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RESEARCH ARTICLE

Assessment of initial admission and discharge parameters in COVID-19-related ARDS patients in terms of outcome

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ABSTRACT

It has been understood that in 2019, coronavirus disease 2019 (COVID-19), believed to have originated in the city of Wuhan, China, and caused by the coronavirus, has a wide range of disease potential, from asymptomatic cases to acute respiratory distress syndrome (ARDS). Some risk factors have been identified for COVID-19-related ARDS (CARDS) patients. These risk factors include old age, the presence of chronic diseases, male gender, and smoking. During the monitoring of patients in intensive care units, there are significant changes in clinical findings, vital signs, and some laboratory findings, especially. Currently, there is still no specific treatment available for both COVID-19 and CARDS.

Keywords: COVID-19, COVID-19 associated acute respiratory distress syndrome, ARDS

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INTRODUCTION

Acute respiratory distress syndrome (ARDS) is a life-threatening condition in which the lungs fail to provide sufficient oxygen to the body's vital organs. It is often a complication of a severe health condition and implies that patients developing ARDS are already in the hospital for some other reason. Symptoms of ARDS include severe shortness of breath, rapid and shallow breathing, fatigue, confusion, and syncope. However, there are also symptoms related to the underlying disease [1].

There are many different types of coronaviruses, and some of them can cause diseases. In 2019, a coronavirus named SARS-CoV-2 caused a respiratory illness pandemic called COVID-19. Some people infected with the coronavirus exhibit no symptoms, while others develop mild COVID-19. However, in some cases, COVID-19 can lead to respiratory failure, lasting lung and myocardial damage, nervous system problems, kidney failure, or even death [2].

Following the SARS-CoV-2 pandemic wave, intensive care unit (ICU) specialists monitored numerous patients with COVID-19-related ARDS (CARDS). From a pathophysiological perspective, prominent mechanisms of CARDS include severe pulmonary infiltration, inflammation leading to edema and disrupted alveolar homeostasis, changes in pulmonary physiology resulting in pulmonary fibrosis, endothelial inflammation (endothelitis), vascular thrombosis, and immune cell activation [3]. In this article, we examined data from some CARDS patients that we have been monitoring in our ICU, including information from the day of admission to the ICU and the day of exit from the unit (either transferred to another unit or in the case of exitus).

MATERIALS AND METHODS

Between March 2020 and December 2021, we retrospectively reviewed 32 CARDS patients who were monitored in our ICU.

Inclusion criteria for the study were, as follows: patients within the age range of 18-80, those diagnosed with ARDS according to the Berlin criteria, individuals who had COVID-19 pneumonia, and patients monitored in the COVID-19 ICU.

Exclusion criteria for the study were, as follows: patients outside the age range of 18-80, individuals who did not meet the

Table 1. Assessment of various characteristics in CARDS patients

	Number of patients	Percentage (%)
Gender	32	100
Male	17	53.1
Female	15	46.9
Comorbidity	28	87.5
Mortality	17	53.1
	Mean (median)	**Standard deviation (inter-quartile rage)**
ICU stay duration	21.2	16.8
Extubated[a]	7.1 (6.0)	5.2 (7.0)
Intubated[a]	14.4 (12.0)	16.7 (21.0)
PEEP[a & b]	13.8	3.1
FiO_2[b]	80.9	17.7
Age[a]	58.3 (62.0)	15.4 (22.0)

Note. [a]Wilcoxon signed-rank test & [b]Student's t-test

Table 2. Data in which the median of the first-day measurement is statistically significantly higher than the median of the last-day measurement in CARDS patients

