ORIGINAL ARTICLE

Car index as a predictor of mortality in hospitalized patients with COVID-19-associated pneumonia

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Summary

Introduction/Aim: COVID-19-associated pneumonia is a serious form of the disease that can result in severe life-threatening complications. This study aims to evaluate the prognostic value of the CAR index in hospitalized patients with COVID-19-associated pneumonia.

Material and Methods: This was a single-centre prospective study conducted at the University Clinical Centre Zvezdara during April 2020 which included hospitalized patients diagnosed with moderate to severe COVID-19-associated pneumonia. The COVID-19 infection was verified by real-time reverse-transcriptase polymerase chain reaction (RT-PCR) test on a sample obtained from a swab of the nasopharynx. The CAR was calculated as CRP and albumin ratio.

Results: Two hundred and eight hospitalized patients with COVID-19-associated pneumonia were enrolled. Average age was 54.5±14.6 years, and participants were predominantly male (64.4%). Comorbidities were present in 67.3% of patients. The overall in-hospital mortality was 14.4%. CAR index level of 2.0 was identified as the cut-off point for predicting mortality, with sensitivity of 86% and specificity of 72% (AUC=0.844). In univariate regression analysis age, comorbidities, breathing difficulties and CAR index were identified as significant predictors of mortality ($p<0.050$ for all). In the multivariate analysis, age (RR=1.06; 95% CI: 1.02-1.09; p=0.001) and CAR index (RR=1.12; 95% CI: 1.02-1.23; p=0.019), were independent predictors of mortality in COVID-19-associated pneumonia patients.

Conclusion: This study demonstrated that routine blood testing can be beneficial in identifying COVID-19 patients with associated pneumonia who are at an increased mortality risk. The CAR index is a widely accessible, simple inflammatory marker that can be a valuable indicator for early differentiating levels of severity in patients hospitalized due to COVID-19-associated pneumonia.

Keywords: CAR index, COVID-19, pneumonia, mortality

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INTRODUCTION

The SARS-CoV-2 pandemic has caused a severe public health crisis and placed considerable pressure on healthcare systems worldwide. It has emerged as a significant threat to global well-being, resulting in over seven million documented fatalities, according to the WHO (1–4). COVID-19 commonly manifests with a range of symptoms, fever, persistent cough, breathing difficulties, extreme fatigue, and muscle aches being the most frequent ones. In addition to the usual symptoms, in some cases, COVID-19 patients have been shown to develop severe pneumonia, which can progress to acute respiratory distress syndrome (ARDS) (5–9)China, was caused by a novel betacoronavirus, the 2019 novel coronavirus (2019-nCoV. This progression can also result in the failure of organs other than the lungs and, in the most severe cases, death (5–7, 10)China, was caused by a novel betacoronavirus, the 2019 novel coronavirus (2019-nCoV.

COVID-19-associated pneumonia is a serious form of the disease that can result in severe life-threatening complications (6). Better patient care and more effective treatment plans require early and accurate predictions of patient outcomes. Although age, comorbidities, and clinical symptoms are helpful indicators of the disease prognosis, identifying more reliable prognostic markers has become a crucial aspect of clinical management for COVID-19-associated pneumonia patients (6, 10–12)especially in patients admitted to ICU as it can provide more useful consumption of health resources, as well as prioritize critical care services in situations of overwhelming number of patients. Materials and Methods. A multivariable predictive model for mortality was developed using data solely from a derivation cohort of 160 COVID-19 patients with moderate to severe ARDS admitted to ICU. The regression coefficients from the final multivariate model of the derivation study were used to assign points for the risk model, consisted of all significant variables from the multivariate analysis and age as a known risk factor for COVID-19 patient mortality. The newly developed AIDA score was arrived at by assigning 5 points for serum albumin and 1 point for IL-6, D dimer, and age. The score was further validated on a cohort of 304 patients admitted to ICU due to the severe form of COVID-19. Results. The study population included 160 COVID-19 patients admitted to ICU in the derivation and 304 in the validation cohort. The mean patient age was 66.7 years (range, 20-93 years.

