Extracorporeal membrane oxygenation experiences during COVID-19 pandemic, third wave with younger patients: A retrospective observational study

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Abstract:
OBJECTIVES: In this article, the results of severe coronavirus disease 2019 (COVID‑19) cases followed with extracorporeal membrane oxygenation (ECMO) support in a 3-month period in the third wave when there were an increased number of cases of young patients in our intensive care unit (ICU) were presented.

METHODS: The study was carried out with all COVID‑19 patients who were given ECMO support in our tertiary referral hospital ICU after obtaining the consent of the Ministry of Health Scientific Research Platform and after the approval of the local ethics committee. Patient data were obtained retrospectively from intensive care bedside follow-up charts and computer records. The demographic and clinical characteristics of the patients were presented in average, median, and percentages. The data of the patients were evaluated and compared with the current literature.

RESULTS: ECMO treatment was applied in seven patients who were followed up with severe COVID‑19 pneumonia in the last 3 months. Venovenous extracorporeal membrane oxygenation (VV‑ECMO) was applied to all patients. Five (71.5%) of seven patients were weaned from ECMO. Four (57.2%) of seven patients were discharged from the ICU and hospital in good health. While two of the patients had a cesarean section (C/S) before ECMO, one patient underwent C/S under ECMO. All three newborns were delivered via C/S and all were premature (C/S dates were 35 weeks, 32 weeks, and 27 weeks), and all were discharged from the hospital in good health.

CONCLUSION: Our experience shows that ECMO in COVID‑19 patients is a lifesaving treatment option that can be successfully applied in severe acute respiratory distress syndrome cases who do not respond to conventional treatments.

Keywords: Coronavirus disease 2019, extracorporeal membrane oxygenation, mortality, pregnancy, SARS-CoV-2

Introduction

Coronavirus disease 2019 (COVID-19)-associated acute respiratory distress syndrome (ARDS) has a high mortality rate and can be seen not only in the elderly and those with chronic diseases but also in young and healthy patients. Venovenous extracorporeal membrane
Performing ECMO treatment is not easy and mortality rates are higher in Turkey than European Union countries, besides the mortality rates are higher in COVID-19 patients than other critical ill patients under ECMO treatment. The main question is: How can we increase our survive rates?

What is the conflict on the issue? Has it importance for readers?
- Mortality rates are higher in Turkey than European Union countries, besides the mortality rates are higher in COVID-19 patients than other critical ill patients under ECMO treatment
- The main question is: How can we increase our survive rates?

How is this study structured?
- This was a single-center, retrospective observational study.

What does this study tell us?
- Contrary to routine recommendation, early weaning from mechanical ventilation (weaning than ECMO) and letting the patients breath can be beneficial in COVID-19 patients.

Method

The study includes all COVID-19 patients who were given ECMO support in our ICU during the third wave; last 3 months (March–May 2021) when the disease was most prevalent among young people in our country. In addition to informed consent of the patients, the study was approved by the Ministry of Health Scientific research platform with registration number of 2021-05-14-T20_34_19 regarding COVID-19–related studies and by the local ethics committee (Karadeniz Technical University, School of Medicine, No: 2021/368 dated November 15, 2021).

The diagnosis of SARS-CoV-2 pneumonia was based on radiological and microbiological (upper respiratory tract SARS-CoV-2 PCR) samples. All data pertinent to the patients were obtained retrospectively from intensive care bedside follow-up charts and computer records.

The clinical characteristics, demographic data, comorbidities, first admission laboratory data, intensive care patient severity scores, mechanical ventilation and ECMO settings, medical treatments for COVID-19, ECMO-related complications, and patient outcomes were recorded. In all patients who underwent ECMO, the lung protective ventilation strategy recommended by the ELSO COVID-19 guideline was followed. This strategy includes achieving a targeting plateau pressure (PPLAT) ≤25 cmH₂O, respiratory rate 4–10, breath per minute, positive end-expiratory pressure (PEEP) 10–15 cmH₂O, driving pressure <15 cmH₂O, and FiO₂ 50% to maintain saturation ≥85%. Again, ECMO decisions were made based on the indications of the same guideline for ECMO. These indications included (1) partial pressure of arterial oxygen (PaO₂) over a FiO₂ ratio of less than 50 mmHg for more than 3 h; (2) PaO₂/FiO₂ less than 60 mmHg for more than 6 h; or (3) arterial blood pH less than 7.25 with a partial pressure of arterial carbon dioxide of 80 mmHg or more for 6 h or more and the absence of absolute contraindications for ECMO.[9]