	First dat		Last day		p
	Mean (median)	Standard deviation (inter-quartile rage)	Mean (median)	Standard deviation (inter-quartile rage)	
GCS[a]	14.0 (15.0)	2.4 (0.0)	8.3 (3.5)	5.9 (12.0)	0.001
HR[a]	94.5 (92.0)	13.1 (16.0)	87.5 (85.0)	16.9 (25.0)	0.020
MAP[a]	79.1 (91.0)	13.1 (13.0)	80.2 (80.0)	3.9 (16.0)	0.001
pH[b]	7.4	0.08	7.3	0.25	0.004
Albumin[a]	9.6 (3.4)	12.3 (1.2)	3.7 (2.6)	5.1 (1.0)	0.001
Fibrinogen[a]	618.9 (601.5)	215.9 (280.0)	405.9 (397.0)	230.2 (277.0)	0.001
Hb[b]	11.3	2.0	10.2	1.7	0.005

Note. [a]Wilcoxon signed-rank test & [b]Student's t-test

Berlin diagnostic criteria, those without COVID-19 pneumonia, patients in the post-operative period, and individuals with an ICU stay of less than 24 hours.

Demographic data, age, clinical, laboratory, and treatment information of the patients were examined by scanning the computer system and files for the data related to the first admission and discharge day.

The following data for the first admission and discharge day were examined: Glasgow coma scale (GCS), heart rate (HR), mean arterial pressure (MAP), saturation level, temperature, arterial blood gas findings (pH, $PaCO_2$, PaO_2, HCO_3, BE, and lactate), hemoglobin (Hb), white blood cell count (WBC), lymphocytes, neutrophils, monocytes, basophils, and platelet (PLT) levels, C-reactive protein (CRP), procalcitonin, ferritin, interleukin 6 (IL-6) levels, activated partial thromboplastin time (APTT), prothrombin time (PT), international normalized ratio (INR), D-dimer, fibrinogen levels, aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), total bilirubin, albumin, glucose levels, creatinine, glomerular filtration rate (GFR), sodium, potassium, calcium levels, creatine kinase (CK), and troponin I levels.

RESULTS

Of the monitored CARDS patients, 53.1% were male, and 46.9% were female. The average age was determined to be 58.3. The average length of stay in the ICU was found to be 21.2 days. Patients were followed for an average of 7.1 days extubated and 14.4 days intubated. The average of the highest positive end-expiratory pressure (PEEP) levels during their follow-up was 13.8. The maximum fraction of inspired oxygen average was 80.9. The average Apache II score for the patients was 21.9. It was observed that the disease had a mortality rate of 53%.

Table 1 shows the assessment of various characteristics in CARDS patients. **Table 2** shows the data in which the median of the first-day measurement is statistically significantly higher than the median of the last-day measurement in CARDS patients.

Table 3. Data indicating that the median of the last day's measurement in CARDS patients is statistically significantly higher compared to the median of the first day's measurement

	First dat		Last day		p
	Mean (median)	Standard deviation (inter-quartile rage)	Mean (median)	Standard deviation (inter-quartile rage)	
Saturation[a]	80.2 (84.0)	13.9 (15.0)	93.1 (94.5)	4.9 (7.0)	0.001
PCO_2[a]	43.0 (39.5)	15.9 (17.0)	55.1 (51.0)	19.8 (19.0)	0.006
Lactate[a]	2.1 (1.7)	1.6 (0.8)	4.8 (2.5)	4.9 (5.3)	0.007
PT[a]	14.4 (12.0)	6.9 (3.8)	21.2 (16.0)	13.7 (12.0)	0.001
APTT[a]	28.5 (25.0)	8.7 (12.0)	41.9 (31.5)	25.0 (26.0)	0.007
INR[a]	1.2 (1.1)	0.5 (2.8)	1.7 (1.3)	0.9 (1.2)	0.001
D-dimer[a]	5.6 (1.7)	11.1 (2.7)	19.1 (7.5)	57.6 (12.7)	0.010
Monocyte[a]	0.45 (0.40)	0.2 (0.3)	0.69 (0.50)	0.5 (0.5)	0.040
Basophil[a]	0.02 (0.01)	0.02 (0.02)	0.06 (0.04)	0.06 (0.07)	0.001
Procalcitonin[a]	0.7 (0.2)	1.4 (0.7)	7.9 (0.3)	18.7 (9.9)	0.030
IL-6[a]	145.5 (68.0)	225.1 (139.5)	8,070.6 (98.0)	14,753.8 (9,682.3)	0.040
Ferritin[a]	984.5 (566.5)	1,333.7 (990.0)	7,838.0 (1,306.5)	14,670.9 (8,884.0)	0.003
AST[a]	53.2 (41.0)	36.7 (29.0)	785.4 (68.0)	1,989.9 (158.0)	0.030
ALT[a]	42.1 (31.0)	34.9 (44.0)	402.9 (50.5)	814.7 (114.0)	0.009
Total bilirubin[a]	0.70 (0.44)	0.7 (0.6)	1.90 (0.79)	2.50 (1.44)	0.001
Sodium[b]	136.3	4.6	140.9	5.9	0.004
Troponin I[a]	0.04 (0.02)	0.05 (0.03)	0.14 (0.04)	0.26 (0.10)	0.001

