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KARAKTERISTIK KLINIS DAN LUARAN PASIEN COVID-19 YANG MENDAPAT TERAPI KANULA HIDUNG ARUS TINGGI DI RUMAH SAKIT UMUM PUSAT PERSAHABATAN JAKARTA

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Abstrak

Latar belakang: *Pasien COVID-19 berat dan kritis memerlukan perawatan intensif bahkan ventilasi mekanis invasif. Penggunaan kanula hidung arus tinggi (KHAT) pada pasien gagal napas akut hipoksemik non COVID-19 dapat menurunkan angka intubasi sedangkan data pada pasien COVID-19 mengenai kemampuan KHAT untuk mencegah ventilasi mekanis invasif masih terbatas.*

Metode: *Penelitian ini merupakan kohort retrospektif pada 62 pasien COVID-19 terkonfirmasi yang menggunakan KHAT dan dirawat di RSUP Persahabatan Jakarta pada bulan maret hingga Juli 2020. Data rekam medis demografi, klinis dan laboratorium diambil sebelum penggunaan KHAT sedangkan tanda vital dan indeks pernapasan diambil 24 jam setelah penggunaan KHAT.*

Hasil: *Mayoritas pasien merupakan laki-laki (67.7%), rerata usia subyek 57.6 tahun dengan komorbid terbanyak berupa hipertensi dan diabetes mellitus. Proporsi pasien dengan luaran berhasil sebesar 45.2%. Terdapat perbedaan bermakna antara kelompok luaran berhasil dengan luaran gagal pada laju napas (24 vs 28.5), laju nadi (88.14 vs 100), saturasi oksigen (98 vs 94), PaO2/Fio2 (139.27 vs 73), SpO2/FiO2 (116.98 v 102.78) dan indeks ROX (4.97 vs 3.5) Tanda vital dan indeks pernapasan 24 jam setelah pemakaian KHAT pada kelompok luaran berhasil memiliki perbaikan yang signifikan dibanding kelompok luaran gagal.*

Kesimpulan: *Penggunaan KHAT dapat menurunkan angka intubasi pada pasien COVID-19. Perbaikan tanda vital dan indeks pernapasan secara signifikan terjadi pada kelompok KHAT dengan luaran berhasil.*

Kata kunci: *COVID-19, Kanula hidung arus tinggi (KHAT), indeks ROX*

CLINICAL CHARACTERISTIC AND OUTCOME OF COVID-19 PATIENT USING HIGH FLOW NASAL OXYGEN IN PERSAHABATAN HOSPITAL, JAKARTA

Abstract

Background: *Severe and critical COVID-19 patient need intensive care and even invasive mechanical ventilation. Use of high flow nasal oxygen (HFNO) in acute hypoxemic respiratory failure on non-COVID-19 patient can reduce the need for intubation while in COVID-19 patient the data is still inadequate.*

Methods: *This is a retrospective cohort study in 62 confirmed COVID-19 patient using HFNO and treated at Persahabatan Hospital from March to July 2020. Demographic, clinical and laboratory data before HFNO and vital sign, respiratory index after 24 hours of HFNO was taken from medical record.*

Results: *Majority of patients are men (67%), mean age 57.6 years, comorbidity is mostly hypertension and diabetes. HFNO Success outcome is 45.2%. Statistically significant difference between success and failure group is noted on respiratory rate (24 vs 28.5), pulse rate (88.14 vs 100), oxygen saturation (98 vs 94), PaO2/Fio2 (139.27 vs 73), SpO2/FiO2 (116.98 v 102.78) and ROX index (4.97 vs 3.5). Vital sign and respiratory index measured after 24 hours of HFNO showed statistically significant improvement in success group.*

Conclusion: *HFNO can reduce intubation rate in patient with COVID-19. Vital sign and respiratory index are significantly improved in HFNO success group.*

