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Relationship Between Intubation and Mortality in COVID-19 Patients with Moderate ARDS, Secondary Bacterial Infection Status

Moderate ARDS'li COVID-19 Hastalarında Entübasyon ve Mortalite İlişkisi, Sekonder Bakteriyel Enfeksiyon Durumu

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ABSTRACT *Objective:* In many studies on patients with ARDS caused by SARS-CoV-2, the mortality rate was found to be high in intubated patients. The aim of this study was to try to understand how intubation affects mortality in patients with COVID PCR-positive ARDS and to understand the relationship between intubation and mortality in the patient group whose PaO2/FiO2 is 100-150 mmHg (moderate) and who have difficulty in intubation decision.
Materials and Methods: Patient information was obtained by retrospectively examining the hospital computer database and patient files. 313 patients were included in the study. The patients were divided into two groups as intubated and non-intubated according to their intubation status after the first 24 h of their admission to the intensive care unit (ICU) and their intubation status when PaO2/FiO2 was 100–150 mmHg (moderate ARDS).
Results: In the group of patients who were intubated after the first 24 h, the number of mechanical ventilator days was 9.15±8.58 ($p<0.001$), the length of stay in the ICU (LOS) was 14.15±10.33 ($p< 0.001$), and the length of hospital stay was 18.33±12.13 ($p < 0.05$), it was longer and statistically significant compared to the non-intubated group. Additionally, 140 (80.92%) of these patients died ($p< 0.001$). The number of mechanical ventilator days was 8.87±8.51 and the LOS days were 13.53±9.6 in the intubated group with moderate ARDS, which was longer and statistically significant than the non-intubated group ($p< 0.001$). Moreover, in 80 (68.4%) of all intubated patients, 60 (37.5%) of the intubated patients with moderate ARDS had secondary bacterial infection ($p< 0.001$) and mortality rates were higher ($p< 0.001$).
Conclusion: All intubated patients with COVID-19, including those with moderate ARDS, had a higher rate of secondary bacterial infection, as well as a higher mortality rate.
Keywords: Acute respiratory distress syndrome, coronavirus, intubation, secondary bacterial infection

ÖZ *Amaç:* SARS-CoV-2 virüsünün neden olduğu ARDS hastaları üzerinde yapılan çok sayıda çalışmada, entübe hastalarda ölüm oranı yüksek bulunmuştur. Bu çalışmanın amacı, COVID PCR pozitif ARDS olan hastalarda entübasyonun mortaliteyi nasıl etkilediği ve PaO2/Fi02' nin 100-150 mmHg olduğu (moderate), entübasyon kararında zorlanılan hasta grubunda entübasyon ile mortalite arasındaki ilişkiyi anlamaya çalışmaktır.
Gereç ve Yöntemler: Hasta bilgileri, hastane bilgisayar veri tabanından ve hasta dosyalarından retrospektif olarak incelenerek elde edildi. 313 hasta çalışmaya dahil edildi. Hastalar yoğun bakıma yatışlarının ilk 24 saatinden sonra ki entübasyon durumuna göre ve PaO2/Fi02' nin 100-150 mmHg (moderate ARDS) olduğunda entübasyon durumuna göre entübe ve non-entübe olacak şekilde iki gruba ayrıldı.
Bulgular: İlk 24 saatten sonra entübe edilen hasta grubunda mekanik ventilatör gün sayısı 9,15±8,58 ($p<0,001$), yoğun bakım gün sayısı 14,15±10,33 ($p< 0,001$) ve hastane gün sayısı 18,33±12,13 ($p< 0,05$)' dü ve non-entübe gruba göre daha uzun ve istatiksel olarak anlamlıydı. Ayrıca bu hastaların 140'ı (%80.92) kaybedildi ($p<0.001$). Moderate ARDS'li entübe grupta mekanik ventilatör gün sayısı 8,87±8,51, yoğun bakım gün sayısı ise13,53±9,6 idi ve entübe olmayan gruptan daha uzun ve istatiksel olarak anlamalıydı ($p< 0,001$). Ayrıca tüm entübe hastaların 80 (68,4%)' inde; moderate ARDS'li entübe hastaların ise 60 (%37,5)' ında sekonder bakteriyal enfeksiyon mevcuttu ($p< 0,001$) ve mortalite oranlarıda daha yüksekti ($p< 0,001$).
Sonuç: Tüm entübe COVID-19'lu hastalarda moderate ARDS' li olgularda dahil olmak üzere sekonder bakteriyal enfeksiyon daha fazla ve mortalite oranları ise daha yüksek tesbit edilmiştir.
Anahtar Kelimeler: Akut solunum sıkıntısı sendromu, koronavirüs, entübasyon, sekonder bakteriyel enfeksiyon

