

ORIGINAL ARTICLE

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The Effect of Co-Morbid Diseases on The Need for Mechanical Ventilation and Mortality of Patients with Covid-19 in Intensive Care Unit**Ulku Ince, Harun Tolga Duran, Yusuf Yildirim, Sule Gokce***Ordu Unye Public Hospital, Clinic of Anesthesiology and Reanimation, Ordu, Turkey*

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**Abstract**

It is aimed to contribute to the literature on Covid 19, a new disease, by examining the mechanical ventilation support, mortality and factors affecting them during the follow-up of patients infected with Covid 19 in the intensive care unit. The clinical course of covid 19 infected patients who were hospitalized in the intensive care unit between March 30 and October 30, 2020, such as length of stay, additional diseases, mechanical ventilation support and mortality rates, were analyzed retrospectively and compared. 66 of 100 patients included in the study required invasive mechanical ventilation, 34 of them did not. The probability of having two or more comorbidities was significantly higher in patients requiring invasive mechanical ventilation ($P:0.007$). The mortality rate was 64% among all patients. Advanced age and additional systemic diseases increase mortality in patients infected with Covid19 treated in intensive care. We believe that patients of advanced age and 2 and above with additional systemic diseases need more invasive mechanical ventilation support and that adequate clinical improvement cannot always be achieved with high flow nasal oxygenation (HFNO) and invasive mechanical ventilation (IMV) support applications in these patients.

Keywords: Covid-19, mechanical ventilation, mortality**Introduction**

In December 2019, an outbreak of pneumonia of unknown cause began in Hubei province of China and was named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It was declared as a pandemic upon its worldwide spread and was named Covid19 by the World Health Organization (WHO) in February 2020 [1]. Acute respiratory failure syndrome (ARDS) and widespread alveolar damage are among the main features of Covid19. Major morbidity and mortality cause of hospitalized patients infected with covid 19 is ARDS due to pneumonia [2]. While mortality rates in covid 19 patients who developed ARDS and were treated in intensive care units vary between 26% and 61%, this rate increases to 64% - 94% in patients with covid 19 mechanically ventilated [3-4]. Especially advanced age and comorbidity increase the mortality rate [5]. Hypoxia is very common in patients with severe Covid19 pneumonia.

In these patients, high flow nasal oxygenation (HFNO), noninvasive mechanical ventilation (NIV) or invasive mechanical ventilation (IMV) support are ventilation methods that can be applied [6-7]. It refers to a system that can provide 40-80 L / min oxygen flow depending on the HFNO manufacturer and can be heated and humidified [8]. With the use of non-invasive ventilation such as HFNO, patients require less invasive mechanical ventilation support [9]. However, NIV may be insufficient to manage respiratory failure caused by Covid-19 [10-11-12]. IMV support is life-saving in patients infected with Covid 19 and with respiratory distress. However, it may cause complications such as barotrauma, volutrauma and atelectasis [9]. Although the need for IMV support and the time of administration of hypoxic patients infected with Covid 19 is not well known, young patients can tolerate moderate hypoxia, while elderly patients have been shown to be associated with high mortality [10]. We aimed to contribute to the literature about a new disease that Covid-19 disease by examining the clinical course of patients infected with Covid-19 and mortality in intensive care followed.

Materials and Methods

Between 30 March and 30 October 2020, the files of patients

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infected with Covid-19 in the intensive care unit of our hospital were retrospectively analyzed. The approval of the local ethics committee and the Ministry of Health was obtained. Local ethics committee number was 2020/257. All patients aged 18 years and over and followed in the adult intensive care unit were included in the study. Criteria for receiving intensive care were respiratory rate above 20 and oxygen saturation at 90 and below despite 100% oxygen support with a 5 lt / min reservoir oxygen mask. In spite of HFNO or NIV support, he was taken to invasive mechanical ventilation support when his oxygen saturation was below 90%, respiratory rate was above 20 and the patient's hemodynamic findings were deteriorated. The criteria for discharge from the intensive care unit were a 4 lt / min oxygen supply from the nasal cannula with a peripheral oxygen saturation of 94% and above and a respiratory rate of 20 or less. Age, gender, comorbidities and length of stay in intensive care unit were examined and recorded. In the follow-up of the patients, it was investigated whether HFNO or NIV or IMV support was applied, and the day of admission and how many days these supports were applied. Antibiotic or antiviral treatments included in the patients' files were examined. In addition, peripheral oxygen saturations of the patients on admission to intensive care, in IMV or NIMV support, while in HFNO support and at discharge were examined. In addition, the discharge processes and mortality of the patients were examined. Patients who received IMV support during their follow-up were classified as Group 1 and patients who did not receive IMV were classified as Group 2. Group 1 and Group 2 patients were compared statistically in terms of age, gender, presence of comorbidity, follow-up and treatment periods in the intensive care unit, oxygen saturation and mortality.