Since its discovery as an acute-phase protein, CRP has served as a systemic marker for tissue damage, infection, and inflammation (13,14). During acute inflammatory responses, CRP expression quickly rises from its referent level (13,14), which makes it a valuable indicator in tracking the progression of COVID-19, enabling early identification of severe cases and helping to reduce mortality rates (6,15–17) making it important to understand the peculiarities of different populations. The aim of this study was to identify the main predictors associated with in-hospital mortality due to COVID-19 in Vilnius, Lithuania. Materials and methods This was a retrospective observational cohort study conducted at Vilnius University Hospital Santaros Clinics, Lithuania. The study included SARS-CoV-2 positive patients aged over 18 years and hospitalized between March 2020 and May 2021. Depersonalized data were retrieved from electronic medical records. The predictive values of laboratory parameters were evaluated using ROC analysis. Multivariable binary logistic regression was performed to reveal predictors of in-hospital mortality due to COVID-19. Results Among 2794 patients, 54.4% were male, the age median was 59 years (IQR 48-70. Albumin is another marker commonly measured in COVID-19 patients. Inflammation greatly influences this hepatically synthesized protein, hindering its formation and accelerating its degradation, leading to reduced quantities in the bloodstream. Hospitalized patients with low admission levels of serum albumin exhibit an increased risk of death, both in the short and long term (18). Observations in COVID-19 patients further support this association between low albumin and poor prognosis, linking low albumin levels to a less favorable outcome (19).

Combining CRP and albumin into a single index offers a valuable approach to assessing inflammation. This method efficiently merges CRP and albumin information by calculating their ratio, resulting in an index that directly correlates with infection severity. An increased ratio indicates a more severe state of inflammation (20). Increased levels of C-reactive protein (CRP) indicate the presence of acute inflammation, while low levels of albumin in the blood signal a state of inadequate nutrition and chronic inflammation. Combining these characteristics into a unified index may provide a more comprehensive understanding of the patient's condition in contrast to analyzing individual indicators separately. The C-reactive protein-to-albumin ratio (CAR) has garnered attention as a reliable prognostic factor in many diseases (21–23) using Cox proportional hazard model and Kaplan-Meier survival analysis. The 28-day mortality was 28.0%. In the univariate analysis, the Acute Physiology and Chronic Health Evaluation II (APACHE II, prompting further investigation about its potential in predicting mortality in patients with COVID-19 and its common complications (24,25). Therefore, this study aims to evaluate the prognostic value of the CAR index in hospitalized patients with COVID-19-associated pneumonia.

MATERIALS AND METHODS

This single-center prospective study was conducted at the University Clinical Centre Zvezdara in April 2020, involving hospitalized patients diagnosed with moderate to severe COVID-19-associated pneumonia. For conducting this research, the approval from the Ethics Committee of the University Clinical Centre Zvezdara was obtained.

COVID-19 infection was confirmed through a real-time reverse-transcriptase polymerase chain reaction (RT-PCR) test on a nasopharyngeal swab sample. Patients were excluded if they had a history of hematological and/or autoimmune cancers. The patients' data were extracted from the electronic hospital information system, while anamnestic data were collected during the first day of hospitalization. Each patient underwent a chest X-ray to verify the diagnosis and location of pneumonia. Hematological and biochemical laboratory values were gathered within the first 24 hours of admission as part of the routine assessment. The neutrophil-to-lymphocyte ratio (NLR) was calculated by dividing the proportion of neutrophils by the percentage of lymphocytes. The CAR was calculated by dividing the value of CRP by the value of albumin. Pulse oximetry was monitored at regular intervals of two hours or continuously in individuals with severe COVID-19-associated pneumonia. Patients whose oxygen saturation levels were equal to or below 92% received oxygen treatment. The discharge criteria for patients were a negative nasopharyngeal swab and a radiographically confirmed reduction of pneumonia symptoms.