Introduction

In the COVID-19 pandemic, physicians, particularly those performing aerosol-generating procedures such as noninvasive ventilation (NIV), a high-flow nasal oxygenation (HFNO), balloon mask ventilation, and intubation, are at a significant risk of developing an infection in the intensive care unit (ICU) (1,2). Endotracheal intubation should be conducted by a clinician who specializes in this field in this patient group, and early intubation should be considered in a patient whose respiratory state worsens (3). The physician's decision to use invasive mechanical ventilation is dependent on his or her clinical judgment, which is impacted by criteria such as oxygen saturation, dyspnea, respiratory rate, chest radiography, and others (4). However, some physicians believe that intubation is linked to a high death rate. A research from China found that intubated COVID-19 patients had a 97 % mortality rate, with a mean ventilation period of 4 days (5). Data from an Italian intensive care cohort of 1591 patients, which was also performed on COVID-19 patients, show that 88 % of the patients were intubated, and that those who finished intensive care therapy had a 64 percent mortality rate (6). However, among 1795 COVID-19 patients who were invasively ventilated, data from a population of inhabitants of England, Wales, and Northern Ireland revealed a 67 percent mortality rate (7). According to a research conducted in New York City and its environs, only 3% of COVID-19 patients who were ventilated invasively survived, while 25% perished (8). When should COVID-19 patients be intubated? There is no clear answer to this question. There is no clear consensus on whether early or late intubation is preferable, or under what circumstances intubation should be conducted. The goal of this study was to examine the link between intubation and mortality in patients with COVID-19 PCR positive acute respiratory distress syndrome (ARDS), as well as the effect of intubation on mortality in patients with COVID-19-related ARDS who had a PaO2/FiO2 mmHg of 100–150. We believe that knowing the link between intubation timing and mortality might help clinicians make better ventilation decisions in COVID-19 pneumonia.

Materials and Methods

Patients who were followed up owing to COVID-19 in adult intensive care units in a tertiary healthcare facility between October 1, 2020 and February 1, 2021 were included in this retrospective analysis. The records of patients admitted to the intensive care unit during the dates mentioned were scanned retrospectively after the study was approved by the hospital ethics committee (ethical permission number: 2021-58, date: 14.04.2021).

The study's inclusion criteria were: 1) cases whose COVID-19 diagnosis was confirmed by RT-PCR, 2) patients diagnosed with ARDS according to Berlin criteria, and 3) patients aged 18 and over.

The study's exclusion criteria were: 1) patients under the age of 18, 2) people who do not have ARDS (n:5), 3) pregnant women (n:8), 4) patients with concurrent malignancy (n: 35), 5) patients with a history of organ transplantation and/ or immunosuppressive drug use (n: 36), 7) patients who had a surgical operation in the previous month (n: 4), 8) COVID-19 PCR test negative but radiologically diagnosed patients (n: 15), 9) patients admitted to the intensive care unit as intubated, and patients intubated within the first 24 hours of admission (n: 38).

