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CLINICAL STUDY

C-reactive protein-to-serum albumin ratio as a marker of prognosis in adult intensive care population

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ABSTRACT
BACKGROUND: Patients in intensive care unit (ICU) require close follow up and clinical attention due to variability in the course of their underlying morbidities. The estimation of prognosis in these subjects has an utmost importance. Recent studies showed that C-reactive protein-to-serum albumin ratio (CAR) could be a reliable marker of inflammation in certain conditions. We aimed to compare CAR levels of deceased patients to those in survived subjects treated in ICU.
PATIENTS AND METHODS: We retrospectively analyzed the data of adult patients. CAR was simply calculated by dividing the levels of CRP by those of serum albumin. Patients were grouped either as deceased or survived according to the prognosis. The data of the survived and deceased ICU subjects were compared.
RESULTS: A total of 208 subjects, 101 deceased and 107 survived, were enrolled in the study. Median CAR levels of the deceased and survived subjects were 49.5 (3–153 %) and 11 (0.2–119 %), respectively ($p < 0.001$). CAR was significantly correlated with PDW ($r = 0.24$; $p < 0.001$) and serum creatinine ($r = 0.27$; $p < 0.001$) levels. In ROC analysis, CAR values higher than 30.2 % have 72 % sensitivity and 70 % specificity in predicting mortality in ICU population (AUC: 0.74; $p < 0.001$; 95% CI: 0.67–0.81).
CONCLUSIONS: We suggest that CAR levels of the subjects in ICU should be evaluated during medical care. Increased CAR levels should alert physicians for a worse outcome in those subjects *(Tab. 1, Fig. 1, Ref. 21)*. Text in PDF *www.elis.sk*
KEY WORDS: C-reactive protein-to-serum albumin ratio, intensive care, mortality.

Introduction

Patients in intensive care unit (ICU) require close follow up and clinical attention due to variability in the course of their underlying morbidities (1). The estimation of the prognosis in these subjects has an utmost importance. For this purpose, various prognostic tools have been developed, such as APACHE II and SOFA scores. However, these scores are not easy to assess while novel prognostic tools to determine prognosis in ICU population are still a necessity.

Recent studies showed that C-reactive protein-to-serum albumin ratio (CAR) could be a reliable marker of inflammation in certain conditions. For instance, the Care Time study suggested CAR as a valuable predictor of diabetic kidney injury in subjects with type 2 diabetes mellitus (2). Moreover, Liu et al found that CAR could predict the outcome in patients with coronary arterial disease (3). Both type 2 diabetes mellitus and coronary heart disease are characterized with an increased burden of inflammation. Subjects in ICU have also increased inflammatory markers in serum. Therefore, we hypothesized that CAR could be associated with the prognosis in ICU population.

We aimed to compare CAR levels of deceased patients to those in survived subjects treated in ICU.

Patients and methods

After obtaining approval from the local ethics committee (as of 13th of July in 2021, approval No: 2021/192), we retrospectively analyzed the data of the adult patients in ICU of Abant Izzet Baysal University hospital between January 2021 and January 2022. Patients with sepsis, rheumatologic conditions, pregnancy, and under 18 years of age were excluded from the study.

General characteristics of the subjects, namely age, gender, duration of stay in ICU, hematological parameters (white blood cell count (WBC), neutrophil count (neu), lymphocyte count (lym), hemoglobin (Hb), hematocrit (Htc), erythrocyte distribution width (RDW), platelet count (PLT), mean platelet volume (MPV), platelet distribution width (PDW)), fasting glucose, serum albumin, creatinine, and C-reactive protein (CRP) were recorded after being obtained from patients' files and institutional database. CAR was simply calculated by dividing the levels of CRP to those of serum albumin. Data about comorbidities, and positive urine or blood culture findings were also recorded. Patients were grouped either as deceased or survived according to

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the prognosis. Data of the survived and deceased ICU subjects were compared.