Note. [a]Wilcoxon signed-rank test & [b]Student's t-test

Table 3 shows the data indicating that the median of the last day's measurement in CARDS patients is statistically significantly higher compared to the median of the first day's measurement.

In CARDS patients, it was found that the median of the first-day GCS levels was statistically significantly higher compared to the median of the last day's measurement.

In CARDS patients, it was determined that the median of the MAP levels and the median value of HR on the first-day measurement were statistically significantly higher compared to the median on the last day's measurement.

In CARDS patients, it was found that the median of the pH levels on the first-day measurement was statistically significantly higher compared to the median of the last day's measurement.

In CARDS patients, it was observed that the median of Hb levels, the median of the albumin levels and the median of fibrinogen levels on the first day's measurement were statistically significantly higher compared to the median on the last day's measurement.

In CARDS patients, it was found that the median of the saturation level and the median of partial pressure of carbon dioxide levels on the last day's measurement was statistically significantly higher compared to the median of the first day's measurement.

In CARDS patients, it was observed that the median of lactate levels on the last day's measurement were statistically significantly higher compared to the median of the first day's measurement.

In CARDS patients, it was determined that the median of the APTT levels, the median of the partial thromboplastin time levels and the median of the INR levels on the last day's measurement were statistically significantly higher compared to the median of the first day's measurement.

In CARDS patients, it was observed that the median of the D-dimer levels on the last day's measurement was statistically significantly higher compared to the median of the first day's measurement.

In CARDS patients, it was observed that the median of procalcitonin levels and the median of IL-6 levels on the last day's measurement were statistically significantly higher compared to the median of the first day's measurement.

In CARDS patients, it was determined that the median of ferritin levels on the last day's measurement was statistically significantly higher compared to the median of the first day's measurement.

In CARDS patients, it was observed that the median of AST and ALT levels on the last day's measurement were statistically significantly higher compared to the median of the first day's measurement.

In CARDS patients, it was found that the median of troponin I levels on the last day's measurement was statistically significantly higher compared to the median of the first day's measurement.

There were no statistically significant differences observed in the levels of LDH, CK, temperature, WBC, neutrophils, PLT, glucose, potassium, calcium, creatinine, GFR, CRP, PaO_2, HCO_3, and base excess between the first day and the last day.

DISCUSSION AND CONCLUSION

Because the COVID-19 disease is relatively new, our knowledge about the course of the disease including clinical findings, vital signs, laboratory results, and treatment is limited when monitoring patients in ICUs. Therefore, it is crucial to determine the clinical findings, vital signs, and certain laboratory results for the course of the CARDS disease for the follow-up and treatment of patients. There are very few studies that assess the clinical features, laboratory findings, disease severity scores, blood gas and vital signs, complications, and treatment differences for the initial and final days. Large randomized controlled trials are needed to understand the course of this disease.