During the COVID-19 pandemic, our hospital collected data from four adult pandemic intensive care units with a total of 16 beds. Symptomatic patients with positive COVID-19 PCR testing are followed in pandemic inpatient care at our hospital, which is a tertiary education and research institution. Patients who require acute care owing to respiratory distress, tachypnea, hypoxia, altered awareness, or hypotension are transported to pandemic intensive care units, where their care is continued. Patients with COVID-19 PCR positive who require intensive care from adjacent provinces and hospitals are also accepted. The hospital's computer database and patient files were used to gather information on the patients. Age, gender, body mass index (BMI), and concomitant sickness status of the patients' sociodemographic data were recorded. On the day of admission to the critical care unit, a complete blood count, kidney (urea, creatinine), and liver function tests (ALT, AST), as well as coagulation indicators, were all conducted. C-reactive protein (CRP), procalcitonin (PRC), and ferritin levels as acute phase reactants, as well as glucose, d-dimer, and lactate dehydrogenesis levels, have all been tracked since the patient's admission to the critical care unit.

The Sequential Organ Failure Assessment Score (SOFA) and and the Acute Physiology and Chronic Health Evaluation II (APACHE II) scores also were taken into account when patients are admitted to the intensive care unit. Mild, moderate, and severe ARDS were assigned to patients diagnosed with ARDS using Berlin criteria. In addition, the forms of oxygen support utilized in critical care were investigated (conventional oxygen support, high flow nasal oxygen (HFNO), invasive mechanical ventilation, and non-invasive mechanical ventilation (NIV). The mechanical ventilation time was measured by keeping a note of when the patients were linked to the ventilator and when they were disconnected. The status of receiving tocilizumab, anakinra, glucocorticoids, IVIG, plasmapheresis, the development of secondary bacterial infection, the number of days in the intensive care unit, the number of mechanical ventilator days, and the number of hospital days were all recorded using electronic medical records during the follow-up period. Fever, high CRP, elevated procalcitonin, culture results (blood culture, urine culture, tracheal aspirate culture), radiological data, and an infectious diseases consultation 48 hours after admission to the critical care unit were used to determine the presence of secondary bacterial infection. The patients' survival status was recorded during the follow-up period.

Statistical Analysis

The SPSS program was used to do statistical analysis on the study data. To see if the continuous data fit the normal distribution, one sample Kolmogorov Smirnov test was employed. Quantitative variables in our study will be expressed as mean and SD or median (min-max) based on their distribution. Numbers and percentages were used to represent categorical variables. For continuous data that fits a normal distribution, the Student-t test will be performed, and for those that do not, the Man Whitney u test will be employed. The Chi-square test was performed to compare categorical data between two groups.

Results

313 patients were included in the study. According to their intubation status after the first 24 hours of critical care admission, patients were separated into two groups: intubated and non-intubated. There were 182 males (58.1%) and 131 females (41.9%) among these patients. The average age of the participants was 65.07±14.55. The intubated group had a mean age of 68.79±11.67 ($p< 0.001$), a neutrophil level of 10.78±6.89 ($p< 0.05$), a white blood cell (WBC) count of 14.60 ±10.38 ($p< 0.001$), ferritin of 1363,5± 1486.18 ($p< 0.05$), and APACHE II score of 18.437.41 ($p< 0.05$), and a BMI of 27.98±4.59 ($p< 0.001$), all of which were higher than the non-intubated group. In addition, the number of mechanical ventilator days in the intubated group was 9.15±8.58 ($p< 0.001$), the number of intensive care days was 14.15±10.33 ($p< 0.001$), the number of hospital days was 18.33±12.13 ($p<0.05$) and was longer than the non-intubated group. In addition, 140 (80.92%) of the intubated patients died ($p< 0.001$) and the mortality rate was higher than the non-intubated group. The demographics, clinical characteristics, APACHE II score, SOFA score, intensive care day duration, mechanical ventilator day duration, hospital day duration, BMI, laboratory data, presence of secondary bacterial infection, NLR, and PLR values for these patients are listed in Tables I and II. Table III summarizes the therapies these patients received as well as the complications they encountered throughout their critical care follow-up. In Table IV, APACHE II score, SOFA score, intensive care day duration, mechanical ventilator day duration, hospital day duration, BMI, laboratory data, presence of secondary bacterial infection, NLR, and PLR data were summarized for intubated and non-intubated patients with a PaO_2/FiO_2 of 100–150 after the 24th hour of admission to the intensive care unit. This analysis revealed that 48 (30%) of the patients who were not intubated were male ($p< 0.05$). The number of mechanical ventilator days was 8.87±8.51 in the intubated group, while the number of intensive care days was 13.53±9.6, which was greater ($p< 0.001$). In this group, 60 (37.5%) patients had secondary bacterial infection, and 79 (49.4%) patients died, with a mortality rate that was greater than in the non-intubated group ($p< 0.001$). A logistic regression analysis of clinical and laboratory data was used to predict mortality, and age, presence of secondary bacterial infection, number of mechanical ventilation days, and number of intensive care days were found to be significant for predicting mortality. These data are summarized in table V.