Statistical Analysis

SPSS v20 program was used in the analysis of data. Categorical variables are presented as number and percentage, numerical

variables as mean and standard deviation. The compatibility of numerical variables to normal distribution was investigated using the Kolmogorov-Smirnov test and graphing methods. Mann Whitney-U was used for comparisons of non-normally distributed numerical variables, and Chi-Square test was used for comparisons of category variables. $P < 0.05$ was considered statistically significant.

Results

It was observed that IMV support was applied to 66 (66%) of the patients (Group 1) and 34 (34%) were not. The mean age of the patients was 73 ± 12 years. The mean age of Group 1 was 75 ± 11 , and that of Group 2 was 68 ± 13 . When Group 1 and Group 2 were compared in terms of age, the mean age of group 1 was found to be significantly higher (0.007). 42 (42%) of the patients were female and 58 (58%) were male. The patients in group 1 were 26 (39.4%) women and 40 (60.6%) men. Group 2 patients were 16 (47.1%) women and 18 (52.9%) men. The mean hospitalization period of the patients was 12 ± 14 , the mean hospitalization time of the patients in Group 1 was 13 ± 17 and the patients in Group 2 were 10 ± 6 . It was observed that 96 (96%) of the patients were taken to the intensive care unit with oxygen support in spontaneous breathing, while 4 (4%) were given intubation and IMV support. It was observed that 62 (64.6%) of 96 patients received IMV support.

It was observed that 36 (36%) patients were discharged from the intensive care unit, and 64 (64%) patients died. While all of the patients in Group 2 were discharged from the intensive care unit, only 2 (3%) of the patients in Group 1 were discharged. It was observed that 24 (57.1%) of the women and 40 (69.0%) of the men died. Both of the patients in Group 1 who were discharged were female. When the patients were compared in terms of discharge by gender, there was no difference ($p: 0.22$).

Additional diseases of the patients are shown in Table 2.

Table 1. Group 1 and Group 2 of patient age, gender, and mean duration of hospitalization

	Group 1 N-66	Group 2 N-34	p
Age	75±11	68±13	0.007
Gender F/M	26 (39.4%) / 40 (60.6%)	16(47.1%) / 18(52.9%)	0.46
Duration of Hospitalizat	13±17	10±6	0.92

Group1: Patients who received invasive mechanical ventilation support Group2: Patients who did not receive invasive mechanical ventilation support F / M: Female / Male, %: percent. N: number of patients

Table 2. Comparison of systemic diseases of the patients in Group1 and Group2

	DM N(%)	HT N(%)	HD N(%)	CLD N(%)	CKD N(%)	ND N(%)	T N(%)
Group1	26 (39.4)	52 (78.8)	20 (30.3)	18(27.3)	5 (7.6)	9 (13.6)	66 (66)
Group2	9 (26.5)	23 (67.6)	5 (14.7)	5 (14.7)	1 (2.9)	9 (26.5)	34 (34)
Total	35 (35)	75 (75)	25 (25)	23 (23)	6 (6)	18 (18)	%100
P	0.19	0.22	0.08	0.15	0.11	0.66	

Group1: Patients who received invasive mechanical ventilation support Group2: Patients who did not receive invasive mechanical ventilation support. DM: Diabetes Mellitus. HT: Hypertension. HD: Heart disease. CLD: Chronic Lung Disease. CKD: Chronic kidney disease ND: Neurological disease. T: Total. N: number of patients %: Percent

Table 3. Comparison of the NIV and HFNO support starting days of the patients in Group1 and Group2

	Group 1	Group 2		Group1(n-66)	Group 2/(n-34)	
	Day	Day	P	Duration	Duration	P
NIV	2.4±1.9	3.7±3.5	0.39	4.2±4 /32(48.5%)	7.5±3 /4 (11.8%)	0.051
HFNO	1.2±0.9	1.7±1.3	0.03	3.1±2 /28(42.4%)	5.6±2/9 (26.5%)	0.006

Group1: Patients who received invasive mechanical ventilation support. Group2: patients who did not receive invasive mechanical ventilation support. NIV: Noninvasive mechanical ventilation, high flow: high flow oxygen. N: number of patients

Two or more systemic diseases were present in 49 (74.2%) patients in Group 1 and 16 (47.1%) patients in Group 2. In paired comparison, the number of patients with two or more comorbidities in Group 1 was found to be significantly higher (p: 0.007). 48 (75%) of 64 patients who died and 17 (47.2%) of 36 discharged patients had two or more additional diseases. When the patients who lost their lives and were discharged from the intensive care unit were compared statistically, the presence of two or more additional diseases in patients who died was found to be significantly higher than the patients who were discharged (p: 0.005).