Keywords: *COVID-19, High flow nasal oxygen (HFNO), ROX index*

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) is caused by Severe acute respiratory syndrome-coronavirus2 (SARS-CoV2), which is an RNA virus in the beta coronavirus family and has phylogenetic similarities to the severe acute respiratory syndrome-coronavirus (SARS-CoV) and middle east respiratory coronavirus (MERS-CoV).[1] The World Health Organization (WHO) in March 2020 declared COVID-19 a pandemic.[2]

Patients with COVID-19 can have different clinical presentations. Data from China concludes that 81% will experience mild symptoms, 14% with severe symptoms, and 5% with a critical condition.[3] Patients with severe and critical symptoms generally experience severe acute respiratory infection (SARI) symptoms that require hospitalization and oxygen therapy. Occasionally, respiratory failure will occur, requiring mechanical ventilation and treatment in the intensive care unit (ICU).[4]

The use of high flow nasal cannula (HFNC) in patients with threatened respiratory failure has the advantages of ease of operation, administration of a constant and maintained oxygen fraction, positive end expiratory pressure (PEEP), decreased anatomic dead space, decreased work of breathing and improved mucociliary clearance. This will lead to an improvement in respiratory rate, oxygen saturation and oxygenation.[5,6]

Research on the characteristics of patients with COVID-19 using (HFNC) and their role in reducing intubation rates and mechanical ventilation is still limited, so research is needed to determine patient characteristics, intubation rates, and mortality of COVID-19 patients using HFNC.

METHOD

This study is a retrospective cohort of confirmed COVID-19 patients with inclusion criteria of 18 years of age or older, using HFNC and being treated at Persahabatan Hospital Jakarta in March-July 2020. Patients with incomplete data and a history of previous COVID-19 treatment did not include.

The initial data were demographic, clinical factors (the duration and type of previous oxygen therapy, duration of use of HFNC, and treatment regimen), and laboratory data before using HFNC. Vital signs and respiratory index data were taken before the patient used HFNC and 24 hours after HFNC. These two data were then compared between the success and failure groups using the Mann-Whitney T/test.

Failed outcomes were defined as death or invasive mechanical ventilation after using HFNC, while successful outcomes were patients who did not experience failed outcomes. The outcome was determined on the 21st day of observation. The required data were taken from patients' medical records who met the inclusion criteria after obtaining approval from the research ethics committee.

RESULT

Data from medical records in the March – July 2020 period showed that 69 COVID-19 patients used HFNC, five people were not included in the sample because the data was incomplete, while two people were not included because the use of HFNC was< 24 hours, so that the total patients who could be analyzed were as many as 62 people.

The research subjects consisted of 42 men and 20 women. The mean age of the research subjects was 57.6 years, and the age group with the most subjects was <65 years, as many as 29. Forty-five people have a record of smoking habits, and most (33 subjects) are recorded as not smoking. The most common comorbidities were hypertension, diabetes mellitus, and cardiovascular disease (36, 32, and 12 subjects). Twenty-three (23) subjects had multiple comorbidities, while 11 subjects did not have any comorbidities.

Table 1 Demographic and clinical characteristics

Variable	N (%)
Age	
<65	45 (73.7)
≥65 years	17 (27.4)
Gender	

Male	42 (67.7)
Female	20 (32.3)
Smoking Habit (n=45)	
Smoke	12 (26.7)
Do not smoke	33 (73)
Comorbid	
No comorbid	11 (17.7)
Diabetes Mellitus	32 (51.6)
Hhypertension	36 (58.1)
Cardiovascular	12 (19.4)
Cerebrovaskular	1 (1.6)
Obstructive Lung Disease	1 (1.6)
Pulmonary Tuberculosis	0
Malignancy	0
HIV	0
Multiple/multiple comorbid	23 (37.1)
WHO clinical level	
Heavy	16 (25.8)
Critical	46 (74.2)
Level of respiratory distress	
Moderate	15 (24.2)
Heavy	47 (75.8)

All patients confirmed COVID-19 through RT-PCR swabs. Most of the subjects entered the critical criteria (46 people) based on WHO clinical criteria and severe respiratory distress criteria (47 people); all patients used non-respirator masks before using HFNC. The average length of treatment was 16.5±9.9 days, while the median length of HFNC use was four days. Oseltamivir was the most commonly used treatment regimen, followed by azithromycin and chloroquine.