Discussion

In this study, we found that patients with ARDS caused by COVID-19 pneumonia who were intubated beyond the first 24 hours of admission to the intensive care unit had a greater fatality rate. Furthermore, intubated patients with a PaO_2/FiO_2 of 100–150 mmHg also had a greater death rate. It's crucial to determine if insufficient oxygenation is caused by a low ventilation-perfusion ratio or by the presence of an intrapulmonary right-left shunt in ARDS caused by COVID-19 pneumonia. In the first situation, increasing the oxygen flow is predicted to result in a significant improvement in oxygenation, hence intubation is avoided in the first place. In

Table 1. Sociodemographic and clinical characteristics of the study population

	Mean ±SD/n	%/min-max
Age	65,07±14,55	18-94
BMI (kg/m²)	27,06±4,98	18-45
Gender		
Male	182	58,1%
Female	131	41,9%
BMI classification		
Normal	115	36,7%
Overweight	147	46,9%
Obese	35	11,1%
Morbid Obese	6	1.9%
Weak	10	3,2%
Comorbidities		
Diabetes mellitus	88	28,1%
Hypertension	139	44,4%
COPD	25	7,9%
Cardiovascular Disease	58	18,5%
Chronic renal failure	50	10,4%
Neurodegenerative disease	45	13,4%
Liver Failure	8	2,5%
Heart failure	7	2,2%
PaO2/FiO2 admission		
Mild ARDS	32	9,9%
Moderate ARDS	160	49,7%
Severe ARDS	121	37,6%
APACHE score	17,17±7,36	8-38
SOFA score at admission	6.32±2,95	3-22
LOS/day	11,81±9,16	1-73
Lenght of stay in hospital/day	16,59±11,74	3-93
Mechanic ventilation days	5,8±7,69	0-52
Entubation	173	55,27%
Mortality	174	55,59%

BMI: Body mass index, COPD: Chronic obstructive pulmonary disease, ARDS: Acute respiratory distress syndrom, APACHE: The acute physiology and chronic health evaluation, SOFA: Sequential organ failure sssessment score, LOS: Lenght of stay in ICU

cases when insufficient oxygenation is caused by an increase in the intrapulmonary right-left shunt, increasing oxygen delivery has little effect. In this condition, lung-protective ventilation is required, especially with prone placement and, if necessary, extracorporeal membrane oxygenation (ECMO) (9). In our study, 173 of the 313 patients were intubated, and 140 (80.92%) of these intubated patients died. Various studies found that mortality rates for COVID-19-associated ARDS patients who were intubated ranged from 25% to 97 percent (5-8). In several trials, including ours, intubated patients had a higher mortality rate. As a result, the answer to the question of when patients with ARDS linked to COVID-19 should be intubated is still unclear and difficult to determine.

