ÖZ Amac: COVID-19 hastalarında akciğer tutulumu sıkılkık görülmektedir, mekanik ventilasyonun ve oksijenasyonun artırılmasında pozisyon desteği de kullanılmaktadır. Çalışmamızda ultrasonografi rehberinde verilen pozisyon uygulamasının etkisi değerlendirilmeye amaçlanmıştır.


Sonuç: Çalışmamızda ultrasonografi rehberinde verilen pozisyonun oksijenasyonu üzerinde pozitif bir etkisi olduğu belirlenmiştir. Pozisyon değişikliği istatistiksel olarak anlamlı olduğu olduğu gözlemlenmiştir.

Anahtar Kelimeler: Akciğer ultrasonografisi, COVID-19, prone pozisyon, yoğun bakım ünitesi, akut solunum yetmezliği

ABSTRACT Objective: Lung involvement is commonly seen in patients with Coronavirus disease 2019. In such cases, mechanical ventilation support and patient positioning are used to improve oxygenation. This study aimed to evaluate the effect of positioning performed under the guidance of ultrasound-guided patient positioning.

Materials and Methods: Patients were divided into two groups: those who underwent lung ultrasonography and those who did not. Patients who underwent lung ultrasonography were positioned in a way that the region with larger infiltration area was upwards and then the groups were compared.

Results: Arterial blood gas values of 103 patients were evaluated. An increased partial pressure of oxygen (PaO2) values at 2 and 12 hours after positioning was statistically significant in patients who were positioned under ultrasound guidance. In the group who did not undergo ultrasonography, an increased PaO2 values was observed at 12 hours.

When patients were evaluated according to their positions, an increased PaO2 values was observed in the right lateral decubitus position. However, it was not statistically significant.

Conclusion: In our study, an increased oxygenation was observed in a short time, i.e., 2 hours, when patients were positioned under ultrasound guidance.

Keywords: Lung ultrasonography, COVID-19, intensive care, prone position, intensive care unit, Acute Respiratory Distress Syndrome
Introduction

Lung involvement is frequently seen in COVID-19 disease, and the incidence of Acute Respiratory Distress Syndrome (ARDS) is reported to be 17-42% (1). Computed tomography (CT) is used for diagnosis, but there are risks such as exposure to excessive radiation, problems in the transfer of critical patients, and transmission of infection, and viral contamination (2-4). Therefore, it is not recommended to use CT in disease follow-up. Posteroanterior chest X-ray can often be used to avoid these risks.

However, the use of lung ultrasonography (LU) is becoming gradually more common in the diagnosis and follow-up of pneumonia and ARDS (5,6). Lung ultrasonography (LU) is also considered to be superior to posteroanterior chest X-ray in the follow-up of COVID-19 patients (7).

Due to reasons such as the pathological progression of COVID-19 pneumonia and the occurrence of peripheral involvement, a surface imaging technique like LU is rather appropriate (4,8). It is also reported that LU has high diagnostic accuracy, is repeatable, noninvasive, ergonomic, and causes less infection, and enables a quick evaluation lung status without using ionizing radiation (8-10). Because of such advantages, LU has readily become a tool for the diagnosis and follow-up of the severity of the lung involvement (3,11).

Besides the mechanical ventilation strategies, the importance of patient positioning is known to improve oxygenation during the treatment of ARDS. Improvements in oxygenation and reduced mortality have been reported in the literature in association with the prone position (12).

The aim of our study was to investigate the effect of LU-guided appropriate patient positioning on improved oxygenation and ventilation to obtain effective use of lung capacity in COVID-19 patients admitted to the intensive care unit (ICU) due to acute respiratory failure.

The primary aim of the study was to evaluate the effect of LU-guided positioning on oxygenation in patients with hypoxemic respiratory failure due to COVID-19. For this purpose, changes in PaO\textsubscript{2} (partial oxygen pressure in arterial blood) levels were examined after patient positioning. The secondary aim of the study was to evaluate the effect of LU-guided patient positioning on ventilation. For this purpose, changes in PaCO\textsubscript{2} (partial carbon dioxide pressure in arterial blood) levels obtained after patient positioning were examined.

