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Use of Soluble Suppression of Tumorigenicity 2 for Predicting the Need for Intubation and Mortality Outcomes in Patients with COVID-19

COVID-19'da Entübasyon İhtiyacı ve Mortaliteyi Öngörmede Soluble Suppression of Tumorigenicity 2

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Abstract

Introduction: Suppression of tumorigenicity 2 (ST2) plays a key role in the serious complications that may occur during Coronavirus disease-2019 (COVID-19), including systemic inflammatory condition, sepsis, Acute respiratory distress syndrome, and fibrosis. In this study, we evaluated the relationship between the serum ST2 concentrations and the mortality and need for mechanical ventilation.
Materials and Methods: A prospective observational study was conducted in patients diagnosed with COVID-19 who presented to the emergency department (ED) between October 2021 and April 2022. Patients with Severe acute respiratory syndrome-Coronavirus-2 infection were consecutively enrolled according to the clinical spectrum defined in the guidelines. Admission to the intensive care unit (ICU), requirement of intubation, and 90-day mortality were the primary study outcomes. Clinical, imaging and laboratory data were assessed to determine the clinical spectrum and severity scores. ST2 was assessed using the micro ELISA method and Sandwich-ELISA principle.
Results: Of the 64 (48.5%) patients admitted to the ICU, 43 (32.6%) required mechanical ventilation. During the 90-day follow-up period, 44 (33.3%) patients died due to clinical deterioration. The median ST2 concentration at admission was 272.5 ng/mL in patients who died and 55.95 ng/mL in patients who survived ($p<0.001$). The median ST2 concentration at admission was 280 and 61.1 ng/mL in patients who did and did not require mechanical ventilation, respectively ($p<0.001$). Areas under the receiver operating characteristic curve of the ST2 level for predicting death and need for mechanical ventilation were 0.77 ($p<0.001$) and 0.79 ($p<0.001$), respectively.
Conclusion: Suppression of tumorigenicity 2 concentration at the time of admission from the ED is a valuable biomarker because it is more effective than lymphocyte count and D-dimer and ferritin levels in predicting the need for mechanical ventilation and mortality in patients with COVID-19.
Keywords: Biomarker, COVID-19, intubation, mortality, soluble ST2

Öz

Giriş: Suppression of tumorigenicity 2 (ST2) sistemik enflamatuvar durum, sepsis, Akut solunum sıkıntısı sendromu ve fibrozis gibi Koronavirüs hastalığı-2019 (COVID-19) hastalık sürecinde ortaya çıkabilecek tüm ciddi komplikasyonlarda anahtar rol oynamaktadır. Bu çalışmada çözünür ST2'nin serum konsantrasyonları ile mortalite ve mekanik ventilasyon gereksinimi arasındaki ilişkiyi değerlendirdik.
Gereç ve Yöntem: Bu prospektif gözlemsel çalışma Ekim 2021 ile Nisan 2022 tarihleri arasında acil servise başvuran ve COVID-19 tanısı alan hastalarla gerçekleştirilmiştir. Şiddetli akut solunum yolu sendromu-Koronavirüs-2 enfeksiyonu ile başvuran hastalar, kılavuzlarda tanımlanan klinik spektruma göre ardışık olarak çalışmaya dahil edildi. Yoğun bakım ünitesine kabul, entübasyon gerekliliği ve 90 gün içinde ölüm, çalışmanın birincil

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Öz

sonuçlarıydı. Klinik, görüntüleme ve laboratuvar verileri klinik spektrum ve şiddet skorlarına göre değerlendirildi. Suppression of tumorigenicity 2 testi mikro ELISA yöntemi ve Sandwich-ELISA prensibiyle çalışıldı.

Bulgular: Altmış dört (%48,5) hasta yoğun bakım ünitesine yatırıldı ve bu hastaların 43'üne (%32,6) mekanik ventilasyon gerekti. Doksan günlük takip süresi içerisinde 44 (%33,3) hasta klinik kötüleşme nedeniyle hayatını kaybetti. Ölen hastaların başvuru anındaki ST2 medyan değeri 272,5 ng/mL, hayatta kalan hastaların ise 55,95 ng/mL olarak saptandı (p<0,001). Mekanik ventilasyon ihtiyacı olan hastaların başvuru anındaki ST2 medyan değeri 280 ng/mL, gelişmeyen hastaların ise 61,1 ng/mL olarak saptandı (p<0,001). Ölümü ve mekanik ventilasyon ihtiyacını tahmin etmek için çözünebilir ST2 seviyelerinin ROC eğrisi altında kalan alanları sırasıyla 0,77 (p<0,001) ve 0,79 (p<0,001) idi.