Statistical analysis

The descriptive statistics, including means, medians, standard deviations, and percentiles for numerical variables and absolute numbers and percentages for categorical variables, were used to characterize the study sample. Associations between categorical data were evaluated using the Pearson chi-square test or Fisher's exact test. Student's t-test or Mann-Whitney U test were used for numerical data to evaluate differences between patients with lethal outcomes and discharged patients. Univariate and multivariate logistic regression analyses were used to establish factors related to overall mortality. Significant variables from univariate analysis were included in multivariate regression, with mortality as the outcome. The results were expressed as relative risk and the corresponding 95% confidence interval (CI). Model discrimination performance was tested by means of sensitivity and specificity. The C statistic, representing the area under the receiver operating characteristic (ROC) curve, was used for the overall assessment of the predictive model. In all analyses, the level of statistical significance was set at $p \leq 0.05$. SPSS version 25 statistical software (Chicago, IL, USA) was used to perform the statistical analysis.

RESULTS

Two hundred and eight hospitalized patients with COVID-19-associated pneumonia took part in the study. The average age was 54.5±14.6 years, and the patients were predominantly male.

Table 1 presents the characteristics of the study population based on the occurrence of the lethal outcome. The overall in-hospital mortality of patients with COVID-19-associated pneumonia was 14.4%. The mean age was significantly higher in the lethal outcome group (67.8±13.0 years) compared to the non-lethal group (52.3±13.6 years) ($p<0.001$). Obesity was significantly more prevalent in patients with lethal outcome (30.0%) compared to discharged patients (14.6%) ($p=0.037$). Similarly, hyperlipoproteinemia (53.3% vs. 20.8%, $p<0.001$), diabetes mellitus (50.0% vs. 17.4%, $p<0.001$), chronic renal failure (16.7% vs. 6.2%, $p=0.046$), cardiovascular disease (73.3% vs. 52.8%, $p=0.036$), hypertension (70.0% vs. 46.1%, $p=0.015$), and the presence of comorbidities (90.0% vs. 63.5%, $p=0.004$) were all significantly more prevalent in the lethal outcome group. Coronary heart disease, autoimmune disease, pulmonary disease, and cancer did not show significant differences between the groups **(Table 1)**.

Table 1. Characteristics of study population according to lethal outcome

Variables	Total n=208	Exitus letalis: No n=178	Exitus letalis: Yes n=30	p
Gender-Male	134 (64.6)	112 (62.9)	22 (73.3)	0.270
Age*	54.6±13.5	52.3±13.6	67.8±13.0	**<0.001**
Smoking	34 (16.3)	32 (18.0)	2 (6.7)	0.121
Obesity	35 (16.8)	26 (14.6)	9 (30.0)	**0.037**
Hyperlipoproteinemia	53 (25.5)	37 (20.8)	16 (53.3)	**<0.001**
Diabetes mellitus	46 (22.1)	31 (17.4)	15 (50.0)	**<0.001**
Chronic renal failure	16 (7.7)	11 (6.2)	5 (16.7)	**0.046**
Cardiovascular disease	116 (55.8)	94 (52.8)	22 (73.3)	**0.036**
Hypertension	103 (49.5)	82 (46.1)	21 (70.0)	**0.015**
Coronary heart disease	25 (12.0)	18 (50.0)	7 (70.0)	0.261
Autoimmune disease	23 (11.1)	19 (10.7)	4 (13.3)	0.667
Pulmonary disease	8 (3.8)	7 (3.9)	1 (3.3)	1.000
Cancer	4 (1.9)	3 (1.7)	1 (3.3)	0.466
Comorbidities	140 (67.3)	113 (63.5)	27 (90.0)	**0.004**

Data are presented as n (%) and Pearson chi-square test or Fisher's exact test were used; *Data are presented as mean±sd and Student's t-test was used;