Materials and Methods

This study was approved by the Ministry of Health (dated 05.04.2020, numbered 2020-05-04T00-50-43) and our Education and Research Hospital’s Clinical Research Ethics Committee (dated 06.26.2020, numbered 66) and written informed consent was obtained from all patients included in the study. The study was registered on clinicaltrials.gov (NCT04432051, date of registration: 06.16.2020). This manuscript adheres to the applicable CONSORT guidelines.

The study was conducted in the intensive care units (ICUs) of our hospital between May 26 and July 26, 2020. 110 patients between 18-80 years of age who were diagnosed with moderate and severe acute respiratory distress syndrome due to COVID-19 were included in the study. All patients included in the study had a PaO\textsubscript{2}:FiO\textsubscript{2} (partial arterial oxygen pressure: fraction of inspired oxygen) ratio of <200 and received mechanical ventilation support was applied to all patients.

In renal and cardiac failure, the respiratory system and oxygenation can be affected independently of acute respiratory failure due to COVID-19. Therefore, patients with cardiac and renal problems were excluded from the study.

Of the 110 patients included in the study; an intubated patient could not tolerate the prone position and was brought back to the supine position because of a sudden drop in SaO\textsubscript{2} and another patient receiving non-invasive mechanical ventilation support was brought back to the supine position because of difficulty adapting to the prone position. When the patients’ arterial blood gas analyses (ABG) were evaluated, 5 patients with initial BE values of <-3 were considered to have metabolic acidosis and excluded from the study. Thus, 7 patients were excluded from the study, and the data from 103 patients were evaluated.

This study was planned as a prospective randomized-controlled, and double-blinded study. Randomization was performed according to the days of the week. The patients were divided into two parallel groups as patients undergoing LU (Group A) and patients without ultrasonography (Group B).

All patients included in the study were examined for respiratory system findings and were evaluated by arterial blood gas analysis. Mechanical ventilation settings have been adjusted. And during the study, FiO\textsubscript{2} levels and other parameters of mechanical ventilation settings were not changed until arterial blood gas was taken at the 12th hour.
The condition of the patients’ lungs was scored via LU in Group A by an anesthesiologist experienced in LU. Six-zone scanning method was performed on for each hemithorax as recommended in previous studies was used (11,13-15). While performing lung ultrasonography (MyLab™ Seven, Esaote, Genova, Italy), each hemithorax was divided into 6 quadrants for the examination as anterior, lateral, and posterior regions and lower and upper sections within each region, using anterior axillary line and posterior axillary line. Thus, each hemithorax was scanned on six quadrants by using a convex ultrasound probe and scored with Lung Ultrasound Score Score (LUS) (16).

In lung ultrasonography; A-lines characterized by the horizontal reverberation artifact and mirror images of the pleural line are formed depending on the reflection of the pleura (Figure 1) (2,17,18). A-lines show normally aerated lung. B-lines are hyperechoic, laser-like, vertical reverberation artifacts, which obliterate the A-lines extending from the pleural line to the bottom of the screen (Figure 2) (4,17,19,20). With synchronization of the breath, B-lines move and up to three B-lines appear per lung window (intercostal space) (4,17).

Diagnosis of interstitial lung disease is made in the presence of >3 B-lines, confluent B-lines (white lung), >0.3 mm thick, irregular pleural line, subpleural consolidations per window (Figure 3,4,5) (4,20). Consolidation regions are observed in advanced cases (Figure 6).

Depending on the LUS score; patients were brought to the supine, prone, right lateral, or left lateral positions with the side with higher scores kept upside.

Mechanical ventilation adjustments were made to the control patients in Group B by taking into account routine respiratory examination and arterial blood gas analysis. The patients were positioned as deemed appropriate by the physician.