When selecting whether or not to intubate, significant respiratory effort and hypoxemia are important considerations. However, measuring esophageal pressure, which can be challenging in a clinical context and is frequently reserved for research, is the most reliable approach to assess high respiratory work. The palpation of phasically rising contractions of the respiratory muscles, notably the sternocleidomastoid muscle, is a simpler method for physicians (10). Because hypoxemia does not always result in end-organ damage, it cannot be used as a sole trigger for intubation (10,11). It's worth noting that tissue oxygen supply is influenced by hemoglobin content and cardiac output in addition to oxygen saturation. Furthermore, the patient's dyspnea is frequently caused by limits in respiratory mechanics rather than oxygenation restrictions (10,11). As a result, deciding whether or not to intubate a patient is a personal decision that should be based on the sum of all of these factors (4,9,10). In COVID-19, there is yet no randomized controlled trial on ventilation therapy. As a result, accurate ventilation recommendations are mostly based on physician expertise and studies in other patient groups (12–14). Based on the oxygenation index (PaO2/FiO2) at PEEP 5 cmH2O, covid-19 associated ARDS were categorized into three categories in one study; mild (200 mmHg ≤ PaO2/FiO2 < 300 mmHg), mild to moderate (150 mmHg ≤ PaO2/FiO2 < 200 mmHg) and moderate to severe (PaO2/FiO2 < 150 mmHg) (15). In our study, we also examined the patient groups whose oxygenation index, PaO2/FiO2 < 100–150 mmHg, which compels clinicians to decide on intubation. We compared patients with this index who preferred invasive mechanical ventilation with groups of patients using NIV and/or HFNO. 79 (49.4%) of 94 (58.4%) patients died in the intubation group with PaO2/FiO2 of 100-150 mmHg. In the non-intubated group with PaO2/FiO2 150-100 mmHg, 17 (12.14%) of 67 (41.6%) patients were intubated during their stay in the intensive care unit, and only 8 (5%) died. Intubating a patient raises the risk of secondary bacterial

Table 2. Comparison of the clinical and laboratory results between intubated and non-intubated groups

	Total (n=313)	Intubated (n=173)	Non-intubated (n=140)	p-value
Age	65,07 ±14,55	68,79±11,67	60,88±16,29	0,00
Gender (male)	182 (%58.1)	92 (% 29,4)	90 (%28,8)	0,05
Glucose (mg/dl)	198,55±103,04	190,09±105,60	208,10±99,58	0,069
BUN (mg/dl)	76,46± 58,18	75,9±55,324	77,09± 61,43	0,88
Creatinine(mg/dl)	1,68±03,16	1,44±1,34	1,94±4,38	0,66
AST(U/L)	65,45±212,05	83,16±287,45	45,48±44,17	0,59
ALTU/L)	49,63±96,03	55,05±110,72	43,50±76,05	0,67
Fibrinogen (mg/dl)	610,71±511,92	640,29±674,18	577,31±210,32	0,872
INR	1,16±0,32	1,15±0,29	1,17±0,36	0,487
D-dimer (mgFEU/mL)	3,38±4,65	3,35±4,86	3,40±4,42	0,62
LDH (U/L)	499,84±383,34	513,83±397,16	484,86±367,82	0,415
Ferritin(ng/mL)	1140,20±1281,75	1363,5±1486,18	887,76±945,34	0,001
WBC (109/L)	14,28±15,00	14,60±10,38	11,42 ± 8,85	0,000
HB (g/dl)	12,79±10,70	11,85±2,44	13,85±15,36	0,227
Platelet	248,70±119,70	238,55±125,52	260,15±112,261	0,064
Lymphocyte (10^9/L)	8,09±90,96	0,94±1,10	0,87±0,67	0,750
Neutrophil (10^9/L)	10,37±7,95	10,78±6,89	9,89±8,49	0,031
CRP (mg/L)	130,99±97	135,37±91,66	126,05±102,79	0,119
PCT (ng/mL)	4,75±24,55	5,57±31,7	3,82±12,29	0,887
Mechanic ventilation days	5,8±7,69	9,15±8,58	2,02±4,01	0,000
LOS/day	11,8±9,15	14,15±10,33	9,18±6,74	0,000
Lenght of stay in hospital/day	16,59±11,74	18,33±12,13	14,61±11,0	0,001
SBIP	117(37,4%)	80(68,4%)	37(31,6%)	0,000
SOFA	17,17±7,36	6,5±2,77	6,1±3,13	0,072
APACHE	6.32±2,95	18,43±7,41	15,74±7,05	0,001
NLR	19,38±22,24	18,27±21,55	20,67±22,98	0,184
PLR	452,26±440,16	433,96±402,73	472,92±479,49	0,199
BMI (kg/m^2)	27,06±4,98	27,98±4,59	26,25±5,19	0,001
Mortalite	174 (%55,59)	140 (%80,92)	34(%24,28)	0,000

