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Predictive value of C-reactive protein to albumin ratio and systemic immune-inflammation index for the long-term mortality in COVID-19

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ABSTRACT

Aim: Several studies have investigated the association between biomarkers and short-term prognosis in the coronavirus infectious disease 2019 (COVID-19). However, data on the long-term prognosis are limited. To determine the predictive value of systemic immune-inflammation index (SII) and C-reactive protein (CRP) to albumin ratio (CAR) for in-hospital and 1-year outcomes during COVID-19.

Material and Method: The primary outcomes were in-hospital and 1-year mortality. The secondary outcomes were the intensive care unit (ICU) need at admission and transfer to the ICU later on.

Results: The study included 449 (53.6%) males and 389 (46.4%) females with a mean age of 53.8±18.5 years. Previously known heart failure (HF), COVID-19-related HF, acute renal failure (ARF), diabetes mellitus, hypertension, coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD)/asthma, high CO-RADS scores (>4), low ejection fraction (EF), higher CAR and SII were associated with an increased in-hospital and 1-year mortality ($p<0.05$). After multivariate analysis; CAR, SII, ARF, and diabetes mellitus were independent predictors of in-hospital and 1-year mortality,whereas CAD was only an independent predictor of 1-year mortality. After ROC analysis, CAR cut-off levels of 2.54 and 2.23 predicted in-hospital and 1-year mortality, respectively ($p<0.001$). The SII cut-off levels of 1274 and 1191 predicted in-hospital and 1-year mortality, respectively ($p<0.001$).

Conclusion: CAR and SII can be used as valuable prognostic indexes to predict both the short-term and long-term mortality in COVID-19.

Keywords: Systemic immune-inflammation index, SII, C-reactive protein to albumin ratio, CAR, long-term mortality, COVID-19

INTRODUCTION

The coronavirus infectious disease 2019 (COVID-19) outbreak has affected about 524 million people worldwide, causing over 6 million deaths despite the application of nearly 12 billion doses of vaccines (1). Several studies have shown that the main factor in COVID-19 is the extreme inflammatory response and the ensuing uncontrolled cytokine storm, which affects not only the respiratory system but many other systems, causing clinical deterioration and death (2). Therefore, the course of infection may be more severe in diseases such as diabetes, hypertension, heart failure (HF), and coronary artery disease (CAD), in which inflammation plays a key role in the pathophysiology (3). The virus may also cause thrombotic events such as myocardial infarction, stroke, and pulmonary embolism through endothelial damage, autonomic dysregulation, and microvascular dysfunction in both short and long term (4-6).

There is a growing number of studies investigating the relationship of thromboinflammatory parameters with the severity of the COVID-19, the intensive care unit (ICU) need, and short-term mortality (7-9). The systemic immune-inflammation index (SII) (calculated

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as neutrophil x platelet/lymphocyte) and C-reactive protein (CRP) to albumin ratio (CAR) are the novel indexes developed to determine the inflammatory and immunothrombotic status of patients with various cancer types (10-11). Then, SII and CAR have been suggested to be more valuable than other many inflammatory biomarkers in predicting major adverse cardiovascular events and the severity of diseases such as CAD and pulmonary embolism (12-13). Recently, several studies have been conducted investigating the role of CAR and SII in the prognosis of COVID-19 but mostly presenting short-term results(7,8).

Since the data on long-term prognostic parameters are lacking, we aimed to investigate the effectiveness of the CAR and SII as inflammatory and immunothrombotic parameters in predicting the ICU need, in-hospital, and 1-year mortality due to COVID-19.

MATERIAL AND METHOD

Study Design, Clinical and Laboratory Parameters

This single-center, case-control, and cross-sectional study was approved by the Kırıkkale University Faculty of Medicine Clinical Researches Ethics Committee (Date: 25.05.2022, Decision No: 2022.05.20). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants. The study included a total of 838 patients having a history of COVID-19 confirmed by positive real-time polymerase chain reaction (PCR) between April 2020 and April 2021. Exclusion criteria were as follows; pregnancy, younger age of 18 years, decompensated HF (not new onset HF or euvolemic patients with known HF), significant valvular heart disease, ongoing systemic inflammatory conditions such as flu, diarrhea, and urinary tract infection unrelated to SARS-CoV-2 infection, history of liver disease (with liver function parameters >3x upper normal value), autoimmune disease and hematologic or malignant disease. Patients' demographics, clinical characteristics, medical history, radiological, and clinical outcome data were obtained through the electronic patient database. The laboratory parameters, measured within the first 24 hours of hospital admission, were obtained through the electronic patient database. The SII was calculated as the ratio of the product of total neutrophil count and platelet count to lymphocyte count. The CAR was calculated as the ratio of serum CRP to the serum albumin level.

