

# The impact of C-reactive protein-to-albumin ratio on mortality in patients with acute kidney injury requiring continuous renal replacement therapy : A multicenter retrospective study

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## Introduction

The C-reactive protein-to-albumin ratio (CAR) is a prognostic marker in various diseases that represents patients' inflammation and nutritional status. Here, we aimed to investigate the prognostic value of CAR in critically ill patients with severe acute kidney injury (AKI) requiring continuous renal replacement therapy (CRRT).

## Methods and Materials

We retrospectively collected data from 8 tertiary hospitals in Korea between 2006 and 2021. Patients were divided into quartiles according to CAR levels at the time of CRRT initiation. Cox regression analyses were performed to investigate the impacts of CAR on the in-hospital mortality.

The mortality prediction performance of CAR was evaluated using area under the curves (AUC), net reclassification improvement (NRI), and integrated discrimination improvement (IDI).

## Results

**Table 1. Baseline characteristics**

variables	Quartile 1 (n=999)	Quartile 2 (n=999)	Quartile 3 (n=1000)	Quartile 4 (n=998)	P
CAR	0.39 (0.13-0.74)	2.17 (1.63-2.76)	5.32 (4.42-6.40)	11.06 (9.28-13.39)	<0.001
Age, years	65.2 ± 15.4	66.2 ± 15.1	66.9 ± 14.8	67.4 ± 14.5	0.007
Sex, male, n(%)	583 (58.4)	604 (60.5)	615 (61.5)	627 (62.8)	0.216
ICU admission body weight, kg	61.6 ± 15.0	61.2 ± 14.0	60.9 ± 13.0	62.1 ± 12.9	0.218
ICU admission BMI, kg/m <sup>2</sup>	23.3 ± 4.6	23.4 ± 7.0	23.0 ± 4.6	23.3 ± 4.3	0.432
CCI	3.4 ± 2.6	3.6 ± 2.8	3.6 ± 2.8	3.5 ± 2.7	0.379
Cause of AKI, n (%)					<0.001
Septic	375 (37.5)	525 (52.6)	607 (60.7)	711 (71.2)	
Non-septic	624 (62.5)	473 (47.4)	393 (39.3)	287 (28.8)	
Comorbidities, n (%)					
Hypertension	416 (41.6)	383 (38.4)	411 (41.1)	368 (36.9)	0.094
Diabetes	282 (28.2)	264 (26.5)	253 (25.3)	248 (24.9)	0.476
Congestive heart failure	218 (21.8)	219 (21.9)	149 (14.9)	119 (11.9)	<0.001
Chronic liver disease	119 (11.9)	111 (11.1)	102 (10.2)	98 (9.8)	0.426
Chronic obstructive pulmonary disease	53 (5.3)	58 (5.8)	54 (5.4)	78 (7.8)	0.065
Leukemia	8 (1.0)	25 (3.1)	38 (4.8)	81 (9.9)	<0.001
Metastatic cancer	36 (3.6)	60 (6.0)	83 (8.3)	71 (7.1)	<0.001
SOFA score	11.2 ± 3.4	12.1 ± 3.3	12.2 ± 3.3	12.8 ± 3.5	<0.001
APACHE II score	26.5 ± 4.4	26.6 ± 7.6	27.9 ± 7.8	29.2 ± 7.7	<0.001
Laboratory findings at CRRT initiation					
WBC count, ×10 <sup>3</sup> /μL	14.4 ± 17.1	16.0 ± 18.6	16.4 ± 18.4	15.0 ± 19.8	0.066
Platelet count, ×10 <sup>3</sup> /μL	126.2 ± 88.6	117.3 ± 94.2	115.7 ± 105.9	100.7 ± 96.1	<0.001
Hemoglobin, g/dL	10.0 ± 2.7	9.6 ± 2.3	9.6 ± 2.1	9.5 ± 2.2	<0.001
Potassium, mEq/L	6.2 ± 2.8	5.9 ± 2.7	5.6 ± 2.4	5.8 ± 2.5	0.002
BUN, mg/dL	50.9 ± 35.9	55.6 ± 33.2	57.5 ± 32.5	57.6 ± 31.1	<0.001
Creatinine, mg/dL	3.3 ± 3.0	3.1 ± 2.4	3.1 ± 2.1	3.1 ± 2.1	0.080
Calcium, mg/dL	8.2 ± 1.3	8.0 ± 2.7	7.8 ± 1.1	7.6 ± 3.3	<0.001
Albumin, g/dL	3.1 ± 0.7	2.8 ± 0.6	2.7 ± 0.5	2.4 ± 0.5	<0.001
CRP, mg/dL	1.4 ± 1.1	6.3 ± 2.2	14.4 ± 4.1	27.6 ± 7.7	<0.001
Lactate (n = 2786)	7.9 ± 6.4	7.0 ± 5.6	6.3 ± 5.3	7.2 ± 5.6	<0.001

Abbreviations: CAR, C-reactive protein-to-albumin ratio; ICU, intensive care unit; BMI, body mass index; CCI, Charlson Comorbidity Index; AKI, acute kidney injury; SOFA, sequential organ failure assessment; APACHE II, Acute Physiology and Chronic Health Evaluation II; CRRT, continuous renal replacement therapy; WBC, white blood cell; BUN, blood urea nitrogen; CRP, C-reactive protein.