Table 2. Patients' symptoms at admission according to lethal outcome

Variables	Exitus letalis		p
	No n=178	Yes n=30	
Asymptomatic form of the disease	6 (3.4)	0 (0)	0.308
Prolonged contact with an infected person	27 (15.3)	3 (10)	0.582
Number of days from the onset of symptoms until admission to the hospital*	6 (1 - 22)	6.5 (2 - 15)	0.431
Breathing difficulties	34 (19.2)	16 (53.3)	**<0.001**
Cough	131 (73.6)	24 (80.0)	0.456
Fever	160 (89.9)	27 (90.0)	1.000
Fatigue	111 (62.4)	30 (100)	**<0.001**
Sore throat	18 (10.1)	1 (3.3)	0.321
Runny nose	10 (5.6)	0 (0)	0.363
Myalgia	28 (15.7)	4 (13.3)	1.000
Smell blindness	11 (6.2)	1 (3.3)	1.000
Taste blindness	12 (6.7)	0 (0)	0.222
Conjunctivitis-No	178 (100)	30 (100)	NA
Headache	17 (9.6)	0 (0)	0.141
Diarrhea	15 (8.4)	4 (13.3)	0.489
Loss of appetite	19 (10.7)	4 (13.3)	0.752
Chest pain	20 (11.2)	4 (13.3)	0.758

Data are presented as n (%) and Pearson chi-square test or Fisher's exact test were used; *Data are presented as median (range) and Mann-Whitney U test was used;

Symptoms experienced by patients with COVID-19-associated pneumonia based on their lethal outcome status are presented in **Table 2**. None of the patients with lethal outcome were asymptomatic. The median number of days from symptom onset to hospital admission was similar between the groups, with 6 days for the non-lethal group and 6.5 days for the lethal group (p=0.431). Breathing difficulties were significantly more prevalent in the lethal outcome group (53.3%) compared to the non-lethal group (19.2%) (p<0.001). Fatigue was present in all patients with lethal outcome (100%). All patients in both groups were free of conjunctivitis **(Table 2)**.

The use of mechanical ventilation was significantly more common among patients with lethal outcome (73.3%) compared to those who survived (5.1%) (p<0.001). Similarly, oxygen (O2) therapy was required for nearly all patients in the lethal outcome group (96.7%). The median number of days on O2 therapy was significantly longer for patients with lethal outcome compared to those who survived (8 days and 4 days, respectively; p=0.003). The median number of days of hospitalization differed significantly between the groups (p=0.001). Patients with lethal outcome had a shorter median hospital stay (8.5 days, range 1-22) compared to those who survived (14 days, range 3-44) **(Table 3)**.

Patients with lethal outcome had significantly higher median leukocyte counts (p<0.001) and neutrophil counts (p<0.001), while lymphocyte counts (p<0.001), eosinophil counts (p<0.001) and total protein levels were significantly lower in the lethal outcome group compared to those who survived. The neutrophil-to-lymphocyte ratio (NLR) was higher in the lethal outcome group than in the non-lethal group (p<0.001). Monocyte counts did not differ significantly between the groups (p=0.306). Patients with lethal outcome had significantly higher median uric acid levels (375.5, range 110-760) compared to

Table 3. Oxygen support in COVID-19-associated pneumonia patients according to lethal outcome

Variables		Exitus letalis		p
		No n=178	Yes n=30	
Mechanical ventilation		9 (5.1)	22 (73.3)	**<0.001**
O2 therapy		87 (48.9)	29 (96.7)	**<0.001**
Number of days on O2 therapy*		4 (0 - 32)	8 (1 - 30)	**0.003**
Oxygen therapy	Up to 5l	33 (40.7)	0 (0)	**<0.001**
	Over 5l to 10l	26 (32.1)	2 (7.7)	
	Over 10l	22 (27.2)	24 (92.3)	
Number of days of hospitalization*		14 (3 - 44)	8.5 (1 - 22)	**0.001**

Data are presented as n (%) and Pearson chi-square test or Fisher's exact test were used; *Data are presented as median (range) and Mann-Whitney U test was used;

Table 4. Patients' hematological and biochemical parameters at admission according to lethal outcome