Statistical analyses

Statistical software (SPSS 15 for Windows, IBM, Chicago, IL, USA) was used for statistical analyses. The comparison of non-parametric data was done with chi-square test and expressed as numbers and percentages. Normality analyses of the study variables were conducted with Kolmogorov-Smirnov test. Since all variables were not fit into normal distribution, they were expressed as median (min–max) and compared with Mann-Whitney U test. Non-parametric correlations among study variables were analyzed with Spearman's correlation test. Sensitivity and specificity of CAR in predicting mortality were conducted with ROC analysis. A p value lower than 5 % was considered statistically significant.

Results

A total of 208 subjects, 101 deceased and 107 survived, were enrolled in the study. Median ages of the deceased and survived patients were 71 (33–94) years, and 68 (18–96) years, respectively (p = 0.02). Sixty-two (61 %) of the deceased subjects were men and 39 (39 %) were women while 63 (59 %) of the survived subjects were men and 44 (41 %) were women. The distribution of sex variable was not different among deceased and survived subjects (p = 0.71).

There were no significant differences between deceased and survived subjects in terms of the presence of comorbidities (p = 0.24), or positive findings in blood (p = 0.59) or urine cultures (p = 0.51). WBC (p = 0.82), neu (p = 0.91), lym (p = 0.83), MCV (p = 0.79), RDW (p = 0.24), fasting glucose (p = 0.99) of the deceased and survived subjects were not statistically different.

Hospitalization duration in ICU (p = 0.01), Hb (p = 0.03), Htc (p = 0.04), PLT (p = 0.02), MPV (p = 0.01), PDW (p = 0.03), CRP (p < 0.001), serum albumin (p < 0.001), serum creatinine significantly differed between deceased and survived subjects (p < 0.001). Table 1 shows the characteristics and data of the study population.

Median CAR values of the deceased and survived subjects were 49.5 (3–153 %) and 11 (0.2–119 %), respectively (p < 0.001).

CAR was significantly correlated with PDW (r = 0.24; p < 0.001) and serum creatinine (r = 0.27; p < 0.001) levels.

In ROC analysis, CAR values higher than 30.2 % have 72 % sensitivity and 70 % specificity in predicting mortality in ICU population (AUC: 0.74; p < 0.001; 95% CI: 0.67–0.81). Figure 1 shows ROC curves of CAR, PDW, serum creatinine and length of hospital stay in predicting mortality.

Tab. 1. Characteristics and laboratory data of the study groups.

	Deceased	Survived	p
	X^2		
sex			
Men (n,%)	62 (61%)	63 (59%)	0.71
Women (n,%)	39 (39%)	44 (41%)	
	Median (Min–max)		
Age (years)	71 (33–94)	68 (18–96)	**0.02**
ICU duration (days)	6 (1–97)	3 (1–118)	**0.01**
WBC (k/mm^3)	12,6 (3–42)	11.8 (3–106)	0.82
Neu (k/mm^3)	10,7 (2–39)	10 (1–42)	0.91
Lym (k/mm^3)	1,24 (0–29)	1.16 (0–77)	0.82
Hb (g/dL)	10,5 (5–18)	11.8 (5–19)	**0.03**
Htc (%)	32,9 (15–59)	35.5 (15–59)	**0.04**
MCV (fL)	88,1 (23–116)	88.1 (63–106)	0.78
RDW (%)	18,3 (13–65)	17.7 (13–31)	0.23
PLT (k/mm^3)	192 (2–808)	216 (1–623)	**0.02**
MPV (fL)	8,8 (6–15)	7.97 (5–15)	**0.01**
PDW (%)	18,3 (15–23)	18 (16–23)	**0.02**
Glucose (mg/dL)	128 (60–746)	131 (68–800)	0.98
CRP (mg/L)	153 (0,1–336)	40 (0.1–333)	**<0.001**
Albumin (g/dL)	2,7 (1–4)	3.2 (2–41)	**<0.001**
Creatinine (mg/dL)	1,3 (0,3–6)	0.9 (0.3–9)	**<0.001**
CAR (%)	49,4 (0,03–152)	10.8 (0.02–119)	**<0.001**

Discussion

The present study showed that CAR was significantly higher in deceased subjects as compared to survived patients in ICU population. Another important finding could be that CAR had high sensitivity and specificity in predicting mortality in subjects receiving intensive care. Finally, CAR levels were significantly correlated with serum creatinine and PDW, a novel inflammatory marker in patients treated in ICU.