VV-ECMO was applied to all patients. Deciding whether to start and leave ECMO in our intensive care clinic is made by the intensive care and cardiovascular surgery team. Cannulation procedure is performed with ultrasonography as recommended and adequate position of the cannulas was verified by ultrasonography and chest X-ray.[3] VV-ECMO was percutaneously and ultrasonographically inserted with a 23–29-Fr drainage cannula and an 18–23-Fr return cannula by two intensive care physicians. A 24-h cardiovascular surgery and perfusionist team is available for possible complications and support. All our patients were anticoagulated with unfractionated (UF) heparin and the partial thromboplastin time (PTT) target was as 40–55 s as in the EOLIA study.[4] In general, recommendation for hemoglobin is >7–8 mg/dl (in the case of resistant hypoxemia, it can be increased up to 10 mg/dl), for platelets >50,000 10⁹/1. Although targets are recommended, low platelet counts and fibrinogen values are tolerated unless a bleeding problem occurs.[3] When ECMO was adjusted, cardiac output (CO) was measured by bedside echocardiography, and the target flow adjustment was set to be at least 80% of CO. Flows were maintained greater than 3 L/min to minimize risk of spontaneous clot formation. EOS ECMO®-Hollow Fiber Oxygenator (LivaNova) and SCP + SCPC® The Centrifugal Pump System (SORIN) were used in ECMO treatments.

Oxygenation (VV-ECMO) for the clinical management of severe respiratory failure has been used effectively during the 2009 influenza A (H1N1) pandemic. ECMO is an invasive support strategy for cardiac, respiratory, or combined cardiorespiratory failure when conventional treatment options have failed. Considering the limited healthcare resources, the use of VV-ECMO as a therapeutic intervention in selected COVID-19 cases who resist to standard medical and mechanical ventilation strategies is recommended by The Extracorporeal Life Support Organization (ELSO).[3] In this study, we present our results on severe COVID-19 patients who received ECMO support in a tertiary referral hospital intensive care unit (ICU).
Statistical analysis
Continuous variables are expressed as mean ± standard deviation or as median (interquartile range [IQR]) according to the distributions examined by the Kolmogorov–Smirnov test. Categorical variables are presented as numbers (proportions). Data were analyzed with SPSS V23, IBM, Chicago, USA.

Results
ECMO treatment was applied to seven patients who were followed up with severe COVID-19 pneumonia in the last 3 months. Four of the patients were men and three were women, and the median age was 40 years. Five (71.4%) of seven patients were weaned from ECMO. Four (57.2%) of seven patients were discharged from the ICU and the hospital in good health. All patients were discharged to the ward and then to their homes with a Glasgow coma scale of 15 and reduced oxygen demand. None of the discharged patients died in the 90-day follow-up. All of them continue their lives with their normal physical performances. The clinical features, ECMO and mechanical ventilation-related parameters, and outcome information of the patients are detailed in Table 1. VV-ECMO cannulation was performed in all patients in the femoral-inner jugular configuration. Before the ECMO, the median P/F ratio of the patients was 65 (61–78). While the median driving pressure value before ECMO was 20 (16–23) mmHg, the median driving pressure value under ECMO was 9 (8–11) mmHg. The median FiO₂ support at initial ECMO settings was 90% (90–90), the median blood flow was 3.7 l/min (3.5–4), and the median sweep gas flow was 5 l/min (5–6). Prone position was applied in 6 of 7 patients. While two of the patients had a cesarean section (C/S) before ECMO, one patient underwent C/S under ECMO. All three newborns were delivered via C/S and all were premature (C/S dates were 35 weeks, 32 weeks, and 27 weeks), and all were discharged from the hospital in good health. Tube thoracostomy was performed after pneumothorax in two patients, while pneumothorax was bilateral in these two patients. During the follow-up period, ventilator-associated pneumonia (VAP) developed in four patients, and catheter-related bloodstream infection developed in three patients. While all patients were anticoagulated with UF heparin, no thrombotic events occurred in the membrane oxygenator during ECMO support.

The median day from diagnosis of COVID to mechanical ventilation in patients was 13 (IQR: 9–17), and the median day from mechanical ventilator to ECMO was 1 (IQR: 1–4). The median duration of mechanical ventilator, median ECMO treatment time, and median intensive care hospital stay were, respectively, 22 (IQR: 8–35) days, 16 (IQR: 8–18) days, 35 (IQR: 17–36) days. The timeline chart of the patients after the diagnosis of COVID-19 is shown in Figure 1.