The mean hemoglobin was 13.20 g/dL with median leukocyte and platelet counts of 9315/μL and 259000/μL. The neutrophil/lymphocyte ratio (RNL) showed a median of 6.82. The mean erythrocyte sedimentation rate (ESR) was 82.06 mm from 29 subjects, the mean c-reactive protein (CRP) value was 146.8 mg/L from 57 subjects, and the median procalcitonin (PCT) value was 0.175 ng/mL. Examination of lactate as a marker of tissue hypoxia was performed on 49 subjects and obtained a median value of 2.5 mmol/L.

Tabel. 2 Perbedaan karakteristik tanda vital

Variable	Outside		p
	Success	Fail	
Respiratory rate (x/minute)	24 (18-34)	28.5 (22-45)	0.000
Pulse Rate (x/minute)	88.21 ± 10.94	99.94±10.21	0.000(6.343-17.111)
O2 Saturation (%)	98 (93-100)	94 (54-100)	0.000
SpO2/FiO2	116.47 (100-166.67)	102.78 (56.84-213.33)	0.000
PaO2/FiO2 (n=58)	138.38 (68.84-267.29)	74.22(36-184.4)	0.000
ROX Index	4.94 (3.26-8.25)	3.58 (1.67-9.69)	0.000

The median values for urea, creatinine, aspartate transferase, alanine transferase, total bilirubin and troponin I were 30 mg/dL, 0.9 mg/dL, 44 u/L, 39 u/L, 0.7 mg/dL and 12.7 pg/ mL. The median value of D-dimer was 1500 g/L, while the median value of fibrinogen was 505 g/L. Profile Analysis of blood gases before using HFNC showed a picture of hypoxemia with median values of PaO2, PaO2/FiO2, and median oxygen saturation of 67.95 mmHg, 111.18, and 93.5%, respectively

Demographic characteristics between patients who succeeded and failed after using 24-hour HFNC did not show a statistically significant difference between the success and failure groups. There are differences in clinical characteristics in the form of the total length of treatment and duration of use of HFNC at 24 hours, 7, 14, and 21 days of observation.

Table 2. Differences in the Characteristics of Laboratory Values

Variable	Outside		
	Success	Fail	p
Hemoglobin (g/dL)	12.83 ±1.79	13.48±2.05	0.192 (-0.337-1.644)

Leukocytes (/μL)	8220 (3670-28450)	10175 (3870-21230)	0.218
Count the type of neutrophil	81.3 (39.6-97.8)	82.8 (53.9-94.1)	0.656
Count the type of lymphocyte	12.7 (1.2-55.9)	10.1 (4-39.2)	0.362
Neutrophil/Lymphocyte Ratio	6.14 (1.38-23.53)	8.02 (1.38-23.53)	0.380
Platelets (/μL)	255500 (141000-608000)	271500 (45000-590000)	0.276
CRP (mg/L) (n=57)	130.74±91.64	159.35±88.51	0.238 (-19.482-76.688)
PCT (ng/ml) (n=58)	0.11 (0.03-5.68)	0.21 (0.05-7.14)	0.028
Urea(mg/dL) (n=61)	26 (11-111)	36 (8-168)	0.160
Creatinine(mg/dL) (n=61)	0.8 (0.4-5.4)	1 (0.4-4.1)	0.165
Aspartate transferase (U/L) (n=62)	38.5 (13-85)	49.5 (15-171)	0.110
Alanine Transferase (U/L) (n=62)	37 (12-143)	48.5 (15-124)	0.329
Troponin I (pg/ml) (n=47)	7.2 (0.9-1008)	18.25 (1.1-285.2)	0.052
Lactate (mmol/L) (n=49)	1.9 (1.2-6.1)	2.9 (1.2-5.4)	0.061
D-dimer (μg/L) (n=56)	1545 (380-22230)	1500 (460-48600)	0.434

There was no significant difference in systolic blood pressure (136.33 mmHg vs 134.22 mmHg), diastolic blood pressure (80 mmHg vs 81 mmHg), respiratory rate (28 vs 28), pulse rate (97 vs 100), O2 saturation (96 vs 95) and PaO2/FiO2 (119.51 vs 107.58) between the success and failure groups. The only visible difference in characteristics is the ratio of SpO2/FiO2 (167.91 vs. 143.94) and FiO2 (58.5% vs. 66%).