Sonuç: Başvuru anında ölçülen ST2, COVID-19'da mekanik ventilasyon ihtiyacını ve mortaliteyi öngörmede lenfosit sayısı, D-dimer ve ferritinden daha etkili olduğu için acil serviste kullanılabilecek değerli bir biyobelirteçtir.

Anahtar Kelimeler: Biyobelirteç, COVID-19, entübasyon, mortalite, çözünebilir ST2

Introduction

Since March 2022, the number of Coronavirus disease-2019 (COVID-19) cases has gradually decreased, and the disease had almost completely disappeared in March 2023. However, since the beginning of August 2023, daily hospital admissions due to the COVID-19 variant XBB Omicron have more than doubled[1]. Although it does not currently pose a significant issue, further studies are required and precautions should be taken in terms of global pandemic risks that may arise[2]. The WHO published a new report on the new EG.5 (Eris) mutated variant of COVID-19 in August 2023[3]. A mutation-induced single amino acid change in the viral genome can increase the virus adaptation to counteract the immune system response[4].

Severe acute respiratory syndrome-Coronavirus-2 (SARS-CoV-2) has the ability to damage several organ systems. Endothelial dysfunction and damage in COVID-19 is associated with inflammation and immune-mediated response. The identified damage mechanism is an important diagnostic and therapeutic target[5]. Cytokines are the main mediators of inflammation. Interleukin (IL)-33 of the cytokine family participates in the pathogenesis of inflammatory diseases. Thus, targeting IL-33/suppression of tumorigenicity 2 (ST2) signaling may be a convenient treatment option for virus-induced lung diseases[6]. The biologically active form of IL-33 binds to a ST2 receptor complex consisting of the IL-1 receptor auxiliary protein. This receptor complex is distributed in the respiratory epithelial barrier sites, peripheral mast cells, mononuclear cells, Th2 cells, and natural killer cells[7]. Increased local activation of IL-33/ST2 and increased blood ST2 concentrations are reportedly associated with the severity of acute viral lower respiratory tract infections in children[8]. In infections such as SARS-CoV-2, overproduction of proinflammatory mediators, known as "cytokine storm," occurs from cytotoxic T lymphocytes and an abnormal systemic inflammatory response develops[9]. In severe acute SARS-CoV-2, the primary site of infection is type 2 alveolar epithelial cells in the distal lung. Patients with chronic pulmonary disease, pulmonary arterial hypertension, and bronchiectasis are more likely to contract SARS-CoV-2 and have a higher risk of severe infection than patients without these comorbidities[10]. Epithelial destruction and repair and the subsequent remodeling are critical features of bacterial infections, viral infections, and chronic obstructive pulmonary disease. Interleukin-33 released from damaged airway epithelium causes ST2-receptor dependent and ST2-independent inflammation[11]. Different host immune responses lead to a wide spectrum of disease severity. Suppression of tumorigenicity 2 plays a key role in all serious complications that may occur during COVID-19, such as systemic inflammatory condition, sepsis, acute respiratory distress syndrome, and fibrosis[12].

In this study, we aimed to evaluate the relationship between the serum concentrations of soluble ST2 and the 90-day mortality and mechanical ventilation requirement.

Materials and Methods

Study Design

In this study, we prospectively analyzed patients who presented to the emergency department (ED) of a tertiary care hospital between October 2021 and April 2022 and who were diagnosed with SARS-CoV-2 infection. The study protocol was approved by the Sakarya University Clinical Research Ethics Committee (no: 428, date: 01.10.2021). All participants provided informed written consent. When patients were in critical condition, their families provided informed written consent. All procedures were carried in accordance with the principles of the Declaration of Helsinki.