Arterial blood gas analysis values of the patients were evaluated in both groups at the beginning (before physical examinations ± ultrasonography) and at the 2nd and 12th hour after physical examinations ± ultrasonography. The researchers who performed ultrasonography and evaluated ABG were different.

Partial oxygen pressure in arterial blood (PaO₂), partial carbon dioxide pressure in arterial blood (PaCO₂), oxygen saturation in arterial blood (SaO₂), base excess (BE), lactate and pH values were examined. The changes in the PaO₂ values of the patients were examined and whether there was a change in oxygenation was evaluated. The changes in the PaCO₂ values of the patients were examined to check whether there was a change in ventilation.

Demographic data including age, gender, body weight, and concomitant diseases of the patients were recorded.

<table>
<thead>
<tr>
<th>Table 1. Original and Modified Lung Ultrasound Scores (LUS Score)</th>
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<tbody>
<tr>
<td><strong>Normal Aeration</strong></td>
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<tr>
<td>---------------------</td>
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<tr>
<td><strong>Scoring</strong></td>
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<tr>
<td><strong>Original lung ultrasound score</strong></td>
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<td><strong>Modified lung ultrasound</strong></td>
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</table>

Figure 1. A-Line
Patients’ PaO$_2$:FiO$_2$ ratios, APACHE-II (Acute physiology and chronic health evaluation-II) scores at admission to ICU, length of stay in ICU, and the length of mechanical ventilation, and mortality rates were evaluated.

The primary aim of the study was to evaluate the effect of ultrasound-guided positioning on oxygenation in patients with hypoxemic respiratory failure due to COVID-19. For this purpose, changes in PaO$_2$ values after positioning were examined. The secondary aim of the study was to evaluate the effect of ultrasound-guided positioning on ventilation. For this, changes in PaCO$_2$ values after positioning were examined.

**Statistics:**

**Power Analysis**

For statistical power analyses, G* power 3 for MacOs (Faul, F., Erdfelder, E., Buchner, A., & Lang, A.-G. 2009) was used. Power analysis was performed as priori among
independent groups based on t test (Effect size: 0.6; Power: 0.8; alpha error: 0.05). In order for the total sample size to generate 0.8 power; it was calculated that a total of 72 people, 36 people in each group, should be included in the study.

**Statistical analysis:** Student’s t-test was used to compare continuous demographic variables in independent groups. The chi-square test and Fisher’s exact tests were used to test the distribution of categorical variables between groups.

The repeated measures analysis of variance (repeated measures ANOVA) technique was used to analyze the trend of change in arterial blood gas levels and other parameters along three different time points as at the beginning and the 2nd and 12th hours after examination ± ultrasonography in 2 different groups (Group A and B) and 4 independent groups (according to patient positioning).

With the repeated measures ANOVA technique, the interaction effect test was performed to determine whether the trends differed between groups over time; main effects test was performed to determine whether there was a difference between groups when the change over time was ignored, and the main effect of time test was performed to determine whether there was a difference between time periods when the changes between groups were ignored. In multiple comparison tests, Bonferroni-corrected p-values were used to control the Type-I error level. For descriptive statistics, mean ± standard deviation and for categorical variables, frequency distributions and percentages were used. A p-value of <0.05 value was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics v.23 software package.

**Results**

A total of 110 patients were included in the study. After excluding 7 patients, the data from 103 patients were evaluated. Mechanical ventilation settings were made for 52 patients according to their initial ABG values, and the patients were positioned under US guidance. 51 patients for whom mechanical ventilation settings were made according to their ABG values, but no evaluation with US, were accepted as the control group.

Demographic data of the patients are shown in Table 2. No significant differences were observed in age, height, body weight, body mass index (BMI), and gender variables between the two groups.

