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ORIGINAL ARTICLE

The 30-day mortality predictor role of c-reactive protein/albumin ratio in critically ill COPD patients.

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ABSTRACT

INTRODUCTION: Chronic Obstructive Pulmonary Disease (COPD) is a progressive disease that develops due to inflammation in the airways. The aim of this study is to demonstrate the effectiveness of c-reactive protein/albumin ratio (CAR) as a 30-day mortality indicator in COPD patients admitted to ICU.

MATERIAL AND METHODS: A total of 235 COPD patients with available data between January 2018 and December 2018 were included in this retrospective cohort study. Demographics, APACHE II, Charlson comorbidity index (CCI), SOFA score, CAR and outcomes were evaluated.

RESULTS: 87 (37%) of the cases were female and 148 (63%) were male. Their ages ranged from 26 to 95 years, with an average of 70.9± 11.4. The non-survivors had significantly higher APACHE II, CCI, SOFA score, procalcitonin, creatinine, mechanical ventilation (MV) time, WBC, CRP and CAR compared to the survivors ($p<0.05$). Albumin and prealbumin were significantly lower ($p<0.05$) in non-survivors. In the univariate model; age, sepsis, inotropic support, APACHE II score, CCI, SOFA, procalcitonin, creatinine, MV time, WBC, CRP, albumin, prealbumin and CAR were observed to be significantly effective ($p<0.05$) in predicting 30-day mortality. In the multivariate reduced model; inotropic support, SOFA, WBC and prealbumin value exhibited significant independent ($p<0.05$) effectiveness in predicting 30-day mortality. Albumin, CRP, CAR, APACHE II, SOFA and CCI value were observed to be significant in predicting mortality ($p=0.000$).

CONCLUSIONS: In the study, the predictive power of APACHE II score, CCI, SOFA score, albumin and prealbumin values alone was found to be significantly higher than that of the CAR.

KEY WORDS: C-reactive protein, albumin, chronic obstructive pulmonary disease, mortality.

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a progressive disease that develops due to inflammation in the airways. It progresses with progressive contraction of the airways and irreversible enlargements and destruction of the alveoli. The patient experiences increased shortness of breath and sputum during periods defined as “exacerbation”, where the symptoms of the disease are worsened. During this period, leukocyte and other infection parameters also increase. In COPD patients, comorbidities such as cardiovascular disease, malignancy and osteoporosis increase mortality. A published review showed a significant correlation between the Deyo-Charlson Index scores and mortality in COPD patients, revealing that individuals with score of five or more (at least four comorbidities) were five times more likely to die in the hospital than those without comorbidity [1]. The presence of diabetes mellitus has also been shown to increase exacerbations and mortality in COPD patients, similar to infection and other comorbidities [2].

Scoring systems are used to assess mortality in critically ill patients. Today, mortality expectation is assessed using different scoring systems such as APACHE II, Sepsis Related Organ Failure Assessment (SOFA) and Charlson Comorbidity Index (CCI). However, these scoring systems do not directly reflect the patient's malnutrition and inflammation status [3,4].

Poor prognosis or mortality indicators bear great importance in intensive care unit (ICU) patients. High c-reactive protein (CRP), an indicator of inflammation, and low albumin, a negative acute phase reactant indicating malnutrition, are important laboratory parameters associated with poor prognosis in ICU patients [5]. CRP/albumin ratio (CAR) has been used as an indicator of prognosis and mortality in studies conducted with different patient groups such as cancer and gastrointestinal diseases [6,7]. CAR was shown to be associated with disease activity in a study conducted with Crohn's patients [8]. COPD patients experience chronic inflammation and malnutrition is a common condition in this patient group. Therefore, the evaluation of CAR in COPD patients admitted to ICU may be valuable in predicting mortality.

The aim of this study is to demonstrate the effectiveness of CAR as a 30-day mortality indicator in COPD patients admitted to ICU, as well as to evaluate the reliability and predictive power of CAR by comparing it with other parameters indicating mortality in ICU.