Discussion
Severe ARDS associated with COVID-19 can rapidly cause profound hypoxemia and death. Although the efficacy of ECMO is unclear in this selected patient group where mechanical ventilation is not sufficient, many of major health organizations recommend the use of ECMO support as a rescue therapy for acute hypoxic respiratory failure associated with COVID-19.[13,16–9] However, due to the limited capacity and constrained resources during the pandemic for hospitalization of patients, the consensus among clinicians is to admit young patients with single organ failure and previously healthy patients who are likely to see maximum benefit.[10,11] In parallel with these predelictions, the average age of our patients was also younger because of the second wave. As the median age was 40, the successful wean rate from ECMO was 71.4%, and the survival rate in the ICU was 57.2%. None of the patients had serious comorbidities, and all of them were taken to ECMO in the early period of mechanical ventilation (day 6 at the latest). Contrary to this result in our small group of the study, initial data on the use of ECMO in COVID-19 patients at the beginning of the pandemic resulted in high mortality.[12] For these critically ill patients, it is recommended that ECMO is better to be implemented in centers with enough number of specialist and also to organize mobile ECMO teams for expedited patient transfer.

Lebreton et al. have published a report on the ECMO results of critically ill patients with COVID-19 from 17 ICUs, covering the Paris region of France with a population of approximately 12 million. The survival rate of 90 days after ECMO was 46% of 302 adult patients who did not have serious comorbidities but requiring ECMO. [13] These results contradict the findings from the 2018 EOLIA study, which reported a 60-day survival of 65% in the ECMO group, suggesting that lung failure due to SARS-CoV-2 has a worse prognosis compared to acute respiratory distress from other causes.[14] On the other hand, in an international registry study, ELSO reported an estimated 90-day survival rate of 62% in 1035 patients treated with ECMO for refractory lung failure associated with COVID-19.[18] In our study, while two patients to whom VV-ECMO applied were in the early postpartum period, while one patient gave birth with C/S under ECMO and two of three survived. All female patients were unvaccinated patients who were admitted to ICU and connected to ECMO in the postpartum/pregnancy period completely by chance. Within the patient profile we accepted in the third wave, there were approximately 37 pregnant/postpartum patients that we followed in the
Table 1: Characteristics of the extracorporeal membrane oxygenation patients due to coronavirus disease 2019*

