001
	Model 2	0.87	0.79–0.94	0.001
	Model 3	0.86	0.78–0.95	0.002

Model 1 adjusted for age, sex, ethnicity, and vital signs. Model 2 was adjusted for age, gender, ethnicity, vital signs, scores, vasopressor use, and mechanical ventilation use. Model 3 adjusted for comorbidities based on model 2. HR, hazard ratio; CI, confidence interval.

hemoglobin, RDW, creatinine, and BUN) in Table 2, were associated with short-term and long-term mortality.

The results of the multivariate Cox regression based on three generalized additives models are summarized in Table 3. Model 1 adjusted for age, sex, ethnicity, and vital signs. Model 2 was adjusted for age, gender, ethnicity, vital signs, scores, vasopressor use, and mechanical ventilation. Model 3 adjusted for comorbidities based on model 2. MCHC initial (Model 1: HR = 0.77, 95% CI = 0.68–0.87, $P < 0.001$; Model 2: HR = 0.79, 95% CI = 0.70–0.89, $P < 0.001$; Model 3: HR = 0.79, 95% CI = 0.70–0.90, $P = 0.001$), MCHC max (Model 1: HR = 0.78, 95% CI = 0.69-0.89, $P < 0.001$; Model 2: HR = 0.72, 95% CI = 0.63-0.82, $P < 0.001$; Model 3: HR = 0.69, 95% CI = 0.61-0.80, $P < 0.001$), and MCHC min (Model 1: HR = 0.76, 95% CI = 0.67-0.87, $P < 0.001$; Model 2: HR = 0.82, 95% CI = 0.71-0.94, $P = 0.004$; Model 3: HR = 0.82, 95% CI = 0.71-0.95, $P = 0.01$) were both positively associated with 30-mortality for all models. Moreover, MCHC initial, MCHC max, and MCHC min were all associated with 1-year mortality and 3-year mortality.

Figure 2 presented Kaplan-Meier survival curves for patients in different MCHC quartiles. For MCHC, the 30-day mortality of the first and second quartiles was higher than that of the third and fourth quartiles. In conclusion, MCHC is an important indicator of APE patients' short-term and long-term prognosis.

Discussion

For the first time, to our knowledge, we found that decreased MCHC was independently associated with a poorer prognosis, both for 30-day mortality, 1-year and 3-year mortality from APE. Three models were used to increase the credibility of the results. We verified the relationship between prognosis and the maximum and minimum levels of MCHC during admission. Based on literature reports, we divided whether MCHC was greater than 33 g/dL into two groups.[24] The results showed that patients with MCHC < 33g/dL had significantly higher 30-day, 1-year, and 3-year mortality rates, grouped by initial, maximum and minimum values (Table S2). It suggests that clinicians focus on APE patients with MCHC ≤ 33 mg/dL on admission. In terms of simplicity and ease of use, MCHC initial was superior to MCHC max and MCHC min in predicting the prognosis of patients with APE. Even if APE does not result in in-hospital death of the patients, severe long-term complications may occur.[14] Patients with MCHC initial ≤ 33 mg/dL had a 30-day mortality rate of 25.0% and a 1-year mortality rate of 43.8%, which helps to assess the long-term prognosis of APE patients after hospital discharge.

MCHC is closely associated with the prognosis of several cardiovascular diseases. Similar to our results, Huang found lower MCHC was an independent risk factor for 1-year term mortality (HR = 0.84, 95% CI = 0.80-0.89, $P < 0.001$) in acute myocardial infarction.[16] Tseng reported lower MCHC as an independent risk factor for acute stroke.[25] The above studies proved the role of MCHC in ischemic disease. However, Low MCHC is also associated with the prognosis of acute and chronic heart failure.[24,26] Subsequently, Cesar Simbaqueba discovered that MCHC is associated with long-term adverse events of right and left ventricular diastolic dysfunction, even independent of RDW and hemoglobin.[27] In contrast, Tomasz Urbanowicz and Serhat Karaman found that high MCHC had a similar role in predicting the severity of carotid artery disease and acute coronary syndromes.[18,19] It suggested that the prognosis of MCHC for cardiovascular disease is mixed.