Variables	Exitus letalis		p
	No n=178	Yes n=30	
Leukocytes	5.4 (1.8 – 19.3)	8.3 (2.6 – 22.5)	**<0.001**
Neutrophils	3.6 (0.9 – 17.6)	7.1 (2.0 – 20.6)	**<0.001**
Lymphocytes	1.1 (0.3 – 32.4)	0.7 (0.1 – 2.3)	**<0.001**
NLR	3.2 (0.7 – 27.6)	7.9 (0.3 – 95.3)	**<0.001**
Eosinophils	0 (0 – 1.9)	0 (0 – 0.1)	**<0.001**
Monocytes	0.4 (0.1 – 0.7)	0.3 (0.1 - 1)	0.306
Uric acid	270 (90 - 645)	375.5 (110 - 760)	**0.038**
D dimer	1.1 (0.1 – 31.1)	2.1 (0.5 – 13.2)	**0.027**
CRP	26.2 (0.2 – 371.8)	98.4 (28.5 – 420.9)	**<0.001**
Albumin	36 (22 - 48)	31 (18 - 38)	**<0.001**
CAR	2.2 (0 – 14.3)	3.2 (0.7 - 15)	**<0.001**
Total protein	71 (54 - 82)	64 (51 - 80)	**<0.001**

Data are presented as median (range) and Mann-Whitney U test was used;

those who survived (270, range 90-645) (p=0.038). D-dimer levels were also significantly elevated in the lethal outcome group compared to the non-lethal group (2.1 vs. 1.1, respectively; p=0.027). CRP levels were significantly higher in the lethal outcome group (p<0.001), while albumin levels were significantly lower in the lethal outcome group (p<0.001) compared to those who survived. In the lethal outcome group, the median CAR index was 3.2 (range 0.7-15), whereas in the non-lethal outcome group, the median CAR index was 2.2 (range 0-14.3). This difference was statistically significant (p < 0.001) **(Table 4)**.

The optimal cut-off value for the CAR index was determined based on ROC curve analysis. The area under the curve (AUC) value for the CAR index was 0.844. This analysis identified a CAR index level of 2.0 as the cutoff point for predicting mortality in COVID-19-associated pneumonia patients, with a sensitivity (Sn) of 86% and a specificity (Sp) of 72% **(Figure 1)**.

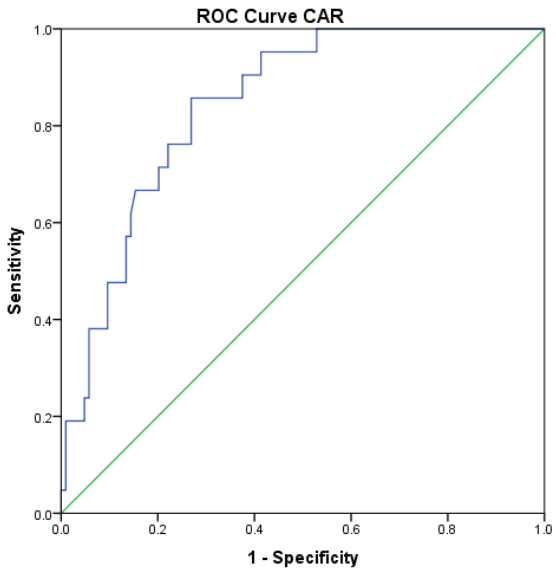

Figure 1. ROC curve for CAR index

The results of univariate and multivariate logistic regression analyses with lethal outcomes are presented in Table 5. In univariate regression analysis, age (p<0.001), comorbidities (p=0.019) and breathing difficulties (p=0.001) were identified as significant predictors of mortality in COVID-19-associated pneumonia patients. The CAR index was another significant factor, with an RR of 1.16 (95% CI: 1.06-1.28, p=0.001) **(Table 5)**.

In the multivariate regression analysis, age, with an RR of 1.06 (95% CI: 1.02-1.09, p=0.001) and CAR index, with an RR of 1.12 (95% CI: 1.02-1.23, p=0.019), were independent predictors of mortality in COVID-19-associated pneumonia patients **(Table 5)**.

DISCUSSION

The results of our study emphasize the significance of the CAR index in predicting mortality risk in hospitalized patients with COVID-19-associated pneumonia. The CAR index of ≥2.0 has been shown to be a reliable prognostic indicator for mortality in patients with COVID-19-associated pneumonia. It demonstrates high sensitivity in identifying those at risk of death and moderate specificity in accurately identifying those not at risk.