| Characteristic                                      | 1          | 2          | 3          | 4          | 5          | 6          | 7          | Median (25th-75th percentiles) |
|-----------------------------------------------------|------------|------------|------------|------------|------------|------------|------------|---------------------------------|
| Age (years)                                         | 46         | 22         | 32         | 40         | 45         | 26         | 63         | 40 (26-46)                      |
| Gender                                              | Male       | Female     | Female     | Male       | Male       | Female     | Male       |                                 |
| BMI<30                                               | Yes        | Yes        | Yes        | Yes        | Yes        | Yes        | Yes        |                                 |
| Smoking                                             | Yes        | No         | No         | Yes        | No         | No         | No         |                                 |
| Score points                                        |            |            |            |            |            |            |            |                                 |
| SOFA score                                          | 8          | 8          | 10         | 15         | 2          | 5          | 5          | 8 (5-10)                        |
| APACHE II score                                     | 16         | 20         | 17         | 14         | 12         | 20         | 18         | 17 (14-20)                      |
| Comorbidity                                         |            |            |            |            |            |            |            |                                 |
| Hypertension                                        | Yes        | None       | None       | Diabetes mellitus | Hypertension | None       | Hypertension |                                 |
| Laboratory values on admission                      |            |            |            |            |            |            |            |                                 |
| C-reactive protein (mg/L)                           | 206        | 103        | 14.3       | 9.1        | 42.9       | 77.4       | 324        | 77.4 (14.3-206)                 |
| White blood cell (10^3 cells/mm^3)                  | 7.95       | 23.5       | 10.29      | 13.6       | 7.9        | 11.1       | 22         | 10.1 (7.9-22)                  |
| Platelet (10^3 cells/mm^3)                          | 134        | 405        | 211        | 142        | 225        | 328        | 302        | 225 (142-328)                  |
| Hemoglobin (g/dl)                                   | 15.5       | 8.4        | 9.7        | 13.3       | 10.8       | 8.8        | 12.8       | 10.8 (8.8-13.3)                 |
| Creatinine (mg/dl)                                  | 1.11       | 0.22       | 0.62       | 0.37       | 1.29       | 0.24       | 0.97       | 0.62 (0.24-1.11)                |
| Lactate dehydrogenase (U/l)                         | 987        | 574        | 594        | 586        | 733        | 551        | 515        | 586 (551-733)                  |
| D-dimer (mg/l)                                      | 0.96       | 6.22       | 5.89       | 0.63       | 1.46       | 2.28       | 2.04       | 2.05 (0.96-5.89)                |
| Lactate (mg/dl)                                     | 20         | 9          | 11         | 10         | 30         | 17         | 18         | 17 (10-20)                     |
| Ferritin (µg/l)                                     | 2116       | 62         | 40         | 279        | 78         | 1812       | 98.1       | 98.1 (62.3-1812)               |
| Median arterial blood gas values before ECMO         |            |            |            |            |            |            |            |                                 |
| pH                                                  | 7.43       | 7.46       | 7.46       | 7.26       | 7.36       | 7.41       | 7.07       | 7.41 (7.26-7.46)               |
| FiO2 (%)                                            | 100        | 100        | 75         | 100        | 100        | 100        | 100        | 100 (100-100)                 |
| P/F                                                | 63         | 61         | 80         | 65         | 78         | 78         | 78         | 65 (61-78)                    |
| PO2 (mmHg)                                          | 83         | 61         | 58.9       | 65         | 78         | 78         | 78         | 63 (58-78)                    |
| PCO2 (mmHg)                                         | 43         | 27         | 48.8       | 114        | 65.3       | 44.1       | 103        | 48.8 (43-103)                 |
| HCO3 (mmol/L)                                       | 28         | 21         | 32.5       | 41.2       | 27.5       | 21.7       | 28         | 21.7 (21.7-33)                |
| sO2 (%)                                             | 85         | 83         | 86         | 84         | 84         | 87         | 87         | 85 (84-87)                    |
| Mechanical ventilation parameters before ECMO       |            |            |            |            |            |            |            |                                 |
| FiO2 (%)                                            | 100        | 100        | 75         | 100        | 100        | 100        | 100        | 100 (93.75-100)               |
| PEEP (mmHg)                                         | 11         | 10         | 13         | 7          | 12         | 10         | 9          | 10 (9-12)                     |
| Tidal volume (ml)                                   | 550        | 310        | 560        | 326        | 530        | 350        | 350        | 350 (326-550)                 |
| Respiratory rate (breath/min)                       | 20         | 20         | 18         | 24         | 20         | 20         | 22         | 20 (20-22)                    |
| Plato pressure (mmHg)                               | 31         | 32         | 29         | 32         | 28         | 30         | 32         | 31 (29-32)                    |
| Driving pressure (mmHg)                             | 20         | 22         | 16         | 25         | 16         | 20         | 23         | 20 (16-23)                    |
| ECHO evaluation before ECMO†                         |            |            |            |            |            |            |            |                                 |
| EF (%)                                              | 55         | 50         | 50         | 60         | 60         | 55         | 55         | 55 (50-60)                    |
| Valve insufficiency                                 | None       | 1º         | 1º         | None       | None       | None       | 1º         |                                 |

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Contd..
Table 1: Contd...