Thorax Computed Tomography Imaging

All patients were imaged at presentation with multidetector computer tomography (CT) using the TOSHIBA Alexion/ Advance Edition (Toshiba Medical Systems Corporation, Japan, 1.25 mm section thickness) with 64-detector rows. All scans were acquired without an intravenous contrast agent, with the patient in a supine position during end inspiration. CT indications were as follows: patients having moderate-to-severe respiratory symptoms and high index of clinical suspicion of COVID-19, showing unexplained clinical deterioration and/or where other concurrent lung pathology needs exclusion, COVID-19-positive patients with associated co-morbidities (age >65 years, diabetes mellitus, hypertension, obesity, cardiovascular disease, chronic respiratory disease, immune-compromise, etc.). CT imaging was also indicated in patients having indeterminate chest X-ray findings despite having mild symptoms and recorded oxygen saturation of <93 percent at rest while breathing room air or de-saturation on six-minute walk test. The CO-RADS classification was used to categorize the level of COVID-19 suspicion (14). According to that system, the degree of suspicion is classified into five levels from very low (CO-RADS 1) to very high (CO-RADS 5).

Echocardiographic Measurement

Standard 2-dimensional echocardiography was performed on all subjects lying in the left lateral decubitus position with a Vivid 7 Doppler echocardiographic unit (GE Vingmed Ultrasound, Horten, Norway) using a 3.5-MHz transducer. Echocardiographic measurements were made according to ACC and AHA standard protocols(15). We utilized two-dimensional and M-mode echocardiography to investigate ejection fraction (EF). An EF of less than 50% was defined as HF.

Outcome

The primary outcomes were in-hospital and 1-year mortality after the diagnosis of the COVID-19. The secondary outcomes were the ICU need at admission and transfer to the ICU later on. In-hospital death was defined as death during the index hospital stay related or non-related to COVID-19. One-year mortality was defined as death related or unrelated to COVID-19 within 1 year from diagnosis. Indications for transfer to the ICU was as follows: i) Respiratory rate>30/minute, ii) SpO2<94% on room air, iii) PaO2/FiO2<300, iv) Lung infiltration>50% on X-ray or CT, v) Need for positive pressure ventilation, ECMO, or mechanical ventilation, vi) Shock vii) Cytokine release syndrome.

Statistical Analysis

SPSS 25.0 (IBM Corporation, Armonk, New York, United States) program was used in the analysis of the variables. Quantitative variables with a normal distribution were specified as the mean±standard deviation and categorical variables were specified with number and percentage values. The conformity of quantitative data to normal distribution was assessed with the Kolmogorov-

Smirnov test. Independent Samples T-Test was applied in the comparison of continuous variables showing normal distribution. Odds ratio with 95% confidence intervals was used to determine how many times more effects were caused by those who were exposed to a risk factor than those who were not. Logistic regression analysis was applied in the univariate and multivariate analyses to determine the independent predictors of both in-hospital and 1-year mortality. The ROC curves were used to determine the cut-off values of cardiac biomarkers to predict mortality. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 838 patients were analyzed in our study, including 449 (53.6%) males and 389 (46.4%) females with a mean age of 53.8±18.56 years. Demographic, clinical, imaging, and laboratory characteristics of the patients were presented in **Table 1**. In our study, in-hospital mortality was 67 (9.7%) and 1-year total mortality was 86 (11.5%) in the follow-up. As presented in **Table 2**, there was a significant relationship between higher values of the CAR and the ICU need at admission, transfer to ICU later on, in-hospital mortality, and 1-year mortality (p=0.001 for the transfer to ICU, p<0.001 for the rest). Similarly, a significant relationship was found between the higher values of SII and ICU need at admission, transfer to ICU later on, in-hospital mortality, and 1-year mortality (p=0.003 for the transfer to ICU, p<0.001 for the rest).