APACHE-II scores at admission to the ICU were found to be significantly higher in Group A (p=0.036) (Table 3). The PaO$_2$:FiO$_2$ ratios of the patients, the length of stay in the intensive care unit, and the length of mechanical ventilation support were similar in both groups (Table 3). Mechanical

<table>
<thead>
<tr>
<th>Table 2. Demographic Data and Concomitant Diseases</th>
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<tbody>
<tr>
<td><strong>Grup A (Mean±S.Dev.)</strong> (n,%)</td>
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<tr>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Height (cm)</td>
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<tr>
<td>Body weight (kg)</td>
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<tr>
<td>Body mass index (BMI) (kg/m$^2$)</td>
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<tr>
<td>Gender</td>
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<tr>
<td>Male</td>
</tr>
<tr>
<td>Women</td>
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<tr>
<td>At least one concomitant disease</td>
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<tr>
<td>Yes</td>
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<tr>
<td>No</td>
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*Fisher’s exact test p value
ventilation support methods used in patients are shown in Table 3.

The mean LUS score was found to be 25.19 (Table 4). No significant difference was found between groups for the variable PaO₂ (p = 0.153) (Table 5).

The change over time between PaO₂ values evaluated at the beginning and 12 hours after positioning was found significant (p = 0.01) (Table 5).

In Group A, the difference between the PaO₂ values evaluated at the beginning and 2 hours after positioning was statistically significant (p = 0.033), and the difference between PaO₂ values evaluated at the beginning and 12 hours after positioning was statistically significant (p = 0.025). In Group A, the difference between PaO₂ values evaluated at 2 hours and 12 hours after positioning was statistically insignificant (p = 0.0921).

In Group B, the change over time between PaO₂ values evaluated at the beginning and at 12 hours after positioning was found significant (p = 0.004).

Of the 52 patients who were positioned under ultrasound guidance, 13 patients were followed up in the prone position (25%), 10 in the right upper lateral position (19.2%), 21 in the left upper lateral position (40.3%), and 8 in the supine position (15.3%).

The results of the repeated measures ANOVA for arterial blood gas parameters according to the patient position categories, revealed that PaO₂ values were similar across the groups (p = 0.94). The change over time in PaO₂ values evaluated at the beginning and 12 hours after positioning was found significant (p = 0.032) (Table 6).

The change in PaO₂ levels over time was not significant in the supine, right lateral, and prone position groups.

| Table 3. PaO₂:FiO₂ ratios and APACHE-II scores of patients, the length of stay in intensive care, the length of mechanical ventilation support, and the method of mechanical ventilation |
|--------------------------------------------|----------------|----------------|----------------|----------|
| Group A | Group B | | | |
| | Mean ± S.Dev. | Median (Min.-Max.) | Mean ± S.Dev. | Median (Min.-Max.) | P |
| PaO₂:FiO₂ | 92,36 ± 34,85 | 80,50(40,0 - 200,0) | 101,25 ± 40,70 | 90,0(46,0 - 200,0) | 0,256 |
| APACHE-II | 18,75 ± 8,39 | 18,0 (7,0 - 33,0) | 15,42 ± 8,96 | 12,0 (5,0 - 34,0) | 0,036 |
| Length of mechanical ventilation (days) | 15,76 ± 9,40 | 14,50(3,0 - 31,0) | 16,21 ± 9,40 | 15,0(4,0 - 39,0) | 0,745 |
| Length of stay in ICU (days) | 17,84 ± 9,90 | 18,0(3,0 - 33,0) | 18,06 ± 10,02 | 18,0(4,0 - 40,0) | 0,907 |
| Number of patients undergoing mechanical ventilation | | n (%) | (%) | n (%) | (%) |
| IMV | 34 (65,4) | 45,3 | 41 (80,4) | 54,7 | 0,064* |
| PSV-CPAP | 7 (13,5) | 87,5 | 1 (2,0) | 12,5 | |
| HFNO | 11 (21,2) | 55,0 | 9 (17,6) | 45,0 | |