| Characteristic                      | Patients | Median (25th-75th percentiles) |
|-------------------------------------|----------|---------------------------------|
| CO (l/min)                          | 4.9      | 5.8 (5-6.2)                     |
| ECMO initial settings               |          |                                 |
| Blood flow (l/min)                  | 4        | 3.2 (3.5-4)                     |
| Sweep gas flow (l/min)              | 6        | 4 (5-6)                         |
| FiO₂ support (%)                    | 100      | 90 (90-90)                      |
| Mechanical ventilation parameters   |          |                                 |
| after ECMO                          |          |                                 |
| FiO₂ support (%)                    | 100      | 50 (50-85)                      |
| PEEP (mmHg)                         | 8        | 11 (9-12)                       |
| Tidal volume (ml)                   | 320      | 240 (200-350)                   |
| Respiratory rate (breath/min)       | 15       | 10 (10-14)                      |
| Plato pressure (mmHg)               | 18       | 20 (18-22)                      |
| Driving pressure (mmHg)             | 10       | 9 (8-11)                        |
| Treatments                          |          |                                 |
| Medical†                            | Pulse steroid | Tocilizumab | Pulse steroid | Pulse steroid | Pulse steroid | Pulse steroid |
|                                    | Tocilizumab | NM blocker                 | Tocilizumab | NM blocker | Tocilizumab | NM blocker |
|                                    | NM blocker  |                          | NM blocker |               | NM blocker |               |
| Prone position                      | Yes       | Yes                         | Yes       | Yes         | No         | Yes          |
| Surgical                            | None      | Tube thoracotomy             | Cesarean section | Thoracotomy | Cesarean section | None |
| Complications                       | None      | Hemorrhax                   | Thrombocytopenia | Cardiac arrhythmia | VAP | CRBSI | Thrombocytopenia | VAP | CRBSI |
|                                    | Pneumothorax |                            | VAP | Septic shock | CRBSI |                                       |
| Outcomes                            | Wean from ECMO | Survived | Survived | Survived | Nonsurvived | Nonsurvived | Survived | Survived |
| Mortality                           | Yes       | Yes                         | Yes       | No         | Yes        | No          | Yes        | Yes      |

*BMI denotes body mass index, †Cardiac output was estimated with the Doppler velocity time integral method and ejection fraction with the Simpson method, ‡Pulse steroid means 250 mg methylprednisolone/day. The P/F ratio equals the arterial pO₂ divided by the FiO₂. CAD=Coronary artery disease, FiO₂=Fraction of inspired oxygen, PO₂=Partial pressure of oxygen, pCO₂=Partial pressure of carbon dioxide, SO₂=Arterial oxygen saturation, SOFA=Sequential organ failure assessment, APACHE II=Acute physiology and chronic health evaluation II, PEEP=Positive end expiratory pressure, ECMO=Extracorporeal membrane oxygenation, ECHO=Echocardiography, EF=Ejection fraction, CO=Cardiac output, NM blocker=Neuromuscular blocker, VAP=Ventilator-associated pneumonia, CRBSI=Catheter-related bloodstream infection, BMI=Body mass index.
ICU, and these three patients were among those patients who needed ECMO. Pregnant women are younger, are healthier than the general population, and thus have probably higher survival than patients undergoing ECMO for other indications.\[14-16\] Case reports on the application of ECMO in COVID-19 ARDS in pregnant women are scarce. Barbaro et al. reported on the successful use of ECMO in COVID-19 in an international cohort study (22 patients out of 1035 were pregnant).\[8\]

Currently, there is no known effective treatment for SARS-CoV-2. All treatments approaches including ECMO are supportive and aim saving time for the body’s immune response to be activated. Appropriate patient selection for ECMO is extremely important, especially in times of inadequacy of equipment. Before choosing the right patient for ECMO, different mechanical ventilation modes that the patient can adapt to should be tried, and clinicians should be encouraged to follow up in the prone position using neuromuscular blocking agents before ECMO. First of all, to provide protection from ventilator-induced lung injury, ultra-protective lung ventilation should be applied to minimize tidal volume (VT), respiratory rate (RR), and airway and driving pressure. Thus, patients who have not been exposed to mechanical ventilation and its harmful mechanical effects for a long time and who have not developed organ failure and are in the early period of intubation after acute progression can be selected. The median duration of mechanical ventilation in our patients was 1 (IQR: 1–4) days before ECMO. It is thought that the most important point in our dropout rates from successful ECMO is the right patient selection.

We decided to VV-ECMO after trying new mechanical ventilation modes, including Airway pressure release ventilation (APRV), Adaptive support ventilation (ASV), and other traditional modes in our patients in the prone position. As VV-ECMO provides a “window period” in which damaged lungs can rest and heal, it is the primary ECMO mode used in patients with ARDS. In our ICU, the decision to start and wean ECMO is made by two of our well-experienced intensive care specialists who also performed cannulation. Since three ECMO devices are available for 24 h a day in our 16-bed unit, ECMO can be started immediately as soon as the decision was made.