Compared with neutrophil-lymphocyte (NLR) and platelet-lymphocyte (PLR), MCHC (hemoglobin-hematocrit) is directly available from routine blood results without calculation. High hematocrit was associated with a 1.5-fold risk of cardiac arterial thrombosis.[28] Regarding pulmonary embolism and hemoglobin, studies have had mixed results. In a cohort study, Jiménez found low hemoglobin to be a risk factor for 90-day all-cause mortality.[29] On the contrary, another study confirmed a positive association between hemoglobin and the prognosis of APE, excluding patients with cancer, acute illness hospitalization, and recent surgery, which may have contributed to the heterogeneity of the results.[30] Consistent with our study, Brett Slajus found elevated RDW in deceased patients while decreased hemoglobin and hematocrit in deceased patients.[31] Changes in hemoglobin

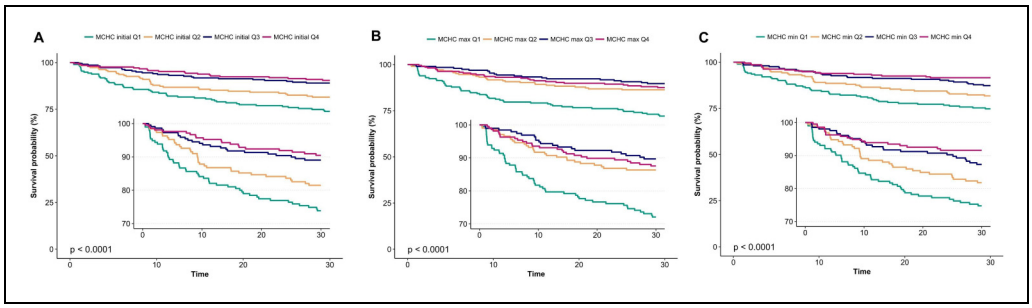

Figure 2. Kaplan-Meier curves of the MCHC for predicting 30-day, 1-year, and 3-year mortality with APE. Low MCHC was significantly associated with higher mortality than high MCHC ($P < 0.001$).

and hematocrit were in the same direction and were ineffective in 30-day mortality (Table S1). MCHC, in contrast, had a significant role in 30-day mortality in patients with APE, indicating that MCHC is a stable predictor.

The mechanism of MCHC and prognosis of pulmonary embolism are unclear. We hypothesize that iron status and NO may play a partial role. MCHC reflects the amount of hemoglobin incorporated into red blood cells and is a reliable indicator of iron loading, with a sensitivity of 96.1% in detecting iron deficiency in red blood cells.[32] Various physiological functions, such as oxygen transport and oxygen metabolism, are associated with iron loading. In addition, NO also plays a vital role in pulmonary embolism (PE). Most of the increase in pulmonary vascular resistance (PVR) during PE is not from obstructing clots but from vasoconstriction.[11] When APE occurs, the systolic pressure in the right ventricle increases significantly, creating turbulence in the tricuspid and pulmonary valves immediately adjacent to the pulmonary vascular system.[14] Ultimately, hemolysis due to turbulence decreases NO utilization by pulmonary vascular smooth muscle cells, increasing PVR and affecting the prognosis of patients with APE.[14,33] Low MCHC increases NO clearance by erythrocytes and affects the prognosis of patients with APE.[15] Inhaled NO may be a promising direction for the treatment of APE.[33]

Our study also has some limitations. First, ICD-9-CM codes to identify APE or other comorbidities may be subject to input errors. Additionally, our study was limited by a retrospective study design and may suffer from selection bias and missing data, but the missing values in our data were less than 0.5%. Due to the limitations of retrospective studies, we could not obtain information about the treatment measures, causes of morbidity, and causes of death in patients with APE. We studied the effect of MCHC on all-cause mortality in all APE patients. Finally, some indicators of APE severity (troponin I, N-terminal pro-BNP, and echocardiographic results) were not available. However, we collected as many variables as possible and used multiple models to demonstrate the stability of the results. Further prospective studies are needed to confirm our findings.

Conclusion

We found that hematological parameters can provide prognostic information in patients with APE. MCHC is an independent predictor of APE patients' short-term and long-term prognosis.

Ethics Approval and Consent to Participate

Ethical approval to report this series of cases was obtained from the MIT Computational Physiology Laboratory.

Authors' Contributions

Zhisen Ruan participated in the study design, analyzed the results, and edited the manuscript. Dan Li for data mining and cleaning. Xianhai Chen and Zhanjun Qiu participated in the research design and editor of the manuscript. Yuanlong Hu directed the study and helped design it.

Consent for Publication

Not applicable.

Availability of Data and Materials

Data in the article can be obtained from the MIMIC-III database (https://mimic.physionet.org/).

Competing Interests

The authors declare that they have no competing interests.

Declaration of Conflicting Interests

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Trial Registration

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