BUN: Blood urea nitrogen, LDH: Lactate dehydrogenase, AST:Aspartate transaminase, ALT: Alanine aminotransferase, WBC: White blood cell, HB: hemoglobin, PCT: Procalcitonin, CRP: C-reactive protein,COPD: Chronic obstructive pulmonary disease, ARDS: Acute respiratory distress syndrom, APACHE: The acute physiology and chronic health evaluation, SOFA: Sequential organ failure assessment score, LOS: Lenght of stay in ICU, SBIP: Secondary bacterial infection positivity, NLR: Neutrophil lymphocyte ratio, PLR: Platelet lymphocyte ratio, BMI: Body mass index

infection and lengthens the time spent in the critical care unit, both of which can lead to an increase in mortality. Many COVID-19 patients require intubation due to hypoxemia; these individuals have dyspnea or distress. Shortness of breath does not usually occur until the PaO2 decreases to 60 mm Hg (or much lower) (11). Patients with PaO2 > 40 mm Hg (equal to ~ 75 percent oxygen saturation) have a tough time demonstrating end-organ damage (4). The product of arterial oxygen content and cardiac output determines the amount of oxygen given to the tissues. Initially, oxygen extraction increases and oxygen intake remains normal in patients with restricted oxygen delivery (16). When oxygen delivery falls below a critical level, this extraction mechanism fails, and metabolism shifts from aerobic to anaerobic pathways, impairing important organ function. In critically ill individuals, this critical threshold is not reached until oxygen

Table 3. Applied treatments and complications

	Total (n=313)	Intubated (n=173)	Non-intubated (n=173)	p-value
Dexamethasone	87(%27,8)	52(%16,6)	35(%11,2)	0,129
Tocilizumab	15(%4.8)	9(%2.9)	6(%1,9)	0,77
Anakinra	42(%13,4)	18(%5,8)	24(%)7,7	0,210
Stem cell therapy	2(%0,6)	2(%0,6)	0	0,5
Methylprednisolone pulse therapy	124(%39,6)	70(%22,4)	54(%17,3)	0,327
IVIG	19(%6.1)	12(%3,8)	7(%2,2)	0,5
Septic shock	153(%48,9)	113(%36,1)	40 (%12,8)	0,000
Survivor	139(%44,4)	28(%8,9)	111(%35,5)	0,000
Acute kidney failure	44(%14,1)	29(%93)	15(%4,8)	0,092
Diabetic ketoacidosis	45(%14,4)	18(%5,8)	27(%8,7)	0,079
Elevated Liver Enzymes	28(%8,9)	15(%4,8)	13(%4,2)	1
Deep vein thrombosis	2(%0,06)	0	2(%0,06)	0,132
Pulmonary embolism	6 (%1,9)	3(%1)	3(%1)	1