Our study has demonstrated that COVID-19 has a significant mortality rate, with the overall mortality of hospitalized patients being 14.4%. This finding aligns with a study conducted in Lithuania, which reported an in-hospital mortality rate of 12.7% (15) and closely matches the 13% mortality rate found by Fakih et al. in the US (26) and 13.9% case fatality rates reported in a systematic review by Rodriguez-Morales et al. (27). In contrast, Gujski et al. in Poland reported a higher in-hospital mortality rate of 18.4% (28). Moreover, research carried out in the UK revealed a death rate of 32.4% among patients who were hospitalized (19). This finding aligns with anoth-

Table 5. Univariate and multivariate regression analysis with mortality as dependent variable

Variables	Univariate analysis				Multivariate analysis			
	RR	95% CI	p		RR	95% CI	p	
Age	1.06	1.03	1.09	**<0.001**	1.06	1.02	1.09	**0.001**
Comorbidities	4.15	1.26	13.69	**0.019**				
Breathing difficulties	3.26	1.58	6.71	**0.001**				
CAR	1.16	1.06	1.28	**0.001**	1.12	1.02	1.23	**0.019**

RR-relative risk; CI-Confidence Interval;

er study that included 16.749 hospitalized patients with COVID-19 in the UK, which indicated a mortality rate of 33% (29). However, it is important to note that mortality rates within hospitals varied between several waves of the COVID-19 pandemic and across different populations (30–32).

From the first COVID-19 cases, it was observed that symptomatic patients had flu-like symptoms: fever, cough, fatigue, slight dyspnea, sore throat, headache, conjunctivitis, and gastrointestinal issues (33)a novel coronavirus from the same family as SARS-CoV and Middle East respiratory syndrome coronavirus, has spread worldwide leading the World Health Organization to declare a pandemic. The disease caused by SARS-CoV-2, coronavirus disease 2019 (COVID-19. In our study, breathing difficulties and fatigue were more frequently present at the beginning of the disease in deceased patients, which aligns with the findings of other authors (5)China, was caused by a novel betacoronavirus, the 2019 novel coronavirus (2019-nCoV.

Patients with COVID-19-associated pneumonia with a fatal outcome were more likely to have pre-existing conditions such as diabetes, obesity, hypolipoproteinemia, chronic renal failure, cardiovascular disease, and hypertension, compared to those who survived in our study. The role of comorbidities in COVID-19 mortality has been well-documented, with one recent meta-analysis specifically examining the prevalence of diabetes, hypertension, obesity, and asthma. This publication reports an overall incidence of hypertension, affecting 39% of patients, diabetes and obesity in 27% of patients. Additionally, the study found an 18% death rate among hospitalized patients with COVID-19 worldwide (34).

Diabetes is a prevalent comorbidity in COVID-19 patients, associated with severe complications (35)Setting, and Participants: Case series of patients with COVID-19 admitted to 12 hospitals in New York City, Long Island, and Westchester County, New York, within the Northwell Health system. The study included all sequentially hospitalized patients between March 1, 2020, and April 4, 2020, inclusive of these dates. Exposures: Confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2. In a study conducted on 5700 COVID-19 patients from 12 hospitals in the USA, diabetes was identified as the third most common comorbidity, present in approximately 34% of patients, following hypertension (56%), and obesity (42%) (35)Setting, and Participants: Case series of patients with COVID-19 admitted to 12 hospitals in New York City, Long Island, and Westchester County, New York, within the Northwell Health system. The study included all sequentially hospitalized patients between March 1, 2020, and April 4, 2020, inclusive of these dates. Exposures: Confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2. As in our study, publications consistently indicate that diabetes exacerbates the severity of COVID-19 outcomes (36). Patients with diabetes who had blood glucose level higher than 10 mmol/L had two to three times higher risk of severe COVID-19 and mortality compared to patients without diabetes (37)219 participants from IDF's Western Pacifi c Region who took part in the survey, there were almost equal numbers of men (2,124.