PaO₂:FiO₂: Partial arterial oxygen pressure: Fraction of inspired oxygen; APACHE-II: Acute physiology and chronic health evaluation; Length of stay in ICU: Length of stay in intensive care unit; IMV: Invasive mechanical ventilation; PSV-CPAP: Pressure Support Ventilation - Continuous Positive Airway Pressure; HFNO: High flow nasal oxygenation; *Fisher’s exact p value

<table>
<thead>
<tr>
<th>Table 4. Lung Ultrasound Scores (LUS)</th>
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<tr>
<td>Group A (Mean±S.Dev.)</td>
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<tr>
<td>R Total</td>
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<tr>
<td>L Total</td>
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<tr>
<td>Total Score</td>
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</tbody>
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However, in the left lateral position group, the difference between PaO₂ values evaluated at the beginning and 2 hours after positioning and the difference between PaO₂ values evaluated at the beginning and 12 hours after positioning were statistically significant (p= 0.009 and 0.038, respectively).

On the other hand, the difference between PaO₂ values evaluated at 2 hours and at 12 hours after positioning was statistically insignificant in the left lateral position group (p= 0.710).

In the prone group, the change between PaO₂ levels evaluated at the beginning and 2 hours after positioning was not statistically significant, but the results were close to reaching statistical significance (p=0.074).

As for the change in PaCO₂ levels, there was not a significant difference between the groups or by the time (Table 5). Therefore, the PaCO₂ variable was not evaluated according to the given position categories.

Also, for the change in the variable SaO₂, no significant difference was found between groups and by the time (Table 5). For the lactate and BE variables, the changes between the groups and by the time were not significant. The 28-day mortality rates were similar in both groups (Table 7).
Discussion

In our study, it was observed that ultrasound-guided positioning improved oxygenation in a short time such as 2 hours in COVID-19 patients with acute respiratory failure.

Bedside ultrasonography has an important place in the diagnosis, follow-up and prognosis of patients and can provide guidance for ventilation (10). One of the main limitations of thoracic ultrasound is that it cannot be used to examine the deep fields of the lung. However, the use of thoracic ultrasound is recommended COVID-19 because the involvement of the distal region is predominant (21,22).

Several studies are available about LU in COVID-19 patients. Characteristic findings of LU in COVID-19 reported by different studies are as follows:

1. Thickening of the pleural line with pleural line irregularities;
2. B-lines in a variety of patterns including focal, multifocal, and confluent;
3. Subpleural small consolidations;
4. Consolidations in a variety of patterns including multifocal small, non-translobar, and translobar patterns with occasional mobile air bronchograms;
5. Appearance of A-lines during the recovery phase;
6. Pleural effusions are uncommon (2,3,9,11,23-25).

Table 7. Comparison of mortality rates

<table>
<thead>
<tr>
<th>n, (%)</th>
<th>Group A</th>
<th>Group B</th>
<th>p</th>
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<tbody>
<tr>
<td></td>
<td>%</td>
<td>%</td>
<td></td>
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<tr>
<td>Survival</td>
<td>15 (% 28,8)</td>
<td>50,0</td>
<td>15 (% 29,4)</td>
</tr>
<tr>
<td></td>
<td>37 (% 71,2)</td>
<td>50,7</td>
<td>36 (%) 70,6</td>
</tr>
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</table>

Pre: Initial value (before examination ± ultrasonography), 2h: Value at the 2nd hour after examination ± ultrasonography, 12h: Value at the 12th hour after examination ± ultrasonography
Studies in the literature report that bedside LU is an effective way to evaluate the severity of lung involvement and follow up disease progression in COVID-19 patients (2,3,9,23,26). Similar to our study, Vetruguna et al. (14) successfully evaluated their patients using LUS scores, and reported that the use of LU resulted in significant reduction in the number of chest X-rays and tomography scans during the pandemic and helped achieve efficient patient care and management.