IVIG: Intravenous Immunoglobulin

Table 4. Comparison of laboratory data of intubated and non-intubated groups with PaO_2/FO_2 =100-150 mmHg

	Total (n=160)	Intubated (n=93)	Non-intubated (n=67)	p-value
Age	65,14±14,41	68,47±13,7	60,53±14,19	0,000
Gender (Male)	92(%57,5) 68(42,5%)	44 (47,3%) 49 (52,7%)	48(71,6%) 19(28,4%)	0,002
Glucose (mg/dl)	194,07±115,51	192,40±115,18	196,38±116,78	0,89
BUN (mg/dl)	70,95±48,15	75,43±55,34	64,72±35,34	0,59
Creatinine(mg/dl)	1,38±1,04	1,41±1,15	1,33±0,87	0,82
AST(U/L)	81,55±291,48	71,12±262,20	96,01±329,36	0,48
ALTU/L)	47,69±87,22	43,72±75,34	53,21±101,80	0,53
Fibrinogen (mg/dl)	639,73±686,20	590,16±170,10	708,53±1042,00	0,95
INR	1,16±0,33	1,17±3,31	1,16±0,33	0,16
D-dimer (mgFEU/mL)	3,41±5,18	3,77±5,81	2,91±4,13	0,77
LDH (U/L)	506,55±391,62	501,24±460,52	513,93±271,56	0,22
Ferritin(ng/mL)	1404,78±1840,25	1321,74±1558,88	1520,05±2178,88	0,77
WBC (10^9/L)	12,26±13,40	12,79±16,51	11,54 ±7,22	0,71
HB (g/dl)	12,72±10,64	12,07±2,42	13,62±16,23	0,22
Platelet	259,32±123,98	248,47±125,56	274,37±121,07	0,24
Lymphocyte (10^9/L)	0,85±0,708	0,86±0,77	0,84±0,60	0,39
Neutrophil (10^9/L)	8,86±5,25	8,9±5,3	8,7±5,22	0,92
CRP (mg/L)	125,84±92,37	117,22±84,15	137,78±102,16	0,286
PCT(ng/mL)	5,55±31,76	6,61±40,37	4,09±12,46	0,110
Mechanic ventilation days	5,51±7,76	8,87±8,51	0,86±2,42	0,000
LOS /day	11,83±9,17	13,53±9,6	9,47±7,9	0,000
Lenght of stay in hospital /day	16,81±12,53	17,09±11,9	16,43±13,9	0,37
SBIP	83(%51,9	60(%37,5)	23(%14,4)	0,000
SOFA	6,08±2,50	6,4±2,79	5,58±1,99	0,11
APACHE	13,55±4,42	13,7±4,31	13,3±5,71	0,72
NLR	17,59±20,16	18,73±23,54	16,02±14,22	0,949
PLR	490,54±526,39	473,97±461,18	513,55±608,38	0,281
BMI (kg/m²)	27,25±5,33	28,31±4,9,	26,49±5,52	0,012
Mortality	87 (%54,4)	79(%49,4)	8 (%5)	0,000

BUN: Blood urea nitrogen, AST:Aspartate transaminase, ALT: Alanine aminotransferase, LDH: Lactate dehydrogenase, WBC: White blood cell, HB: Hemoglobin, PCT: Procalcitonin, CRP: C-reactive protein, COPD: Chronic obstructive pulmonary disease, ARDS: Acute respiratory distress syndrom, APACHE: The Acute Physiology and Chronic Health Evaluation, SOFA: Sequential Organ Failure Assessment Score, LOS: Lenght of stay in ICU, SBIT: Secondary bacterial infection positivity, NLR: Neutrophil lymphocyte ratio, PLR: Platelet lymphocyte ratio, BMI: Body mass index

Table 5. Logistic regression analysis of clinical and laboratory factors for predicting mortality (intubated and non-intubated groups with PaO2/FO2 =100-150 mmHg)