Study Setting and Population

The inclusion criteria were detection of SARS-CoV-2 in real-time polymerase chain reaction, presence of COVID-19 symptoms, and age >18 years. The following were the exclusion criteria: advanced heart failure, acute renal failure, rheumatological disease, active pulmonary tuberculosis, history of surgery and

infection in the last month, acute cerebrovascular disease, acute coronary syndrome, liver cirrhosis, or refusal to participate in the study. The following data were recorded from the public health management system and medical charts by investigators blinded to the results: age, sex, comorbidities, laboratory test results [white blood cell (WBC) count, neutrophil count, lymphocyte count, and levels of C-reactive protein (CRP), troponin, D-dimer, ferritin, pH, and lactate], dispositions, and outcomes. Before assessing the results, the investigators were blinded to the ST2 concentrations. Decisions for all clinical processes were taken independent of the soluble ST2 levels. Blood levels of the biomarker were measured after study termination. Requirement of mechanical ventilation and mortality within 90 days were the primary outcomes of the study. Each patient's vital status was verified using the social security death index. The public health management system was used to track the patients' hospital stays and subsequent 90-day follow-up.

Laboratory Analysis

Blood samples obtained at the time of admission to the ED were collected in tubes containing EDTA. The collected samples were used immediately for routine biochemical evaluations. After routine biochemical evaluations, the remaining serum and plasma samples were stored in a freezer at -80 °C until the day of further analysis. The physician who performed the biochemistry analysis was blinded to the patient's clinical characteristics. On the day of the analysis, the kit and samples to be used were brought to room temperature. Suppression of tumorigenicity 2 test (Human ST2 Kit; Elabscience Co., Wuhan, China) utilizes the micro ELISA method and Sandwich-ELISA principle. ELISA was performed using the Triturus automated device (Grifols Diagnostic, Spain). By comparing the optical density of the samples with that of the standard curve, the ST2 value was quantitatively calculated and recorded in ng/mL (signal/cut-off).

Statistical Analysis

The sample size was calculated on the basis of diagnostic efficacy of other pneumonia-related markers in previous studies. Sample size analysis with a 5% margin of error and 95% power in the large effect size (d=0.8) revealed that at least 72 patients were required for the study. Descriptive statistics are presented as frequency and percentage, mean and standard deviation, or median and 25-75% percentile (Q1-Q3). Normality assumption was evaluated by analyzing histograms, q-q plot, skewness, and kurtosis values using the Shapiro-Wilk test. To compare the numerical data between two groups, the independent samples t-test was used when the data were normally distributed. However, the Mann-Whitney U test was used when the data were not normally distributed. The relationships between the categorical data were analyzed using the Fisher's exact test when the number of cells with an expected value of <5 was actually >20%; if not, the Pearson chi-square test was used. The sensitivity, specificity, positive predictive value, negative predictive value of the levels of CRP, D-dimer, ferritin, lymphocyte, ST2, and troponin, WBC count, and PSI score in the mortality and intubation groups were presented as numerical variables. The cut-off points of these parameters were evaluated by receiver operating characteristic (ROC) analysis. A p value of <0.05 was considered statistically significant. All analyses were performed using Statistical Package for the Social Sciences (version 20.0; IBM Corp., Armonk, NY, USA).

Results

In this study, 132 patients (72 females; mean age, 65.9±18.2 years) with a diagnosis of SARS-CoV-2 were included. Of the 64 (48.5%) patients admitted to the intensive care unit (ICU), 43 (32.6%) required mechanical ventilation. During the 90-day follow-up period, 44 (33.3%) patients died due to clinical deterioration. Demographic characteristics of the study population are summarized in Table 1. Only 11.5% of the patients hospitalized in the ward required mechanical ventilation, whereas the rate was 88.4% in the ICU. The mortality rate of patients hospitalized in the ICU was 84.1%. The soluble ST2 concentration and other laboratory parameter values in patients who did and did not require mechanical ventilation are presented in Table 2. There were statistically significant differences in the CRP, troponin, ferritin, D-dimer, and ST2 levels at admission between patients who did and did not require mechanical ventilation. Furthermore, there were statistically significant differences in the CRP, troponin, ferritin, D-dimer, and ST2 levels at admission between patients who died and those who survived (Table 3). The ROC curves demonstrating the role of laboratory test results at admission in predicting the need for intubation and mortality rate are shown in Figures 1 and 2, respectively. The AUCs generated from the ROC analysis are compiled in Table 4. All the biomarkers, except lymphocyte count, proved useful in predicting the need for mechanical ventilation and mortality.