Table 2. The relationship of inflammatory indexes with the intensive care unit need and mortality

	n,%	CAR Mean±SD	p	SII Mean±SD	p
ICU (at admission)			<0.001		<0.001
No	661 (75,3%)	1.18±1.80		940.35±1225.39	
Yes	177 (24.7%)	4.18±4.19		2976.72±3241.18	
Transfer to ICU			0.001		0.003
No	682 (82%)	1.66±2.80		1270.21±2066.37	
Yes	156 (18%)	2.51±2.59		1808.79±1749.30	
In-hospital mortality			<0.001		<0.001
No	771 (90.3%)	1.26±1.70		1204.13±1870.97	
Yes	67 (9.7%)	8.24±4.34		3284.68±2630.48	
1-year mortality			<0.001		<0.001
No	752 (88.5%)	1.14±1,46		1144.03±1671.62	
Yes	86 (11.5%)	4.25±0.45		3350.51±3333.72	

Abbreviations: ICU: Intensive care unit, Independent Samples T Test (Bootstrap), Mean±standard deviation for normal distribution, and n (%) for categorical data.

Table 1. Demographic, clinical, imaging, and laboratory characteristics of the patients

	Total (n=838)	In-hospital mortality (n=67)	1-year mortality (n=86)
Gender (male), n (%)	449 (53.6)	34 (50.7)	41 (47.7)
Age, years	53.8±18.56	71±14.22	71.3±13.25
BMI, kg/m²	21.31±3.12	21.02±3.58	21.01±3.57
Smoking, n (%)	359 (42.8)	27 (40.3)	38 (44.2)
Clinical risk factor, n (%)			
Hypertension	255 (30.4)	38 (56.7)	52 (60.5)
Coronary artery disease	117 (14.0)	33 (49.3)	44 (51.2)
Diabetes mellitus	136 (16.2)	39 (58.2)	47 (54.7)
Heart failure (known)	71 (8.5)	28 (41.8)	37 (43.0)
Heart failure (COVID-19-related)	23 (2.7)	14 (20.9)	15 (17.4)
Acute kidney failure	28 (3.3)	24 (35.8)	26 (30.2)
COPD/Asthma	172 (20.5)	22 (32.8)	29 (33.7)
Stroke	9 (1.1)	8 (11.9)	9 (10.5)
Transfer to ICU, n (%)	158 (18.6)	12 (17.9)	15 (17.4)
ICU need (at admission), n (%)	177 (21.1)	47 (70.1)	63 (73.3)
Laboratory and Imaging Findings			
Ejection fraction,%	55.10±8.10	43.07±13.92	43.78±13.76
CO-RADS score	3.05±1.65	4.66±0.70	4.62±0.72
CAR	1.82±2.78	8.24±4.34	7.72±4.25
SII	1370.47±2021.07	3284.68±2630.48	3350.51±3333.72
C-reactive protein, mg/dL	6.51±9.22	26.75±13.44	25.28±13.27
Albumin, g/dL Normal range (3.5-5.5 g/dL)	3.82±0.42	3.28±0.36	3.32±0.36
White blood cells, (10^9/L)	8.98±4.26	14.29±6.16	13.47±6.18
Neutrophils, (10^3/μL)	6.52±4.18	12.19±5.70	11.46±5.72
Lymphocytes, (10^3/μL)	1.93±1.06	1.43±1.02	1.36±0.96
Platelets, (10^9/L)	246±77.5	246.2±87.1	249.9±85.2

Mean±standard deviation for normal distribution, and n (%) for categorical data. Abbreviations: BMI: Body mass index; CAR: c-reactive protein/albumin ratio; COPD: Chronic obstructive pulmonary disease; CO-RADS: Coronavirus Disease 2019 (COVID-19) Reporting and Data System; ICU: Intensive care unit; SII: Systemic immune-inflammation index

Table 3 provides information about univariate and multivariate logistic regression analysis results of patients' in-hospital and 1-year mortality. Univariate logistic regression analysis results revealed that patients with known HF, COVID-19-related HF, acute renal failure (ARF), diabetes mellitus, hypertension, CAD, chronic obstructive pulmonary disease (COPD)/asthma, high CO-RADS scores (> 4), low EF, higher CAR and SII were significantly associated with both the increased in-hospital and 1-year mortality (p=0.011 of in-hospital mortality for the COPD/Asthma, p=0.002 of 1-year mortality for the COPD/Asthma, p<0.001 for the rest). After the multivariate logistic regression analysis, CAR values (odds ratio (OR): 1.46; 95% confidence interval (CI): 1.29-1.65; p<0.001) and SII values (OR: 1.00; 95% CI: 1.00-1.00; p=0.021) remained as significant predictors of the in-hospital mortality as well as ARF (OR: 12.6; 95% CI: 3.20-49.61; p<0.001) and diabetes mellitus (OR: 2.99; 95% CI: 1.23-7.26; p=0.015). In addition, CAR (OR:1.72; 95% CI: 1.50-1.99; p<0.001), SII (OR: 1.00; 95% CI: 1.00-1.00; p<0.001), ARF (OR: 15.74; 95% CI: 2.77-89.36; p=0.002), diabetes mellitus (OR: 2.63; 95% CI: 1.09-6.34; p=0.031), and CAD (OR: 3.99; 95% CI: 1.34-11.83; p=0.013) were independent predictors of 1-year mortality.