The benefits of prone position in addition to the mechanical ventilation strategies to provide oxygenation in the treatment of ARDS are known, and it is reported that, with prone position, oxygen is improved, and mortality is decreased (12,27).

Sztajnbok et al. (28) reported an improvement in oxygenation in their patients who remained in the prone position for 8 to 10 hours. Ghelichkhani et al. (29) recommended the prone position for at least 12 hours. Özbilen et al. (30) reported that they used the prone position in their patients for 4 hours and reported improvements in oxygenation. In our study, we observed improvements in oxygenation in the 2-hour period after appropriate positioning in the patients under ultrasonography guidance. No significant differences occurred between the measurements at 2nd and 12th hours after the positioning.

We found that hypoxia was effectively treated in the left lateral position. In the prone position group, there was an increase in $\text{PaO}_2$ values evaluated 2 hours after positioning, though not statistically significant. The low number of patients may be an important factor in this result.

Studies suggest that the prone position is not preferred by physicians and causes hemodynamic instability (31). In the prone position, accidental removal of the tracheal tube may occur, as well as limited venous access, decubitus ulcer, and bruising around the mouth, edema around the eyes and facial edema due to the presence of endotracheal tube (32). For such reasons, physicians are reluctant to use prone positioning in patients.

We also think that it is not necessary to use prone positioning in every patient. This process is both difficult and risky, in addition to being difficult to tolerate (33). In our study, we had to exclude two of our patients that we applied the prone position because they could not tolerate the position.

In our study, we observed that there was an increase in oxygenation after 2 hours in the patients who were positioned under ultrasonography guidance. The short duration will increase the tolerance of especially noninvasive supported patients, and also complications such as pressure ulcers and edema formation will be prevented.

A study performed during the pandemic reported that; of the 15 patients, who were kept in the prone position for three hours and received non-invasive mechanical ventilation, the respiratory rate decreased, $\text{SO}_2$ increased, and the $\text{PaO}_2$ : $\text{FiO}_2$ ratio improved in 73% of the patients during the prone positioning and in 86.7% of the patients at the end of the prone positioning (34).

As a result, we found that, if the infiltrative region in the lung is defined with bedside LU in a short time so as to know which positioning to prefer for which region, there is an increase in oxygenation in COVID-19 patients shortly after the application. In our study, we observed that especially the patients in the left lateral position benefited from the position. Instead of bringing all patients to the prone position, we think that customized positioning of the patient according to LU-guided findings can increase oxygenation in a short time like 2 hours. Thus, the potential negative effects of the prone positioning can also be avoided, and proper positioning can be attempted in more patients commonly.

Limitations
A more specific lung scoring technique to evaluate patients with COVID-19 may be better in grading the severity of the disease. For this purpose, we suggest that a new classification should be developed immediately.

After positioning our patients for 12 hours, we could have evaluated and scored them again with LU, so that we could have evaluated both the success of the position and the correlation between LUS score and ABG. Finally, the number of patients included in the study could have been higher so that more patients could be evaluated in each position group.

Main Points:
Ultrasound-guided patient positioning improves oxygenation in COVID-19 patients with respiratory failure.

The increase in $\text{PaO}_2$ values at 2 and 12 hours after positioning was statistically significant in the patients who were positioned under the guidance of ultrasound guidance. When the patients were evaluated according to their positions, the increase in $\text{PaO}_2$ values at 2 and 12 hours after positioning was statistically significant in the right lateral decubitus position.

Positioning the patient by determining the required
position with lung ultrasonography can provide an increase in oxygenation in a short time like 2 hours.

Ethics

Ethics Committee Approval: This study was approved by the Ministry of Health (dated 05.04.2020, numbered 2020-05-04T00-50-43) and our Education and Research Hospital’s Clinical Research Ethics Committee (dated 05.26.2020, numbered 66).

Informed Consent: Written informed consent was obtained from all patients included in the study.

Peer-review: Externally peer-reviewed.

Authorship Contributions


Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.
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