Discussion

To the best of our knowledge, this is the first prospective study to evaluate and compare the combined prognostic accuracy of ST2, CRP, troponin, ferritin and D-dimer levels in patients with SARS-CoV-2 infection. The study results demonstrate that the ST2, troponin, and CRP levels are the most reliable biomarkers for predicting the prognosis of COVID-19.

In the management of viral pandemics, the biggest challenge is distinguishing patients who may require hospital care from patients who can be managed at home. Although clinical risk classification is the key to effective patient management, the

pathophysiological basis for predicting prognosis remains to be fully elucidated[13].

Interleukin-33 is usually released after cell or tissue damage, and it activates the signaling pathways in cells expressing the ST2 receptor[14]. Interleukin-33 plays a significant role in the progression of SARS-CoV-2 disease at every stage (i.e., mild-moderate, severe-critical, and chronic-fibrotic)[12]. Furthermore, the antiviral immune response regulated by IL-33 correlates with the duration of infection. Following tissue damage caused by an acute viral infection, IL-33 synergizes with other epithelial cytokines and chemokines to promote homeostasis and repair. Thus, IL-33 activation prevents persistent inflammation that may develop during chronic infection. The protective and detrimental effects of the IL-33/ST2 axis in different inflammatory conditions vary according to the type and stage of infection[15]. Severe acute respiratory syndrome-Coronavirus-2 may cause autoinflammatory lung disease by inducing T-cells to release IL-33 from injured lower respiratory cells. Thus, monoclonal antibodies directed at the IL-33/ST2 axis may be useful in fighting against the COVID-19 pandemic[12]. Blocking of IL-33 can alleviate excess pulmonary inflammation. Furthermore, anti-ST2 therapy is currently the subject of multiple active clinical trials for inflammatory lung disease[16]. Alveolar damage and endothelial cell damage are the most likely cause of death in patients with severe respiratory failure associated with SARS-CoV-2. Thus, assessment of the cytokine profile in COVID-19 may aid in the early recognition of

Table 1. Demographic characteristics of the study population

	Total (n=132)	Need for intubation			90-day mortality		
		No (n=43)	Yes (n=89)	p	No (n=88)	Yes (n=44)	p
	n (%) or median (IQR)	n (%) or median (IQR)	n (%) or median (IQR)		n (%) or median (IQR)	n (%) or median (IQR)	
Age, year	67 (25.3)	63 (26)	76 (18)	**<0.001**	62.5 (22.5)	78.5 (15.3)	**<0.001**
Sex							
Female	72 (54.5)	49 (68.1)	23 (31.9)	0.865	48 (66.7)	24 (33.3)	1.000
Male	60 (45.5)	40 (66.7)	20 (33.3)		40 (66.7)	20 (33.3)	
CAD							
No	115 (87.1)	79 (68.7)	36 (31.3)	0.418	79 (68.7)	36 (31.3)	0.198
Yes	17 (12.9)	10 (58.8)	7 (41.2)		9 (52.9)	8 (47.1)	
HT							
No	66 (50)	48 (72.7)	18 (27.3)	0.194	48 (72.7)	18 (27.3)	0.140
Yes	66 (50)	41 (62.1)	25 (37.9)		40 (60.6)	26 (39.4)	
DM							
No	92 (69.7)	66 (71.7)	26 (28.3)	0.109	64 (69.6)	28 (30.4)	0.284
Yes	40 (30.3)	23 (57.5)	17 (42.5)		24 (60)	16 (40)	
CVD							
No	127 (96.2)	89 (70.1)	38 (29.9)	**0.003**	88 (69.3)	39 (30.7)	**0.004**
Yes	5 (3.8)	0 (0)	5 (100)		0 (0)	5 (100)	
Fever							
No	106 (80.3)	71 (67)	35 (33)	0.826	71 (67)	35 (33)	0.877
Yes	28 (19.7)	18 (69.2)	8 (30.8)		17 (65.4)	9 (34.6)	
Sore throat							
No	122 (92.4)	80 (65.6)	42 (34.4)	0.165	79 (64.8)	43 (35.2)	0.164
Yes	10 (7.6)	9 (90)	1 (10)		9 (90)	1 (10)	
Cough							
No	77 (58.3)	49 (63.6)	28 (36.4)	0.272	49 (63.6)	28 (36.4)	0.382
Yes	55 (41.7)	40 (72.7)	15 (27.3)		39 (70.9)	16 (29.1)	
Dyspnea							
No	80 (60.6)	60 (75)	20 (25)	**0.021**	59 (73.8)	21 (26.3)	**0.032**
Yes	52 (39.4)	29 (55.8)	23 (44.2)		29 (55.8)	23 (44.2)	