MATERIAL AND METHODS

A total of 235 COPD patients with available data were included in the study. We retrospectively analyzed patients who were admitted to the Department of Anaesthesia and Intensive Care of Health Sciences University Ankara Atatürk Chest Diseases and Thoracic Surgery Training and Research Hospital between January 2018 and December 2018. Demographics, comorbidities, body mass index (BMI), APACHE II score, CCI, SOFA score, CRP, albumin, CAR, procalcitonin, outcomes including duration of ICU, length of stay (LOS) and 30-day mortality were evaluated. Patients with no COPD and patients with missing data were excluded from the study. At the end of 30 days, patients were divided into two groups as survivors and non-survivors. With the ethical committee decision numbered 624 dated 19/04/2019.

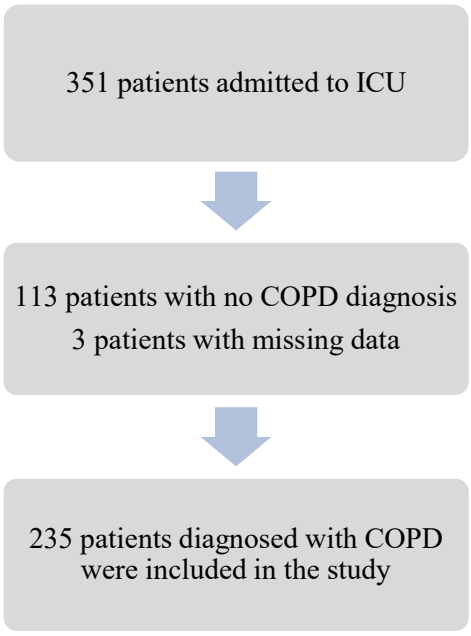

Figure 1. CONSORT flow diagram of patients

Statistical analysis

Data were expressed using mean, standard deviation, median, minimum, maximum, frequency and ratio values. The Kolmogorov–Smirnov test was used to measure the distribution of variables. The Mann–Whitney U test was used to analyze quantitative independent data. Paired sample t test and Wilcoxon test were used to analyze dependent data. The Chi-square test was used to analyze qualitative independent data. The level of effect was investigated using univariate and multivariate logistic regression. Statistical analysis was performed with SPSS version 22.0 software.

RESULTS

Table 1 lists demographics, comorbidities and clinical characteristics of the cases. Accordingly, 87 (37%) of the cases were female and 148 (63%) were male. Their ages ranged from 26 to 95 years, with an average of 70.9± 11.4.

Table 1. Demographic properties, comorbidities and clinical findings of the patients

		Min-Max	Median	Mean±SD/ n-%
Age (years)		26.0-95.0	71.0	70.9±11.4
Gender	Female			87 37.0%
	Male			148 63.0%
BMI		15.0-53.3	26.0	25.9±6.7
LOS (days)		0.0-50.0	3.0	5.4±6.4
Duration of hospitalization (days)		0.0-127.0	14.0	18.8±15.8
COPD				235 100%
Sepsis				26 11.1%
Coronary artery disease				12 5.1%
Congestive heart failure				49 20.9%
Acute renal failure				10 4.3%
Hypertension				70 29.8%
Diabetes mellitus				44 18.7%
Malignancy				18 7.7%
Comorbidity				158 67.2%
Inotropic support				51 21.7%
Repeated ICU admission				36 15.3%
APACHE II		10.0 - 46.0	20.0	21.6 ± 7.0
CCI		2.0 - 13.0	6.0	5.8 ± 2.0
SOFA		4.0 - 17.0	6.0	6.4 ± 2.1
Procalcitonin		0.0 - 97.0	0.2	2.2 ± 9.5
Creatinine		0.3 - 6.5	0.9	1.1 ± 0.8
Mechanical ventilation time		0.0 - 48.0	0.0	2.7 ± 6.7
WBC		0.4 - 110.0	10.7	12.4 ± 8.7
CRP		0.0 - 34.0	4.5	7.2 ± 8.1
Albumin		1.6 - 4.7	3.2	3.2 ± 0.6
Prealbumin		0.1 - 31.0	13.0	12.8 ± 5.6
CAR		0.0 - 14.4	1.4	2.5 ± 3.0