Obesity is a recognized risk factor for cardiovascular and respiratory complications, and its prevalence has raised concerns about its impact on COVID-19 outcomes (38,39). It increases the expression of ACE-2 receptors, contributes to organ damage, increases abdominal pressure, limits chest expansion and movement, and leads to insufficient respiratory compensatory function (40–43). Additionally, it impairs immune function and promotes inflammation, all of which may exacerbate the severity of COVID-19 (39). Studies indicate that higher body mass index (BMI) correlates with increased risks of hospitalization, ICU admission, and death in COVID-19 patients (44). The results of our study provide additional supporting evidence for the association between obesity and increased COVID-19 mortality rates.

Existing research has established a clear association between chronic cardiac disease and worse outcomes in COVID-19 patients. Studies have consistently shown that pre-existing chronic cardiac disease is a major risk factor for worse outcomes in COVID-19 patients who develop pneumonia (45). This increased risk is likely due to the significant strain severe pneumonia places on the heart's ventricles. This strain can lead to left ventricular dysfunction, potentially progressing to cardiogenic shock. Our findings align with existing research demonstrating a strong correlation between chronic cardiovascular disease (CVD) and increased mortality in patients with COVID-19 (46)epidemiology, clinical features, progression, and prognosis of the disease. Early identification of risk factors and clinical outcomes might help in identifying critically ill patients, providing appropriate treatment, and preventing mortality. We conducted

a prospective study in patients with flu-like symptoms referred to the imaging department of a tertiary hospital in Iran between March 3, 2020, and April 8, 2020. Patients with COVID-19 were followed up after two months to check their health condition. The categorical data between groups were analyzed by Fisher's exact test and continuous data by Wilcoxon rank-sum test. Three hundred and nineteen patients (mean age 45.48 ± 18.50 years, 177 women. A meta-analysis by Zhao et al. revealed that CVD elevated the mortality risk for COVID-19 patients by approximately fivefold (47).

Arterial hypertension is one of the most prevalent comorbidities found in COVID-19 patients. Despite its common occurrence, it remains unclear whether hypertension itself is a direct aggravating factor or if its impact is mainly due to its frequent association with older age and the resultant weakened immune system (48).

Recent meta-analysis reported an increase in mortality in overweight and obese COVID-19 patients in ten out of eleven analysed studies. Only one study did not find a difference in mortality between overweight and normal-weight patients. However, overweight patients demonstrated an increase in the severity of symptoms (12,34,49–52)and the clinical and laboratory characteristics associated with severity of illness. Design Prospective cohort study. Setting Single academic medical center in New York City and Long Island. Participants 5279 patients with laboratory confirmed severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2.

The majority of routine laboratory parameters measured at admission were significantly different in deceased patients compared to patients who survived. These included the number of leukocytes, neutrophils, lymphocytes, and eosinophils, as well as D dimer, CRP, albumins, total protein, uric acid, and the NLR and CAR index. Our findings are in agreement with those of other authors (17,53–55) and highlight the potential prognostic value of these markers in COVID-19-related pneumonia. Considering that each of these parameters may be performed routinely, the significance of their predictive value lies in their wide availability.

Age and the CAR index were independent predictors of fatal outcomes in our study. Older patients were recognized to be at risk for mortality in almost all studies (24,56). CRP and albumin are often used to measure the level of inflammation (22). After the production of various cytokines in the infection (and some other conditions), the increase in C-reactive protein (CRP) is stimulated, and its high levels are associated with poor prognosis in critically ill patients (21,57)using Cox proportional hazard model and Kaplan-Meier survival analysis. The 28-day mortality was 28.0%. In the univariate analysis, the Acute Physiology and Chronic Health Evaluation II (APACHE II. Decreased serum albumin concentration was also shown to be a predictor of mortality in previous studies (18,21). CRP and albumin are known as positive and negative acute phase reactants, but their ratio (CRP/albumins) is considered a more precise indicator of inflammation (20,22).