CAD: Coronary artery disease, CVD: Cerebrovascular disease, DM: Diabetes mellitus, HT: Hypertension, IQR: Interquartile range

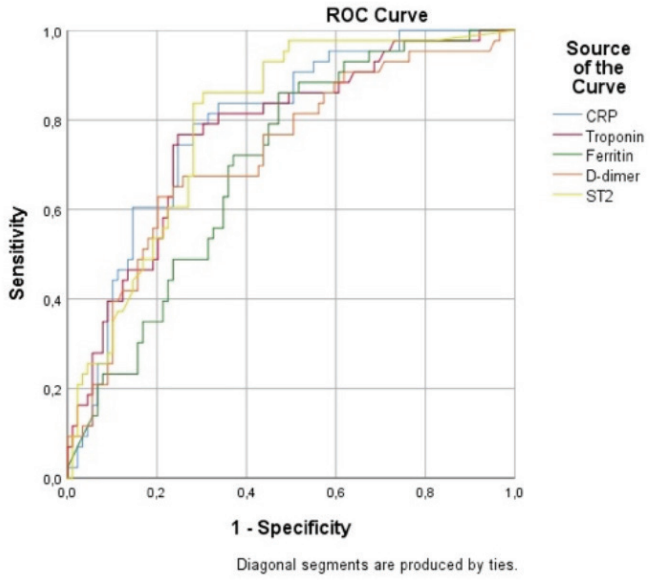

Figure 1. Receiver operator characteristic curve of the CRP, D-dimer, ferritin, troponin, and ST2 levels at the time of admission for determining the requirement for intubation in patients with SARS-CoV-2

CRP: C-reactive protein, ST2: Suppression of tumorigenicity 2, SARS-CoV-2: Severe acute respiratory syndrome-Coronavirus-2, ROC: Receiver operating characteristic

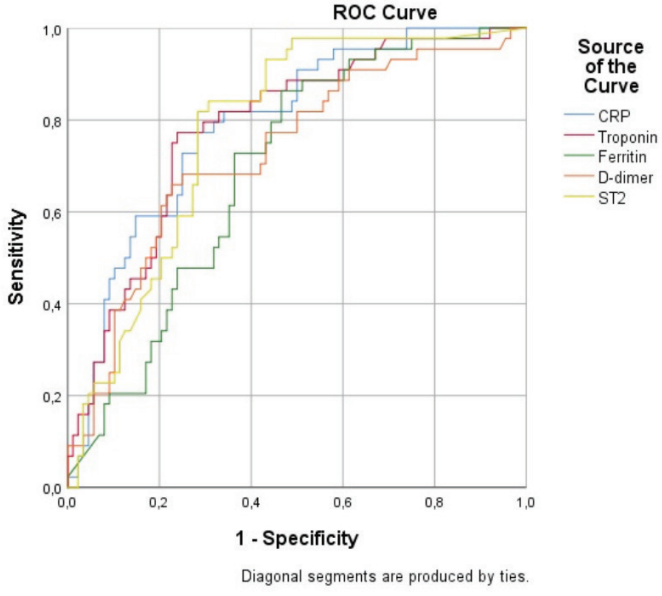

Figure 2. Receiver operator characteristic curve of the CRP, D-dimer, ferritin, troponin, and ST2 levels at the time of admission for determining 90-day mortality in patients with SARS-CoV-2

CRP: C-reactive protein, ST2: Suppression of tumorigenicity 2, SARS-CoV-2: Severe acute respiratory syndrome-Coronavirus-2, ROC: Receiver operating characteristic

worsening prognosis and progression to inflammation-related multiple-organ failure[9].