Vital signs and respiratory index after using HFNC 24 hours showed a statistically significant difference between patients with successful and failed outcomes. Significant differences were seen in respiratory rate, pulse rate, oxygen saturation, SpO2/FiO2 ratio, PaO2/FiO2 ratio and ROX index with better median or mean parameter values in the successful group compared to the failed group.

There was a significant difference in the PCT value between the successful and failed outcome groups. Still, there was no significant difference in the value of haemoglobin, leukocyte count, neutrophil type count, lymphocyte type count, neutrophil/lymphocyte ratio, platelet count, CRP, urea, creatinine, aspartate transferase, alanine transferase and D-dimer. The values of troponin I and lactate showed significant differences at the outcomes of 24 hours and 7 days but became insignificant at the outcomes of 14 and 21 days.

DISCUSSION

The majority of the subjects in this study were male (67.7%), and the mean age of the subjects in this study was 57.6 years, with the most age group being <65 years. This is slightly different from Wang et al.'s study, which found the median age of patients was 56 years, and only 41% of patients were male.[7] Demoule et al. found that the median age of patients using HFNC was 60 years, with the majority (79%) male.[8] Patel et al.'s study showed a mean age of 55.6, with 51% male.[9]

In old age, the innate immune function decreases so that related cells (macrophages, neutrophils, dendritic cells) are not activated effectively and efficiently when an infection occurs. It causes the adaptive immune system to be inactive properly and completely, thereby reducing viral clearance and increasing the possibility of immune system dysregulation. It can lead to excessive release of pro-inflammatory cytokines, resulting in a cytokine storm.[10]

The activity and expression of ACE2 in males are known to be greater than that in females, which is thought to be because estrogen causes downregulation of ACE2 expression in females. In contrast, testosterone causes an increase in the

amount of ACE2.[11] Comorbidities and lifestyle-related major comorbidities in COVID (hypertension, diabetes and cardiovascular disease) such as smoking and alcohol consumption are also more common in men. These three things cause men to have a greater tendency for immune system dysregulation and worse outcomes in COVID-19.[11].

The most comorbid found in this study were hypertension (58.1%) and diabetes mellitus (51.6%). A total of 37.7% of the subjects had multiple comorbidities. Wang et al. also found that hypertension and diabetes mellitus were the most common comorbidities in patients taking HFNC. The same thing was obtained by Demoule et al. and Patel et al.[9] The data from the above study shows that hypertension and diabetes mellitus have a relationship with the severity of COVID-19.

In this study, only 26.7% of patients had a smoking record. Patel et al. found that almost half of the patients had a smoking habit (43.4%), while Gupta et al. found that 29.3% of patients requiring ICU care due to COVID-19 had a smoking habit or were previously smokers.[9,12] Patanavanich et al. conducted a meta-analysis of the relationship between smoking with worsening in COVID-19 patients and found that smokers have a 1.91x risk of worsening if they experience COVID-19.[13]

Demographic characteristics (age, gender, and comorbidities) between patients with successful or failed outcomes at 24 hours, 7 days, 14 days and 21 days did not show statistically significant differences in this study. Studies on COVID-19 patients using HFNC by Patel et al. and Calligaro et al. also did not find significant differences in age, gender, comorbid diabetes and hypertension between the intubated and non-intubated groups.[9,14] The findings in this study were because the two outcome groups had almost the same mean age (55.9 and 59.9 years), equal distribution of male gender and almost the same number of people with diabetes and hypertension between the groups with successful and failed outcomes.