The first study to report a significant and positive correlation between the CAR index and the severity of COVID-19 was published in 2020 by Wang et al. Consistent with our study's results, this study found that the level of CAR index was significantly higher among patients with severe COVID-19 in comparison with patients with non-severe symptoms. The results of the multivariate regression analyses that were reported in this research further demonstrated that CAR is an independent risk factor for the severity of COVID-19 (25). Another study, conducted in Turkey in 2021, evaluated the predictive value of the CAR index among COVID-19 patients. The authors of this study demonstrated the effectiveness of using the CAR for early differentiation of COVID-19 severity in hospitalized patients. The multivariate logistic regression analysis model in this study supports the claim that in severe cases of COVID-19, CAR can be considered a distinct risk factor. The ROC curve analysis performed in this study identified 0.9 as the relevant cut-off value of the CAR index for discrimination of severe COVID-19 patients, with 69.1% sensitivity and 70.8% specificity. In addition, the CAR index demonstrated a higher AUC in ROC analysis compared to CRP, indicating its superiority as a marker for early identification of severe COVID-19 (24).

This study has several limitations. Due to the small sample size, single-centre design, and inclusion of only hospitalized patients, it is not possible to generalize our results to the population of COVID-19 patients not requiring hospital admission. Larger multi-centre studies are necessary to confirm the use of CAR as a cost-effective prognostic index.

CONCLUSION

This study demonstrated that routine blood testing can be beneficial in identifying COVID-19 patients with associated pneumonia who are at a higher risk of mortality. The CAR index is a widely accessible, simple inflammatory parameter that can be a valuable indicator for early differentiating levels of severity in patients who have been admitted to hospital due to COVID-19-associated pneumonia. Using the CAR index ensures patient monitoring and management during pandemics such as COVID-19.

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CAR INDEKS U PREDIKCIJI MORTALITETA KOD PACIJENATA HOSPITALIZOVANIH USLED PNEUMONIJE IZAZVANE KOVIDOM 19

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Sažetak

Uvod/Cilj rada: Pneumonija izazvana kovidom 19 predstavlja ozbiljan oblik bolesti koji može dovesti do teških komplikacija koje ugrožavaju život. Ova studija ima za cilj da proceni prognostičku vrednost CAR indeksa kod hospitalizovanih pacijenata sa pneumonijom izazvanom kovidom 19.

Metod: Istraživanje je sprovedeno kao prospektivna kohortna studija u Univerzitetskom kliničkom centru Zvezdara tokom aprila 2020. Godine. U studiju su uključeni pacijenati koji su hospitalizovani zbog dijagnostikovane umerene do teške pneumonije uzrokovane kovidom 19. Infekcija usled kovida 19 potvrđena je reakcijom lančane polimeraze reverznom transkripcijom u realnom vremenu (RT-PCR) iz brisa nazofarinksa. CAR indeks je izračunat kao količnik CRP-a i albumina.

Rezultati: U studiju je uključeno 208 hospitalizovanih pacijenata sa pneumonijom izazvanom kovidom 19, prosečne starosti 54,5±14,6 godina, pretežno muškog pola (64,4%). Komorbiditeti su bili prisutni kod 67,3% pacijenata. Ukupan bolnički mortalitet iznosio je 14,4%. Vrednost CAR indeksa od 2,0 identifikovana je kao tačka preseka za predikciju mortaliteta, uz senzitivnost od 86% i specifičnost od 72% (AUC=0,844). U univarijantnoj regresionoj analizi, starost, komorbiditeti, otežano disanje i CAR indeks identifikovani su kao značajni prediktori mortaliteta (p<0,050, za sve analize). U multivarijantnoj analizi, starost (RR=1,06; 95% CI: 1,02-1,09; p=0,001) i CAR indeks (RR=1,12; 95% CI: 1,02-1,23; p=0,019) bili su nezavisni prediktori mortaliteta kod hospitalizovanih pacijenata sa pneumonijom izazvanom kovidom 19.

Zaključak: Rutinska analiza krvi može biti korisna u identifikaciji pacijenata sa pneumonijom izazvanom kovidom 19 koji su pod povećanim rizikom od letalnog ishoda. CAR indeks je široko dostupan, jednostavan inflamatorni marker koji može biti indikator za ranu diferencijaciju težine bolesti pacijenata sa pneumonijom uzrokovanom kovidom 19.

Ključne reči: CAR indeks, kovid 19, pneumonija, mortalitet

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