Table 2. Comparison of clinical parameters between survivors and non-survivors

		30-day mortality (-)			30-day mortality (+)			p	
		Mean±SD/n %		Median	Mean±SD/n %		Median		
Age (years)		69.3±11.4		68.5	74.2±10.9		74.0	*0.002*	m
Gender	Female	59	37.3%		28	36.4%		0.884	X^2
	Male	99	62.7%		49	63.6%			
BMI		25.9±6.9		25.2	25.3±6.1		24.2	0.408	m
LOS (days)		4.7±5.5		3.0	6.8±7.8		3.0	0.182	m
Duration of hospitalization (days)		19.9±16.7		15.0	16.4±13.5		12.0	*0.040*	m
COPD		158	100%		77	100%		1.000	X^2
Sepsis		9	5.7%		17	22.1%		*0.000*	X^2
Coronary artery disease		7	4.4%		5	6.5%		0.500	X^2
Congestive heart failure		30	19.0%		19	24.7%		0.314	X^2
Acute renal failure		7	4.4%		3	3.9%		0.849	X^2
Hypertension		46	29.1%		24	31.2%		0.746	X^2
Diabetes mellitus		24	15.2%		20	26.0%		*0.047*	X^2
Malignancy		12	7.6%		6	7.8%		0.957	X^2
Comorbidity		100	63.3%		58	75.3%		0.065	X^2
Inotropic support		13	8.2%		38	49.4%		*0.000*	X^2
Repeated ICU admission		23	14.6%		13	16.9%		0.642	X^2
APACHE II		19.3 ± 5.0		19.0	26.5 ± 8.1		26.0	*0.000*	m
CCI		5.4 ± 1.7		5.0	6.5 ± 2.3		6.0	*0.000*	m
SOFA		5.5 ± 1.0		5.0	8.1 ± 2.6		8.0	*0.000*	m
Procalcitonin		0.7 ± 2.5		0.1	5.2 ± 16.1		0.3	*0.000*	m
Creatinine		1.0 ± 0.7		0.8	1.3 ± 0.9		1.1	*0.000*	m
Mechanical ventilation time		1.4 ± 5.3		0.0	5.6 ± 8.4		2.0	*0.000*	m
WBC		10.9 ± 4.6		10.3	15.3 ± 13.3		12.5	*0.001*	m
CRP		5.5 ± 6.3		2.9	10.9 ± 10.0		7.6	*0.000*	m
Albumin		3.4 ± 0.5		3.4	2.9 ± 0.5		3.0	*0.015*	m
Prealbumin		14.2 ± 5.3		14.0	10.1 ± 5.1		10.0	*0.000*	m
CAR		1.8 ± 2.1		0.8	4.1 ± 4.0		2.3	*0.000*	m

[m] Mann-whitney u test / [X^2] Chi-square test

The mean age of non-survivors was significantly higher ($p<0.05$) than the surviving group, and the distribution of gender did not differ significantly between the groups ($p>0.05$). There was no significant difference in BMI values ($p>0.05$) and duration of ICU ($p>0.05$) between two groups. Duration of hospitalization was significantly lower ($p<0.05$) and the incidence of sepsis was significantly higher ($p<0.05$) in non-survivors. There was no significant difference in the rate of coronary artery disease (CAD), the rate of congestive heart failure (CHF), the rate of acute renal failure (ARF), the rate of hypertension (HT), the rate of malignancy, the rate of comorbidity and the rate of ICU admission ($p>0.05$) between the groups.

The rate of inotropic support was significantly higher ($p<0.05$) in the 30-day mortality group. The non-survivors had significantly higher APACHE II score, CCI, SOFA score, procalcitonin, creatinine, mechanical ventilation (MV) time, white blood cell (WBC), CRP and CAR compared to the survivors ($p<0.05$). Albumin and prealbumin were significantly lower ($p<0.05$) in non-survivors (Table 2).