High ST2 concentrations are associated with endothelial or pneumocyte inflammation and damage. Furthermore, studies on the effectiveness of ST2 in predicting the clinical spectrum of patients with COVID-19 are limited. In the study by Zeng et al.[17], the patients were divided into mild and moderate clinical groups. They found a statistically significant difference in the ST2 levels between the two groups. Furthermore, the serum ST2 levels were significantly increased in patients with COVID-19 and positively correlated with the CRP levels, which reflected the inflammatory status and disease severity, respectively. Omland et al.[18] and Abers et al.[19] reported that high ST2 levels can predict 30-day mechanical ventilation requirement or mortality. Collectively, these results suggest that ST2 levels may predict mortality in patients with SARS-CoV-2 infection and be an early indicator of disease outcome.

The Coronavirus Clinical Characterization Consortium Mortality Score (4C Score) includes parameters such as comorbidities, sex, age, CRP level, oxygen saturation, respiratory rate, level of consciousness, and urea level (negative predictive value of 99%). A low 4C score indicates that the incidence of patient mortality is low. Although scores showing high power are useful for following up patients being treated on an outpatient basis or for making a decision regarding hospitalization, the use scores or biomarkers alone is not recommended for decision-making in patients[20]. The use of CRP in combination with simple clinical scores appears to be useful in the determination of hospitalization or discharge. In our study, ST2 level exhibited similar effectiveness to CRP level in the early identification of patients who may require mechanical ventilation. The combined use of a biomarker such as ST2, which can be easily adapted to daily practice in the ED, and the 4C score may provide a cost-effective approach to identifying poor outcomes. Furthermore, positive correlations were observed between elevated ST2, CRP, and high-sensitive cardiac troponin levels following SARS-CoV-2 infection in patients without prior cardiovascular disease. This indicates that ST2 is a potential new and powerful marker of inflammation[21].

The use of different IL pathways such as IL-6, IL-8, and IL-17 for the development of different management strategies may play a role in clarifying therapeutic targets. The prospective validation of cardiac biomarkers such as troponins and B-type natriuretic peptide (BNP) to guide clinical decision-making may provide more effective management of viral pandemics[22]. In our study, the troponin level was one of the most important predictors of mortality. In previous studies, the mortality significantly increased in patients with SARS-CoV-2 in whom abnormal transthoracic echocardiography findings were observed, as well as those with high BNP, N-terminal proBNP,

Table 2. ST2 concentrations and other laboratory parameter values in patients who did and did not require intubation

Laboratory values	Need for intubation	n	Median	Q1	Q3	p
WBC	**No**	89	7.12	5.95	9	**0.033**
	Yes	43	8.95	5.76	13.55	
Neutrophil count	**No**	89	5.37	3.84	6.63	**0.008**
	Yes	43	7.27	4.59	12.39	
Lymphocyte count	**No**	89	1.08	0.74	1.65	0.336
	Yes	43	1.02	0.72	1.47	
CRP	**No**	89	67.03	14.4	133.41	**<0.001**
	Yes	43	182.1	128.78	241.73	
Lactate	**No**	78	1.5	1.1	1.9	**0.001**
	Yes	43	2	1.5	2.8	
Troponin	**No**	89	5.4	2.5	15	**<0.001**
	Yes	43	33.6	15.1	126.3	
Ferritin	**No**	89	211.32	91.5	592	**<0.001**
	Yes	43	518.77	268.98	941.91	
D-dimer	**No**	89	554	410	743	**<0.001**
	Yes	43	1180	591	1990	
pH	**No**	78	7.4	7.37	7.44	**0.003**
	Yes	43	7.36	7.28	7.42	
ST2	**No**	89	61.1	4.8	238	**<0.001**
	Yes	43	280	204	424	

CRP: C-reactive protein, WBC: White blood cell, ST2: Suppression of tumorigenicity 2

Table 3. ST2 concentrations and other laboratory parameter values in survivors and patients who died