	Beta	SE	OR: Exp (B)	Lower95%	Upper95%	Sig
Age	-0,046	0,015	0,955	0,928	0,983	0,002
BMI	0,015	0,037	1,015	0,944	1,091	0,693
Gender (Male)	-0,321	0,408	0,726	0,326	1,615	0,432
NLR	-0,001	0,017	0,999	0,967	1,032	0,94
PLR	0	0,001	1	0,999	1,001	0,545
PCT	-0,004	0,008	0,996	0,981	1,012	0,649
CRP	-0,001	0,002	0,999	0,994	1,003	0,545
APACHE	0,003	0,046	1,003	0,916	1,098	0,953
SOFA	-0,025	0,087	0,975	0,823	1,155	0,77
SBEP	-0,995	0,414	0,37	0,164	0,833	0,016
Mechanic ventilation days	-0,139	0,04	0,871	0,804	0,942	0,001
LOS/day	-0,014	0,039	0,986	0,914	1,065	0,726
Lenght of stay in hospital/day	0,079	0,028	1,082	1,023	1,144	0,005

BMI: Body mass index, NLR: Neutrophil lymphocyte ratio, PLR: Platelet lymphocyte ratio, PCT: Procalcitonin, CRP: C-reactive protein, APACHE: The acute physiology and chronic health evaluation, SOFA: Sequential organ failure sssessment score, SBIP: Secondary bacterial infection positivity, LOS: Lenght of stay in ICU

delivery is 25% of normal (17). The main problem after a patient is put on a ventilator is avoiding complications (18). The best way to minimize ventilator-related complications is to avoid intubation unless necessary (19,20). In addition to increased ventilator-associated pneumonia in intubated patients, the use of sedation-muscle relaxants during long intensive care unit stays may have contributed to the high mortality rate by causing an increase in secondary bacterial infections. According to our findings, secondary bacterial infections develop more frequently in intubated patients.

A logistic regression analysis of clinical and laboratory data was used to predict mortality, and age, presence of secondary bacterial infection, number of mechanical ventilation days, and number of intensive care days were found to be significant for predicting mortality.

The retrospective nature of this study is one of its limitations. Because the physician made the decision to intubate, the time it took to intubate was vary. The second limiting factor is that the causes of death have not been fully invastigated. More research is needed to see if the onset of symptoms, the time of hospitalization following the beginning of symptoms, the timing of intubation, the intubation PaO2/FiO2 ratio, and pharmacotherapies are all factors that could affect the patient's clinical path. Our study's strength is that we observed that patients with moderate ARDS can survive using oxygenation modalities like HFNC/NIV. Furthermore, there is no other study in the literature that compares intubated and non-intubated patients with ARDS who had a PaO2/FiO2 of 150 mmHg.

Finally, deciding whether or not to intubate individuals with COVID-19-associated ARDS is challenging. In this patient group, fear of contaminating health workers should not be a factor in intubation. While substantial oxygenation impairment caused by a large intrapulmonary shunt is a key intubation criterion in classic ARDS, COVID-19 patients often respond well to HFNO and / or NIV treatments. Intubation should always be possible due to probable pathophysiological instability and the risk of rapid clinical deterioration, but it should be remembered that invasive mechanical ventilation has a high rate of complications and mortality.

Ethics

Ethics Committee Approval: The records of patients admitted to the intensive care unit during the dates mentioned were scanned retrospectively after the study was approved by the Başakşehir Çam and Sakura Hospital Ethics Committee (ethical permission number: 2021-58, date: 14.04.2021).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: D.T., G.H.A., K.B., B.İ.F., A.Ö., Consept: G.H.A., K.B., Design: D.T., B.İ.F., A.Ö., G.T., Data Collection or Processing: D.T., G.H.A., K.B., B.İ.F., A.Ö., Analysis or Interpretation: D.T., G.H.A., K.B., G.T., Literature Search: D.T., G.H.A., K.B., Writing: D.T.

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