Table 3. Logistic regression analysis in univariate and multivariate model

	Univariate Model				Multivariate Model			
	OR	95% Confidence I.		p	OR	95% Confidence I.		p
Age	1.04	1.01	- 1.07	*0.002*				
Sepsis	4.69	1.98	- 11.10	*0.000*				
Inotropic Support	10.87	5.28	- 22.38	*0.000*	7.25	2.54	- 20.69	*0.000*
APACHE II	1.19	1.13	- 1.26	*0.000*				
CCI	1.37	1.17	- 1.59	*0.000*				
SOFA	2.74	2.06	- 3.63	*0.000*	2.45	1.71	- 3.52	*0.000*
Procalcitonin	1.13	1.02	- 1.24	*0.016*				
Creatinine	1.53	1.07	- 2.20	*0.021*				
MV time	1.11	1.05	- 1.17	*0.000*				
WBC	1.09	1.04	- 1.15	*0.000*	1.14	1.05	- 1.24	*0.001*
CRP	1.09	1.05	- 1.13	*0.000*				
Albumin	0.18	0.10	- 0.33	*0.000*				
Prealbumin	0.85	0.80	- 0.91	*0.000*	0.81	0.73	- 0.89	*0.000*
CAR	1.29	1.16	- 1.43	*0.000*				

In the univariate model; age, sepsis, inotropic support, APACHE II score, CCI, SOFA, procalcitonin, creatinine, MV time, WBC, CRP, albumin, prealbumin and CAR value were observed to be significantly effective ($p<0.05$) in predicting 30-day mortality. In the multivariate reduced model; inotropic support, SOFA, WBC and prealbumin value exhibited significant independent ($p<0.05$) effectiveness in predicting 30-day mortality (Table 3).

Table 4. Investigation of measurements effective in estimating mortality

	AUC	95 % CI	p
Albumin	0.701	0.621-0.782	0.000
CRP	0.665	0.581-0.748	0.000
CAR	0.682	0.600-0.764	0.000
APACHE II	0.767	0.699-0.835	0.000
SOFA	0.840	0.781-0.899	0.000
CCI	0.655	0.579-0.732	0.000

Albumin, CRP, CAR, APACHE II, SOFA and CCI were observed to be significant ($p = 0.000$) in predicting 30-day mortality (Table 4).

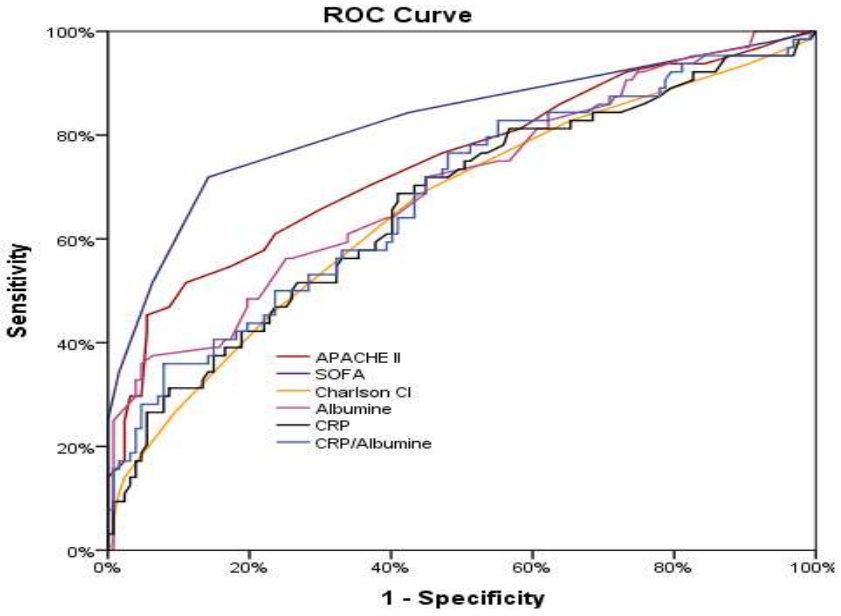

Figure 2. The ROC curves for prediction of 30-day mortality for APACHE II, SOFA, CCI, albumin, CRP and CAR