Most of the patients using KHAT in this study had a high respiratory rate (>25), an oxygen demand of 10-15 liters per minute via MNHU, and bilateral infiltrates with hypoxemia (median PaO2/FiO2 111.18 and median SpO2/FiO2 146.21) so that they fit the criteria. Acute and severe respiratory distress. Patel et al. also reported that patients using KHAT were patients who required oxygen supplementation of 15 liters/minute (severe hypoxemic respiratory failure). In contrast, Calligaro et al. reported that patients using KHAT had a respiratory rate of 30 breaths/minute and a saturation of 92% with O2 15 liters/minute (severe respiratory failure).[9,14]

Patel et al. assessed the chest radiograph using the radiographic assessment of lung edema score (RALES) with a mean value of 18.17 at the beginning of KHAT use. However, they did not explain whether the infiltrates were bilateral or unilateral.[9] Demoule et al. reported that patients who received KHAT therapy were patients with the category of heavy and had the involvement of 4 quadrants on chest radiograph.[8]

Patients who fall into the critical criteria have a KHAT failure rate significantly different from the first 24-hour outcome but not significantly different from the 7, 14, and 21-day outcomes. This is because there are patients who switch from a successful outcome to a failed outcome, so overall, it can be concluded that the clinical degree is not significantly different between the two groups.

Most patients (75.8%) were admitted with severe respiratory distress before using KHAT, and the rest were admitted with moderate respiratory distress. There was no significant difference in the degree of respiratory distress between the patients who succeeded and those who failed, which may be due to the high rate of severe respiratory distress in the two groups. Wang et al. found that patients with a higher respiratory rate (26 vs. 23) and lower PaO2/FiO2 (159 vs. 223) were more likely to fail with KHAT.[7]

Administration of chloroquine/hydroxyl-chloroquine, azithromycin, and oseltamivir did not give different outcomes in patients with KHAT. The same thing was reported by Patel et al., who found no difference in the number of intubations in the group receiving drugs from hydroxychloroquine, azithromycin, and redeliver.9 The SOLIDARITY and

RECOVERY study conducted by WHO also did not find any difference in mortality and the need for mechanical ventilation between patients who received these drugs and those who did not.[15]

Before using KHAT, the patient's vital signs did not show a significant difference between the success and failure outcome groups. Significant differences were seen in the SpO2/FiO2 ratio (lower in the failed group) and the fractional requirement for inspired oxygen (higher in the failed group). This shows that the patient characteristics between the two groups are almost the same.

In this study, there were significant differences in respiratory rate, pulse rate, oxygen saturation, PaO2/Fio2, SpO2/FiO2, and ROX index measured 24 hours after using KHAT on outcomes 24 hours, 7, 14, and 21 days. In the group with successful outcomes, there was an improvement in vital sign parameters and respiratory index compared to the failed outcome group, which showed worsening or no improvement in vital signs and respiratory index parameters 24 hours after using KHAT. Wang et al. reported a significant difference in PaO2/FiO2 values between successful patients. They failed patients after using KHAT for 2 hours, while Calligaro et al. reported significant differences in the respiratory rate, pulse rate, SpO2, and ROX index, assessed 6 hours after KHAT. 7,14 Patel et al. reported that the changes in SpO2/FiO2 measured on day 7 were significantly different in the non-intubated KHAT group compared to the intubated group (141.4 vs. 40.5). [7,14]

The use of KHAT has a positive effect in the form of decreasing the workload of breathing and increasing patient comfort and compliance so that clinical improvements appear in the form of decreased respiratory rate and improved oxygenation (PaO2 and SpO2). This can be seen from the results of this study which illustrates that the group with successful outcomes will experience improvements in respiratory rate, pulse rate, O2 saturation, PaO2/FiO2 ratio, SpO2/FiO2 ratio, and ROX index. In contrast, the failed group will experience worsening or no improvement in these parameters compared with the initial value.[16]

Data from patients using KHAT, Wang et al. obtained the median results of peripheral blood tests, respectively, hemoglobin (12.8 g/dL), leukocytes (5400/μL), platelets (154000/μL), and lymphocyte count 700/L.[7] Patel et al. found a lymphocyte count of 1020/μL while Calligaro et al. of 1180/μL.[9,14] In this study, the average hemoglobin was almost the same (13.2 mg/dL) but with the value of leukocytes (9315/μL) and platelets (259000/μL).) higher. The lymphocyte count (1113/μL) was almost the same as in other studies.