Table 4 presents the analyzes of CAR and SII values in predicting in-hospital and 1-year mortality. CAR predicted in-hospital mortality at the cut-off value of ≥ 2.54 with a sensitivity of 89.6% and a specificity of 88.8% (p<0.001). The sensitivity and specificity of SII at the cut-off value of ≥ 1274.07 were 77.6% and 77.4%, respectively (p<0.001). Similarly, CAR had a sensitivity of 88.4% and a specificity of 88.4% at the cut-off value of ≥ 2.23 in predicting 1-year mortality (p<0.001). The sensitivity and specificity of SII at the cut-off value of ≥ 1191.20 were 76.7% and 76.9%, respectively (p<0.001). In the ROC analysis of CAR and SII values designed to estimate in-hospital mortality, the area under the curve (AUC) values were 0.956; (95% CI: 0.936-0.976; p<0.001) and 0.809; (95% CI: 0.752-0.865; p<0.001), respectively. In the ROC analysis of CAR and SII designed to estimate 1-year mortality, the AUC values were 0,953; (%95 CI: 0,932-0,974; p<0.001) and 0,807; (%95 CI: 0,758-0,857; p<0.001), respectively (**Figure**).

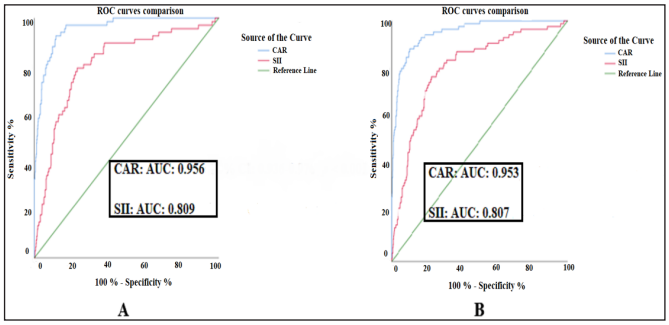

Figure. Comparison of ROC curves of CAR and SII values for predicting in-hospital (A) and one-year mortality (B) in patients with COVID-19

Abbreviations: AUC: Area under the curve; CAR: C-reactive protein/albumin ratio; CI: Confidence interval; SII: Systemic immune-inflammation index

Table 3. Risk factors associated with in-hospital and 1-year mortality according to univariate and multivariate logistic regression analysis

Risk Factors	In-hospital mortality (n=67)				1-year mortality (n=86)			
	Univariate		Multivariate		Univariate		Multivariate	
	OR (95%CI)	p	OR (95%CI)	p	OR (95%CI)	p	OR (95%CI)	p
HF (known)	12.15 (6.84-21.59)	<0.001	1.13 (0.11-10.41)	0.925	15.94 (9.21-27.58)	<0.001	1.40 (0.16-11.82)	0.754
HF (COVID-19 related)	22.36 (9.25-54.05)	<0.001	3.16 (0.33-29.84)	0.314	19.94 (8.05-47.93)	<0.001	1.61 (0.13-19.10)	0.705
ARF	107.02 (35.54-322.21)	<0.001	12.60 (3.20-49.61)	<0.001	162.50 (37.66-701.16)	<0.001	15.74 (2.77-89.36)	0.002
DM	9.67 (5.69-16.44)	<0.001	2.99 (1.23-7.26)	0.015	8.97 (5.56-14.49)	<0.001	2.63 (1.09-6.34)	0.031
HT	3.34 (2.01-5.56)	<0.001	1.07 (0.41-2.81)	0.882	4.13 (2.60-6.56)	<0.001	2.40 (0.94-6.15)	0.066
CAD	7.93 (4.67-13.48)	<0.001	1.79 (0.56-5.68)	0.321	9.74 (5.98-15.85)	<0.001	3.99 (1.34-11.83)	0.013
COPD/Asthma	2.02 (1.17-3.47)	0.011	0.94 (0.36-2.46)	0.912	2.16 (1.33-3.51)	0.002	0.81 (0.32-2.05)	0.664
CO-RADS (> 4)	19.55 (7.04-54.24)	<0.001	2.76 (0.62-12.25)	0.180	14.58 (6.64-32.02)	<0.001	1.66 (0.49-5.62)	0.409
EF (< 50%)	0.87 (0.85-0.90)	<0.001	0.95 (0.88-1.03)	0.293	0.87 (0.85-0.89)	<0.001	0.93 (0.85-1.00)	0.930
CAR	1.75 (1.60-1.93)	<0.001	1.46 (1.29-1.65)	<0.001	1.89 (1.70-2.09)	<0.001	1.72 (1.50-1.99)	<0.001
SII	1.00 (1.00-1.00)	<0.001	1.00 (1.00-1.00)	0.021	1.00 (1.00-1.00)	<0.001	1.00 (1.00-1.00)	<0.001
	R2=0.71, -2 log-likelihood=162.56				R2=0.76, -2 log-likelihood=164.70			