DISCUSSION

The results of our study have shown the effectiveness of CAR is effective in predicting 30-day mortality in COPD patients admitted to ICU. In addition, APACHE II, CCI, SOFA scores, procalcitonin, creatinine, MV duration, WBC, CRP, CAR, sepsis rate, inotropic support rate and age were significantly higher in the non-survivors ($p<0.05$) while admission albumin, prealbumin and duration of hospitalization were significantly lower ($p<0.05$) compared to the survivors. However, there was no significant difference in the duration of ICU stay, CAD rate, CHF rate, ARF rate, HT rate, malignancy rate, comorbidity rate and repeated ICU admission between two groups ($p>0.05$).

CRP and albumin, acute phase reactants, are considered to be important markers predicting morbidity and mortality in critically ill patients as they are indicators of inflammation and malnutrition [9,10]. Accordingly, available studies investigated CAR, which assesses both inflammation and malnutrition, in postoperative patients, patients with an infection, cancer or other patient group as a prognostic marker [11-19]. A study showed that increased CAR was associated with increased 28-day mortality in ICU patients, but it was concluded that sensitivity and specificity were not sufficient to predict mortality so multicentre studies were needed. The same study emphasized the effectiveness of APACHE II score in predicting mortality [20]. Several studies reported that CAR could be a useful prognostic factor in predicting mortality in patients with sepsis, septic shock patients, or critically ill patients requiring parenteral nutrition [11,21-23]. While available studies mostly focus on 28 or 30 days of mortality, a study investigating the effectiveness of CAR in predicting 180-day mortality stated that CAR can be used to predict 180 days of mortality in patients diagnosed with sepsis and septic shock [11]. Another study investigating the patients admitted to the postoperative ICU reported that the CAR was effective in predicting 30-day and 1-year mortality [12].

There is a quite limited number of studies in the literature examining the relationship between CAR and morbidity and mortality in COPD patients. COPD patients experience chronic inflammation and malnutrition is also common in this group of patients. Accordingly, COPD patients may be expected to have increased CRP with reduced serum albumin. Likewise, high CAR is correlated with severe inflammation and infection in COPD exacerbations [24]. Therefore, the evaluation of CAR in terms of mortality may differ in the

group of COPD patients and can provide us with valuable insight. A study by Atalay et al. [24] where they investigated patients hospitalized with COPD exacerbation concluded that CAR was correlated with 1-year mortality. Additionally, it was stated that CAR was more effective in predicting mortality compared to albumin and CRP alone. The same study stated that CAR may be an important determinant in predicting mortality with other parameters, and it may be used as a reliable prognostic marker in the clinical setting with new prospective and randomized controlled studies. Similarly, our study investigated patients diagnosed with COPD and found that CAR was correlated with mortality. However, unlike the study of Atalay et al. [24], only critical COPD patients who were admitted to ICU were included in our study. Additionally, we also assessed APACHE II, CCI, SOFA score and prealbumin values and compared the power of CAR to predict mortality with the predictive power of these values. Review of the literature reveals that most studies focus on whether the CAR predicts mortality or not. There is a limited number of studies comparing the predictive power of CAR with scoring systems such as APACHE II, SOFA or CCI, which are conducted during patient admission to ICU. A study evaluating the clinical benefit of CAR in predicting 30-day mortality in critical patients admitted to ICU revealed that CAR was independently associated with 30-day mortality. However, clinical usefulness of the CAR in predicting 30-day mortality was questioned since the predictive power of APACHE II and CCI was higher than that of the CAR while the area under curve of albumin alone was higher than that of CAR [25].

CONCLUSIONS

In the study, the predictive power of APACHE II, CCI, SOFA score, albumin and prealbumin values alone was found to be significantly higher than that of the CAR. This significant finding was found by calculating the logistic regression analysis and the area under the curve in the multivariate model. Therefore, we do not recommend using the CAR to routinely predict mortality in COPD patients admitted to ICU. However, we think that further research should be conducted to determine an acceptable cut-off value for CAR in predicting mortality in COPD patients.

Disclosure statement

The authors did not report any potential conflict of interest.

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