In severe and critical cases, viral replication occurs rapidly and causes inhibition of interferon production, which causes T cell apoptosis so that the virus cannot be removed quickly. This leads to activation and excessive recruitment of neutrophils and monocytes to the site of infection. The mechanisms thought to cause the decrease in lymphocyte count are the cytopathic effect of SARS-CoV2 on lymphocytes, myelosuppression due to excessive inflammation, activation of lymphocyte apoptosis, and redistribution of lymphocytes to tissues due to high levels of proinflammatory cytokines (IL-2, IL-6, TNF)[17,18] Wang et al. found that a neutrophil/lymphocyte ratio (RNL) 2.14 is associated with more severe clinical severity and mortality.[18]

The value of inflammatory markers in several studies gave varying results. In patients using KHAT, Wang et al. had a lower median CRP value of 39 mg/L and a PCT value of 0.07 ng/ml, while Patel et al. and Calligaro et al. reported higher results of 117.7 mg/L and 118 mg/L. L.[1,9,14] The median lactate value in Demoule et al.'s study was 1.5 mmol/L, while Chen et al. reported a mean of 2.4 mmol/L.[8,19] In this study, the average CRP value was 146.8 mg/L, the median PCT value was 0.175 ng/ml, and the median lactate value was 2.5 mmol/L.

This study obtained a median value of D-dimer of 1500 g/L. There are variations in the study D-dimer value in patients using KHAT. Patel et al. reported a much higher value of 5659.6 g/L, while Calligaro et al. reported a lower value of 830 g/L.[9,14] PaO2/FiO2 values in Calligaro's study were reported as 68, which is almost the same as that obtained in this

study.[14]

Severe and critical COVID-19 patients have a hyperinflammatory state with the occurrence of cytokine storms due to dysregulation of the immune system. It is also associated with cardiopulmonary collapse and multiple organ failure. Clinically, an increase in pro-inflammatory cytokines and biomarkers such as IL-1, Il-6, IL-7, granulocyte-colony stimulating factor, macrophage inflammatory protein 1-α, tumor necrosis factor-α (TNF-α), CRP, PCT can be found. D-dimer and ferritin are associated with poor outcomes of increased mortality, more severe clinical course, the occurrence of ARDS, and the need for intensive care. Huang et al. concluded in their meta-analysis that cut-off values of increased PCT(≥0.5 mg/L), CRP(≥10 mg/L), and D-dimer (>0.5 mg/L) were associated with poor outcomes in COVID-19.[20]

This study found that the median values for urea, creatinine, aspartate transferase, alanine transferase, total bilirubin, and troponin I were in the normal range. Research on patients using KHAT by Wang et al. obtained a median creatinine value of 0.678 mg/dL and a total bilirubin value of 0.124 mg/dL.[7] Patel reported a higher mean creatinine of 2.61 mg/dL and a mean of aspartate and alanine transferase values of 56.8 U/L and 38.6 U/L. In comparison, Calligaro et al. reported a median creatinine value of 0.905 mg/dL.[9,14]

Abnormal values of blood chemistry parameters can indicate the severity of organ dysfunction. COVID-19 can cause damage to other organs outside the lungs due to the systemic inflammatory response.[21] Meta-analysis by Deng et al. found that 20% of COVID-19 patients had elevated transaminases, 8% had elevated total bilirubin, 34% had lower albumin values, and 8 % experienced an increase in creatinine values. Changes in these parameters are more clearly seen in patients who experience worsening clinical symptoms.[22]

This study showed significant differences in procalcitonin values between the groups with successful and failed outcomes at 24 hours, 7, 14, and 21 days. The troponin I and lactate values were also significantly different in the two groups at 24 hours and 7 days but were not significantly different at 14 days and 21 days of observation. Until now, there is no data comparing procalcitonin, troponin I, and lactate values in COVID-19 patients using KHAT, but it is known that increased PCT and troponin in COVID-19 patients can increase the risk of poor outcomes and death.[20,23]