Abbreviations: ARF: Acute renal failure; CAD: Coronary artery disease; CAR: C-reactive protein/albumin ratio; CI: Confidence interval; COPD: Chronic obstructive pulmonary disease; CO-RADS: Coronavirus Disease 2019 (COVID-19) Reporting and Data System; DM: Diabetes mellitus; EF: Ejection fraction; HF: Heart failure; HT: Hypertension; OR: Odds ratio; SII: Systemic immune-inflammation index

Table 4. Analysis of predictive values of inflammatory biomarkers in predicting in-hospital and 1-year mortality

	AUC	%95 CI	Cut-off	Sensitivity (%)	Specificity (%)	p
In-hospital mortality						
CAR	0.956	0.936-0.976	≥ 2.54	89.6	88.8	<0.001
SII	0.809	0.752-0.865	≥ 1274.07	77.6	77.4	<0.001
1-year mortality						
CAR	0.953	0.932-0.974	≥ 2.23	88.4	88.4	<0.001
SII	0.807	0.758-0.857	≥ 1191.20	76.7	76.9	<0.001

Abbreviations: AUC: Area under the curve; CAR: C-reactive protein/albumin ratio; CI: Confidence interval; SII: Systemic immune-inflammation index

DISCUSSION

The main findings of this study are as follows i) CAR and SII were independent predictors of in-hospital mortality as well as ARF and diabetes mellitus were other independent predictors; ii) CAR, SII, ARF, diabetes mellitus, and CAD were independent predictors of 1-year mortality; iii) Higher values of CAR and SII were significantly associated with increased ICU need at admission and transfer to ICU later on.

Several studies have been conducted on the predictive values of laboratory parameters and scoring systems such as the CO-RADS, regarding the severity and short-term prognosis of COVID-19 (7,8,14). However, data on the long-term consequences of COVID-19 in patients with and without comorbid diseases are limited to only special populations such as the elderly and patients with chronic kidney disease (16-18). Walle-Hansen et al. (16) investigated the functional status, age-related changes in health-related quality of life, and mortality in the elderly at a 6-month follow-up after COVID-19 onset. They found that more than half of patients had negative changes in cognitive and physical function, and that one out of three had significant deterioration in mobility to sustain their daily lives. Similarly, in a large cohort, the 1-year mortality was high in the elderly irrespective of the severity of the disease (17). In another study, Carriazo et al. (18) investigated the effect of COVID-19 on 1-year mortality in hemodialysis patients and concluded that mortality was significantly higher in those with COVID-19, particularly within 3 months after onset. Furthermore, basal CRP levels were higher in those with COVID-19 and 30% of deaths were due to vascular endothelium deterioration suggesting the possible long-term effect of inflammation on the risk of ischemic and bleeding events.