Patients in ICU are characterized with an increased inflammatory burden (4). Recent studies found that inflammatory markers were associated with the outcome of ICU population (5). Neutrophil-to-lymphocyte ratio, another hemogram-derived inflammatory marker, was suggested to be associated with mortality in patients treated in ICU wards (6). Thus, increased inflammatory markers could be considered as a hallmark finding in patients with ICU. On the other hand, CAR is also associated with inflammatory conditions such as diabetic nephropathy (2), pancreatitis (7), spondyloarthritis (8), neuro-inflammatory conditions (9, 10), and infections

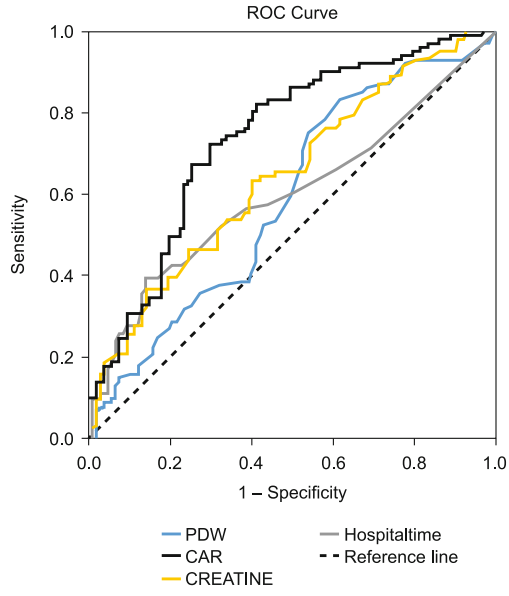

Fig. 1. ROC curves of CAR,PDW, serum creatinine and length of hospital stay in predicting mortality.

(11). All of these conditions are characterized with some degree of inflammation as is common in the ICU population. Therefore, elevated CAR levels in deceased subjects in present study is a finding which is consistent with literature knowledge.

Results of the present study suggested that CAR was associated with the prognosis in patients treated in ICU. Accordingly, in a recent study by Gyawali et al, it has been suggested that CAR could be useful in determining patients with a high risk of sepsis development (12). In contrast, CAR levels of survivals and non-survivals were not statistically different in ICU subjects with sepsis (13). However, subsequent works suggested CAR as a reliable prognostic marker in critically ill subjects (14). The results of the present study confirmed the previous works which suggested CAR as a prognostic marker in ICU population.

We should speculate why CAR levels were associated with mortality in patients in ICU. The inflammatory burden is increased in this population and CRP is one of the widely used inflammatory markers (15, 16). As a result, elevated CRP levels are noticed in ICU subjects while those even higher are frequently found in patients with poor prognosis (17). In accordance with literature data, we reported higher CAR levels in deceased ICU subjects as compared to the survivors.

Elevated CAR levels have been linked to a worse prognosis in recent studies. A Chinese study reported that CAR was associated with outcomes of patients with esophagus cancer (18). Similarly, a study conducted by Frey et al. claimed that CAR was a predictor of mortality in lung cancer (19). In addition, CAR has been introduced as a prognostic factor in metastatic colon cancer (20). Subsequently, their results were confirmed by a study by Zhou et al. study who suggested CAR as an independent prognostic marker in patients with colorectal carcinoma (21). In accordance with the studies in the literature, we found increased CAR levels in deceased patients as compared to the survived patients in ICU.

Our study has several limitations. Firstly, the design was retrospective which could have led to a selection bias. Secondly, the study population was relatively small. And thirdly, the single-center nature of our work may limit the globalization of the results of the present work. However, our work supports previous data in literature suggesting that elevated CAR could be associated with worse outcomes in ICU patients.

We suggest that CAR levels of the subjects in ICU should be evaluated during medical care. Increased CAR levels should alert physicians for worse outcomes in those subjects.

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