The meta-analysis by Huang et al. found that an increase in PCT value of 0.5 mg/L in COVID-19 patients had consequences in the form of increased mortality, more severe clinical degrees, the occurrence of ARDS, and the need for intensive care. In this study, the PCT values were relatively low (< 0.5 mg/L) in both groups. In viral infections, the antiviral activity of interferon-γ will reduce PCT production. This explains why in uncomplicated COVID-19 patients, the PCT value is still within the reference value limit. Increased PCT on serial measurements may indicate the deteriorating clinical status of COVID-19 patients.[20]

In this study, the troponin values in the two groups were significantly different in the 24-hour and 7-day outcomes. However, they were still within the reference range, so the detected troponin levels may not reflect myocardial injury in most study subjects. Loss of significance at the 14-day and 21-day outcomes may have occurred due to failed outcomes in subjects with extreme troponin values. A meta-analysis by Zhao et al. found that 20.8% of COVID-19 patients had elevated troponin values above the reference value at the time of admission and described myocardial injury. An increase in troponin values at the beginning of hospitalization that exceeds the reference value can predict mortality risk.[23]

The CRP value in this study did not significantly differ in the outcome of 24 hours, 7, 14, and 21 days. Both groups had a mean CRP above 100 mg/L at the start of treatment, although the group with the failed outcome had a higher mean CRP value than the group with the successful outcome. Calligaro et al. found significantly different CRP values in patients who succeeded and failed after

using KHAT for 6 hours. However, the new CRP value gave significance as a predictor of KHAT failure at values > 500 mg/L. The CRP value of the failed group was also higher than that of the successful group (235 mg/L vs. 173 mg/L).[14]

This study found that D-dimer values were not significantly different at 24 hours, 7, 14, and 21 days. The median value of D-dimer in the group with successful outcomes was higher than in the failed group. Calligaro et al. reported significantly different D-dimer values between the successful and failed groups after 6 hours of KHAT; the successful group had a lower median D-dimer value (560 g/L vs. 1030 g/L) but only the D value. -dimer > 5000 g/L, which is statistically significant as a predictor of KHAT failure.[14]

This study did not find significant differences in hemoglobin, leukocyte, neutrophil count, lymphocyte count, RNL, and platelet count. Both groups had almost the exact characteristics of hematological parameters. However, the group with failed outcomes had a median leukocyte, neutrophil count, higher NLR, and lower lymphocyte count than the group with a successful outcome. Although not statistically significant, Patel et al. and Calligaro et al. also found lower lymphocyte count values in patients who failed with KHAT.[9,14]

The characteristics of blood chemistry parameters often used as organ damage markers did not show significant differences in the group with successful and failed outcomes. However, the urea, creatinine, and transaminase values in the group with failed outcomes were higher than those with successful outcomes. Patel et al. and Calligaro also reported similar results in baseline blood chemistry values of patients with HBV.[9] The course of COVID-19 disease is dynamic and clinical deterioration may occur as the length of stay increases. It is possible that the values of blood chemistry parameters in the patients in this study would be different between the two outcome groups if serial examinations were performed.

The success of using KHAT on this study's 21st day of observation was 45.2%. Calligaro et al. reported successful use of KHAT (defined as patients who were not intubated and did not die) of 47%, while Patel et al. reported a 64.42%.[7,9,14] intubation prevention rate. requiring NIV or intubation) Moreover, Demoule et al. reported that 56% of patients with KHAT required intubation at 28-day follow-up.[7,8]

This study was conducted retrospectively so that the quality of the data depends on the completeness of the medical record. Laboratory data also cannot be analyzed serially because examination intervals are not uniform. Prospective studies and serial laboratory studies are needed to confirm the findings.

CONCLUSION

There were significant differences between the success and failure outcomes in respiratory rate, pulse rate, oxygen saturation, PaO2/Fio2, SpO2/FiO2, and ROX index. Patients with failed outcomes showed no improvement or worsening, while patients with successful outcomes showed improvement in these parameters after using KHAT.

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