In a multicenter study in Spain in 2020, 740 COVID-19 patients were analyzed [4]. Among these patients, 504 (68.1%) were identified as male, and 236 (31.9%) were identified as female. In our study, 17 (53%) of the patients were male, and 15 (46%) were female. It was observed that the patients were predominantly elderly males with comorbid conditions. The median length of stay in the ICU was found to be 21 days, which is consistent with our study. On average, patients were managed using low tidal volumes and moderate PEEP levels within the standard lung-protective tidal volume paradigm. The average PEEP was determined to be 13, which also aligns with our study. In the study, the average number of days without mechanical ventilation was found to be 4, whereas in our study, it was determined to be 7.1 days. These findings indicate that CARDS disease affects both genders, patients require extended ICU stays, and high PEEP levels are necessary for ventilation [4].

In a study conducted in 2021 [5], focusing on risk factor analysis, the levels of ALT, AST, CK, and D-dimer increased in a small number of COVID-19 patients under observation. In our study, we also found that AST, ALT, total bilirubin, and D-dimer levels were higher on the last day compared to the first day. This finding correlates with our study. ALT and AST are markers of acute liver damage. We believe that the harmful effects of abnormal liver tests in COVID-19 patients are mainly related to the use of antiviral drugs during hospitalization. Therefore, liver function should be closely monitored and evaluated during drug treatment.

In a study conducted in 2021 [6], biochemical markers of inflammation and disease severity, such as LDH, D-dimer, and ferritin, were consistently higher in patients who received prone positioning at least once. While our study is not identical to this research, in our study, we also found that D-dimer and ferritin levels on the last-day were statistically significantly higher than the median of the first-day measurements. This result indicates that the severity of inflammation increases or continues despite treatment.

In a study conducted in 2021 [7], a significant decrease in lymphocyte counts was found, with this decrease being more pronounced in elderly adults. It was shown that COVID-19 leads to lymphocyte impairment in the immune system [7]. While this study is not identical to our own research, the results are not correlated with our study. In our study, we evaluated the low lymphocyte counts concerning the first and last-day measurements, and the results did not show statistical significance. Our recommendation is that further research is needed regarding lymphocyte count.

The study in [8] detected an increase in troponin during COVID-19 infection, although the exact cause remained unexplained. This finding correlates with our study. In our study, we found that the troponin I levels in CARDS patients was statistically significantly higher on the last-day measurement compared to the median of the first-day measurement. The reason for this could be the impact of hypoxia on myocardial perfusion or the possibility of myocardial infarction as a result of prothrombotic system activation.

There were 16 cases in the embolization group and 54 cases in the non-embolization group [9]. The INR did not show a significant difference between the embolization and non-embolization groups; however, it was observed that INR tended to be higher in the embolization group, although not significantly (9). While this study is not identical to our own research, in our study, we found that the INR levels in CARDS patients was statistically significantly higher on the last-day measurement compared to the median of the first-day measurement. The reason for this may be related to prothrombotic system activation.

In a meta-analysis study conducted in 2021 [10], unlike APTT, it was shown that fibrinogen levels increased. Most studies indicate higher fibrinogen levels in severely affected COVID-19 patients, while other studies did not report significant differences [10]. In our study, we found that in CARDS patients, fibrinogen levels were statistically significantly higher on the last-day measurement compared to the median of the first-day measurement. This could be related to the increase of fibrinogen in sepsis.

In a study conducted in 2021 [11], which included IL-6, CRP, and procalcitonin levels, it was observed that patients had significantly increased levels of IL-6, CRP, and procalcitonin upon admission. This finding was consistent with the concept of a cytokine storm, indicating the role of

inflammatory factors in patients with elevated IL-6, CRP, and procalcitonin levels [11]. While this study is not identical to our own research, in our study, we found that in CARDS patients, both procalcitonin and IL-6 levels on the last-day measurement were statistically significantly higher compared to the median of the first-day measurement. This could be due to cytokine storm-related factors and may also be an indicator of CARDS patients being more susceptible to secondary infections.

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Declaration of interest: No conflict of interest is declared by the authors.

Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

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