Laboratory values	90-day mortality	n	Median	Q1	Q3	p
WBC	**No**	88	7.12	5.95	9.05	**0.042**
	Yes	44	8.81	5.85	13.42	
Neutrophil count	**No**	88	5.33	3.83	6.67	**0.009**
	Yes	44	7.04	4.64	12.25	
Lymphocyte count	**No**	88	1.1	0.74	1.69	0.172
	Yes	44	1.02	0.67	1.47	
CRP	**No**	88	62.57	13.09	139.61	**<0.001**
	Yes	44	188.17	127.91	241.92	
Lactate	**No**	77	1.5	1.1	1.9	**0.002**
	Yes	44	1.9	1.5	2.8	
Troponin	**No**	88	5.34	2.5	14.7	**<0.001**
	Yes	44	34.35	16.5	125.45	
Ferritin	**No**	88	207.44	85.4	595.2	**<0.001**
	Yes	44	506.4	278.27	938.03	
D-dimer	**No**	88	542.5	408	736	**<0.001**
	Yes	44	1145	592.5	1885	

Table 3. Continued

Laboratory values	90-day mortality	n	Median	Q1	Q3	p
pH	**No**	77	7.4	7.37	7.43	**0.016**
	Yes	44	7.38	7.32	7.43	
ST2	**No**	88	55.95	4.65	238	**<0.001**
	Yes	44	272.5	202.5	369.5	

CRP: C-reactive protein, WBC: White blood cell, ST2: Suppression of tumorigenicity 2

Table 4. Comparison of the efficacy of ST2 concentration and laboratory parameters in predicting patient groups

	Group	AUC	Cut-off	Sensitivity	Specificity	PPV	NPV	+LR	-LR
CRP	Intubation	0.79	126.66	79.07	71.91	57.6	87.7	2.71	0.3
	Mortality	0.79	126.66	77.27	71.59	57.6	86.3	2.62	0.32
Troponin	Intubation	0.77	15.1	76.74	75.28	60	87	3.1	0.31
	Mortality	0.78	15.1	77.27	76.14	61.8	87	3.24	0.3
Ferritin	Intubation	0.70	218.4	86.05	51.69	46.8	88.7	1.78	0.27
	Mortality	0.69	218.4	86.36	53.41	48.1	88.7	1.81	0.26
D-dimer	Intubation	0.73	898	62.79	79.78	60	81.6	2.94	0.47
	Mortality	0.73	729	68.18	75	57.7	82.5	2.61	0.43
ST2	Intubation	0.80	166	86.05	69.66	57.8	91.2	2.64	0.21
	Mortality	0.78	166	84.09	69.32	57.8	89.7	2.55	0.24

AUC: Area under the ROC curve, CRP: C-reactive protein, LR: Likelihood ratio, NPV: Negative predictive value, PPV: Positive predictive value, ST2: Suppression of tumorigenicity 2

and cTnt levels, left and/or right ventricular dysfunction, right ventricular strain, and ST segment abnormalities[23,24]. Given the association between COVID-19 and coronary vascular diseases, the combined use of biomarkers of cardiac injury, stress, and inflammation for risk classification may enable appropriate risk stratification.

We believe that a sufficient number of cases have been included in the study, and the results obtained can be generalized to patients with a similar diagnosis of viral pneumonia.

Study Limitations

However, an important limitation of our study was that not all the risk factors that may worsen viral infections in patients with deteriorating conditions, such as living or working environment or care home, were recorded. Furthermore, additional measurements of proBNP and monitoring of changes in ST2 levels could have provided more precise prognostic information in terms of cardiac damage and COVID-19.

Conclusion

In conclusion, ST2 concentration at the time of admission to the ED can be used to predict the need for intubation and mortality in patients with COVID-19. Furthermore, ST2 is more effective than ferritin, troponin, and D-dimer levels and lymphocyte count and just as effective as CRP level in predicting the need for intubation and mortality in COVID-19. Based on these results, we propose that ST2 can be used for the early detection of poor prognosis in patients with COVID-19 who present to the ED.

Ethics

Ethics Committee Approval: The study protocol was approved by the Sakarya University Clinical Research Ethics Committee (no: 428, date: 01.10.2021).

Informed Consent: All participants provided informed written consent.

Authorship Contributions

Surgical and Medical Practices: F.Ç., Concept: F.Ç., M.Ö., O.K., Y.Y., Design: F.Ç., M.Ö., O.K., H.T., N.G.G., Y.Y., Data Collection or Processing: F.Ç., H.T., N.G.G., Y.Y., Analysis or Interpretation: F.Ç., M.Ö., O.K., H.T., N.G.G., Y.Y., Literature Search: F.Ç., M.Ö., Writing: F.Ç., M.Ö., Y.Y.

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