CRP, a positive acute-phase reactant, plays an important role in many stages of the host response to infection including apoptosis, phagocytosis, nitric oxide (NO) release, and production of cytokines, particularly interleukin-6 and tumor necrosis factor-α (19). Albumin, a negative acute phase reactant, has several functions such as antioxidant/anticoagulant activity, anti-inflammatory, and anti-platelet aggregation (20). Increased CRP and decreased albumin levels are associated with increased inflammatory status and thrombotic events such as ischemic heart disease, acute coronary syndrome, and stroke (20, 21). CAR, calculated as the proportion of CRP-to-albumin level, is thought to be a more accurate indicator of inflammatory status than CRP or albumin alone (7). In many studies, CAR has been used as an important parameter to predict the severity and short-term prognosis of COVID-19 and compared or combined with many other parameters (9,22). Different cut-off values have been determined for CAR to predict mortality risk. Li et al. (9) investigated the in-hospital mortality of 465 patients diagnosed with COVID-19 and showed that compared to the NLR and PLR, high CAR levels (>1,843) were the strongest independent predictor of in-hospital mortality, ICU admission, invasive mechanical ventilation, and a longer hospital stay. Lucijanic et al. (22) defined and validated four CAR prognostic categories (<1.0, 1.0–2.9, 3.0–5.9, and ≥6.0) and found that higher CAR values were associated with the increased in-hospital mortality. Moreover, the 6-month mortality in patients with a CAR >2.92 after discharge was 11.4%. In our study, the cut-off values of ≥2.54 and ≥2.23 were significant predictors of in-hospital and 1-year mortality, respectively.

SII is another inflammation parameter having a prognostic value in many cancer types (10). In the pathophysiology of COVID-19, gene expression changes in platelets and increased platelet-platelet and platelet-leukocyte interactions are important in terms of increasing thrombotic events in the prognosis (23). Therefore, that index has been investigated in many studies with different cut-off values regarding the predictive value of the severity and prognosis of COVID-19 (8,24,25). Fois et al. (8) investigated COVID-19-related in-hospital mortality using the SII, total index of systemic inflammation (AISI), NLR, derived NLR (dNLR), PLR, mean platelet volume/platelet ratio (MPR), neutrophil/lymphocyte x platelet ratio (NLPR), monocyte/lymphocyte ratio (MLR), and systemic inflammation response index (SIRI). They found that only SII was the strongest parameter to predict in-hospital mortality with a cut-off value of 1835. Similarly, Acar et al24 found that SII was an independent predictor of in-hospital mortality with a cut-off value of 2699. In contrast, Kudlinski et al25 suggested that SII and CRP did not predict in-hospital mortality. We found the cut-off values of SII to predict in-hospital and 1-year mortality as 1274 and 1191, respectively. The reason for our lower cut-off values can be explained by the fact that the patients included in those studies had comorbid diseases that may affect the results. The study conducted by Kudlinski et al. (25) included 285 patients, and more than 10% of the study participants were composed of patients with diseases such as cancer, autoimmune disease, and immunosuppression, which may cause higher baseline SII values. Moreover, those with thyroid disorders comprised 8% of all patients included in the study. Endocrine disorders such as thyroid gland dysfunction may also cause significant changes in circulating levels of neutrophil, and platelet in the blood which explains the higher cut-off values compared to our study (26). We excluded the patients with any type of cancer and endocrine disorders to evaluate the relationship of the CAR and SII with the prognosis more objectively.

Although both SII and CAR may provide important information about the prognosis of COVID-19, in the study of Xue et al. (27) in which these two parameters were compared, although SII was superior in predicting disease severity compared to many parameters such as NLR, it was inferior to CAR. Supporting this study, we found that CAR had higher sensitivity and specificity than SII in predicting in-hospital and 1-year mortality which makes CAR more preferable.

Our study has many different aspects from previous studies. To the best of our knowledge, this is the first study presenting the data on the long-term mortality of COVID-19 in the general population. It is very important to use systemic scoring systems to minimize the risk of error in the interpretation of imaging findings of COVID-19. Therefore, we confirmed that the CAR and SII values correlated with disease severity using the CO-RADS scoring system. As an advantage compared to many other studies, ejection fraction values of patients with pre-existing HF and COVID-19-related HF were available in our study. Importantly, our study included a larger number of patients than many previous studies.

Our study has several limitations. First of all, this was a retrospective and single-center study. Second, the treatments such as steroids used in COPD/Asthma patients may have caused changes in inflammatory parameters. Third, the arrhythmias such as atrial fibrillation may affect the prognosis of the patients by causing thrombosis with a synergistic effect and pulmonary congestion, so the ECG findings of the patients could also be presented. Fourth, the D-dimer levels and viral load could also be presented with CAR and SII, as it provides valuable information in predicting thrombotic events and mortality. Fifth, we did not present the accurate cause of the deaths within one year after the diagnosis of COVID-19.

CONCLUSION

CAR and SII can be used as key parameters to predict both short-term and long-term prognosis from the time of diagnosis in patients with COVID-19.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Kırıkkale University Faculty of Medicine Clinical Resaerches Ethics Committee (Date: 25.05.2022, Decision No: 2022.05.20).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the manuscript, and they have approved the final version.

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