Although ECMO treatment is considered as lifesaving in selected patients, the number of serious complications is quite high, especially as a result of the pathophysiological effects of COVID-19–related disease in the vascular bed. In contrast to the previous EOLIA study, high number of serious complications such as intracranial hemorrhage, VAP, and pulmonary embolism were reported with ECMO in COVID-19 patients.\[13,17\] Furthermore, as opposed to the previous reports, pump failure, oxygenator dysfunction, and circuit embolism, among other mechanical complications reported in COVID-19 patients were not seen in our patients.\[8\] In one of our patients, the cannula in the right femoral vein was switched to the left femoral vein in the following days since the target oxygenation could not be achieved because of insufficiency in the drainage cannula. An increase in the frequency of secondary hospital-acquired infections was observed due to some reasons such as high-dose steroid administration and infusion catheter...
requirements due to multiple medications. On the other hand, erythrocyte replacement was required due to leaks from the tracheotomy area, especially in our patients who were heparinized and tracheotomized. In our patients, thrombocytopenia was generally observed in the 2nd week of ECMO follow-up (in 4 of our patients (57.2%), but interruption of heparinization for a short time due to of massive chest tube bleeding was needed in two of our patients (Patient No.: 2 and 6).

Considering that the resources for ECMO may be limited, the ELSO recommends weaning COVID-19 patients from ECMO as early as possible before mechanical ventilation. Desired targets for obtained to facilitate weaning from ECMO are; sweep gas remaining at 01/min, increasing of ventilatory support as needed until the VT ≤6–8 ml/kg, PPLAT ≤30 cmH2O, PEEP ≤16 cmH2O, FiO2 ≤0.5, pH >7.3 and arterial oxygen saturation >88%. It has been suggested that the patient can be decannulated if gas exchange is adequate for a period of 2–4 h. Most of our patients were extubated in 9.5 (IQR: 7.25–22.25) days and weaned from ECMO in 10 (IQR: 8–17.5) days. The reason for this approach is the variability of COVID-19–related radiological involvement between days, the re-progression phase following rapid regression, the increase in oxygen consumption, and the need in cases such as sepsis/septic shock due to frequent secondary infections. In these cases, it would be rational to benefit from ECMO support against the possibility of reintubation in the early period.

Another important issue in the follow-up of the ECMO patient is the effective provision of anticoagulation. All our patients were anticoagulated with UF heparin with the recommendations of the guideline. Although there were higher PTT target recommendations, PTT values were close to the lower limit (PTT 45–55 s) in our patients due to mucosal leaks and bleeding from the tracheotomy areas, in general, but no thrombotic complications were encountered. Tranexamic acid 10–20 mg/kg and fibrinogen 1–2 g/day were additionally used in a patient with heavy bleeding but closely monitored for the circuit and the oxygenator thrombosis. Heparinization was interrupted for a maximum of 24–48 h in our patients who had active bleeding and were planned for invasive intervention. In our patients, platelet transfusions were not used except in the case of severe thrombocytopenia (<50 × 10³/mm³ cell) or bleeding.

**Limitations**

We are aware of that our data and interpretations are limited by the small sample size. However, as management strategies and treatments are constantly evolving during the pandemic, we felt that it was important to share our data to assist clinicians at the bedside.

**Conclusion**

Our experience shows that ECMO in COVID-19 patients is a lifesaving treatment option that can be successfully applied in severe ARDS cases who do not respond to conventional treatments. To have faster access to the equipment, fast and accurate communication between the referring team, cardiovascular surgery department, and intensive care teams is crucial when a transfer to a reference site for ECMO is made, since there are no dedicated ECMO teams in our country. With the experience of intensive care specialists and intensive care teams, and 24-h uninterrupted follow-up, less complications and satisfactory results can be obtained.

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**Author contributions**

AOK: Conceptualization (equal), Formal analysis (lead), Writing – original draft (equal), Methodology (equal). MPK: Conceptualization (equal), Writing – original draft (equal), Methodology (equal). OA: Writing – review and editing (support), Supervision (support), Methodology (equal). GA: Writing – review and editing (support), Supervision (support), Methodology (equal). ACÖ: Writing – review and editing (support), Supervision (lead), Methodology (equal)

**Conflicts of interest**

None Declared.

**Consent to participate and Ethics committee approval**

The STROBE guideline was used as a guide for this manuscript. The study was prepared in accordance with the rules of the Helsinki Declaration. Our study was planned as a retrospective examination of the patient records of the Faculty of Medicine, Pulmonary Medicine Clinic, ICU. In addition to the informed consent of the patients, the study was approved by the Ministry of Health Scientific research platform with registration number of 2021-05-14-T20_34_19 regarding COVID-19 related studies and by the local ethics committee (Karadeniz Technical University, School of Medicine, No: 2021/368 dated November 15, 2021).

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