**Table 2. Cox regression analyses for in-hospital mortality in CAR quartile groups**

	Model 1		Model 2		Model 3		Model 4	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Quartile 1	Reference		Reference		Reference		Reference	
Quartile 2	1.08 (0.96-1.20)	0.203	1.07 (0.96-1.20)	0.239	1.07 (0.95-1.19)	0.257	1.11 (0.98-1.26)	0.098
Quartile 3	1.19 (1.07-1.33)	0.002	1.18 (1.06-1.32)	0.003	1.20 (1.07-1.34)	0.001	1.15 (1.02-1.30)	0.023
Quartile 4	1.43 (1.23-1.60)	<0.001	1.41 (1.27-1.58)	<0.001	1.40 (1.26-1.57)	<0.001	1.33 (1.18-1.50)	<0.001

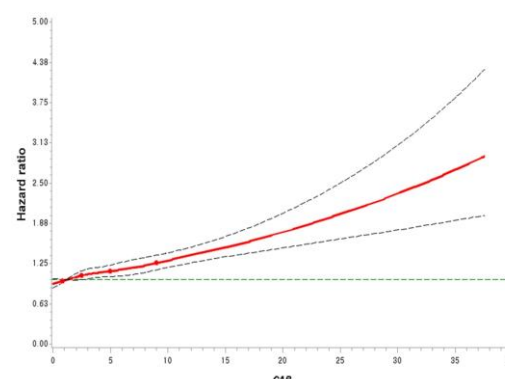
Model 1: unadjusted.  
Model 2: adjusted for age and sex.  
Model 3: adjusted for age, sex, hypertension, and CCI.  
Model 4: adjusted for age, sex, hypertension, CCI, APACHE II score, and mechanical ventilator use.

**Table 3. Comparison of the AUC and predictive power of prognosis for in-hospital mortality**

Variables	AUC (95% CI)	P	NRI (95% CI)	P	IDI (95% CI)	P
CAR	0.580 (0.564-0.595)	Reference				
CRP	0.555 (0.540-0.571)	<0.001				
APACHE II	0.665 (0.646-0.684)	Reference	Reference		Reference	
APACHE II + CAR	0.674 (0.656-0.693)	0.016	0.151 (0.084-0.223)	<0.001	0.007 (0.004-0.010)	<0.001
SOFA	0.669 (0.650-0.687)	Reference	Reference		Reference	
SOFA + CAR	0.677 (0.658-0.695)	0.004	0.134 (0.065-0.204)	<0.001	0.007 (0.004-0.010)	<0.001
APACHE II + SOFA	0.697 (0.679-0.715)	Reference	Reference		Reference	
APACHE II + SOFA + CAR	0.702 (0.683-0.720)	0.036	0.130 (0.060-0.200)	<0.001	0.005 (0.003-0.007)	<0.001

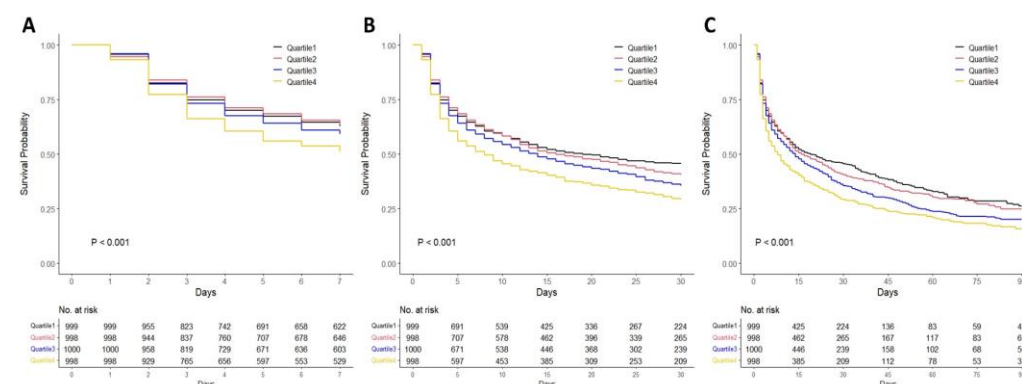
Abbreviations: AUC, area under the curve; CI, confidence interval; NRI, net reclassification improvement; IDI, integrated discrimination improvement; CAR, C-reactive protein-to-albumin ratio; CRP, C-reactive protein; APACHE II, acute physiology and chronic health evaluation II; SOFA, sequential organ failure assessment.

**Figure 1. Relationship between the CAR and in-hospital mortality hazard ratio according to the restricted cubic spline regression model.**



The reference value is the upper limit of quartile 1 (1.57). The red line indicates the estimated hazard ratio; the dashed green line indicates the reference line of null hypothesis that the hazard ratio is 1; the dashed black lines indicate the upper and lower 95% confidence limits.

**Figure 2. Kaplan-Meier curves for in-hospital mortality according to CAR quartiles.**



The (A) 7-day mortality, (B) 30-day mortality, (C) 90-day mortality are significantly different according to CAR quartiles.

## Conclusions

In conclusion, among critically ill patients requiring CRRT, those with a high CAR had an increased in-hospital mortality rate. CAR enhanced the predictive performance when combined with the conventional ICU severity scoring system, such as APACHE II and SOFA scores. Overall, CAR can be a complementary predictor of mortality in critically ill patients with severe AKI.



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