It was observed that oxygen support with HFNO was started on an average of 1,3 days and was applied for 3,7 days in all patients, and NIV support was applied on an average of 2,6 days and for 4,6 days. It was observed that IMV support was started on the 4.9th day and applied for 8.5 days to the patients in group 1. It was observed that HFNO administration was started earlier and applied for a shorter time in the patients in group 1 (p: 0.03). No difference was found between the groups in terms of the day and time of NIV support application (p: 0.051). The days and durations of HFNO and NIV support were compared in Table 3. In group 1, the mean duration of imv support was 7.3 ± 6 days for patients who lost their lives, while the duration of imv for patients discharged was 47.5 ± 20 days.

While the peripheral oxygen saturation was $86\% \pm 5$ lt / min with 100% oxygen support from the reservoir mask when the patients were admitted to intensive care; The average peripheral oxygen saturation was $88 \pm 8\%$ in IMV support, 91 ± 2 in oxygen support with High Flow, 89 ± 5 in NIMV support, and $96 \pm 1\%$ with 100% oxygen support at 4 lt / min from the nasal cannula at discharge.

Discussion

Covid-19 is characterized by progressive respiratory failure due to lung infection [13]. Acute respiratory failure syndrome (ARDS) and widespread alveolar damage are among the main features of Covid-19 [2]. As a result of covid pneumonia developing due to this disease, the number of patients hospitalized in intensive care units has also increased. Clinical characteristics of these patients who receive treatment in intensive care units, such as age, gender, comorbid disease, IMV or NIMV support, and the duration of the application of these supports, as well as the length of stay in the intensive care unit are discussed and shown among the features that affect mortality rates [14]. In a study conducted in Italy, it was observed that the rate of those under the age of 65 who died due to covid 19 infection was 8.5%, while this rate was 91.5% for people over 65 years [15]. In a study conducted in 1590 patients

infected with covid-19 in hospital, it was shown that advanced age, smoking, chronic lung disease, heart disease, DM, HT, presence of neurological disease cause an increase in mortality and the need for IMV support [16]. In our study, when we compared the patients who received IMV support (Group 1) and those who did not (Group 2), the mean age of Group 1 was statistically higher than the average age of Group 2. There was no difference in gender and length of stay in both groups. It was observed that the most common comorbidities in intensive care patients were hypertension, diabetes mellitus, chronic heart diseases, chronic lung diseases, chronic kidney diseases and neurological diseases, respectively. The frequency of these comorbidities was similar in patients treated with IMV. The number of patients with two or more diseases in Group 1 was significantly higher than Group 2. It was also determined that the prevalence of two or more systemic diseases in patients who died was higher than those who were discharged.

Some previous studies have shown that patients infected with covid-19 often require mechanical ventilation support [17,18]. Mechanical ventilation support is inevitable in patients with insufficient oxygenation, and some studies show that initial use of NIV reduces the need for intubation and mortality [19]. In a study on mortality rates in China infected with covid 19 treated with IMV, it was 97% [5] and 88% in a study conducted in New York [18]. In our study, we found the mortality rate as 64% in patients treated in the intensive care unit and 97% in patients receiving IMV support.

Mechanical ventilation support is inevitable in patients with insufficient oxygenation, and some studies show that initial use of NIV reduces the need for intubation and mortality. Again, in a study conducted in China, continuous positive airway pressure (CPAP) was applied and the rate of preventing entubation in patients was found to be 70%, and it was stated that cpap should be applied in hypoxic patients [19]. Implementation of IMV or NIV support in hypoxic Covid 19 patients, especially in intensive care, is of great importance and the time and duration of administration are critical. When the high mortality risk of invasive mechanical ventilation was evaluated [3,19], it was seen that the patients in the intensive care unit were given oxygen support with a reservoir oxygen mask first, and then HFNO and NIV, respectively, on the grounds that it was not sufficient. However, it was observed that if adequate oxygenation could not be achieved with these methods and there was no relief in clinical findings, endotracheal intubation was applied and IMV support was switched to. In our study, it was observed that HFNO support was started earlier in Group 1 compared to the other group (p: 0.003) and applied for a shorter

time ($p: 0.006$). In patients who underwent invasive mechanical ventilation, it was observed that highflow oxygen support was started earlier and the application time was shorter. As a reason, it can be thought that patients who need invasive mechanical ventilation support have a faster clinical progression and therefore switch from reservoir mask to HFNO support earlier, when sufficient oxygen saturation is not achieved and the patient does not have clinical relief, NIV or IMV support can be considered.

The starting day of NIV administration was also earlier in Group 1 and the duration of administration was shorter, but there was no statistically significant difference ($p: 0.051$). When it is considered that clinical progression is faster in patients receiving IMV support in case of studies with more patients, a significant difference can be seen. Peripheral oxygen saturation with oxygen support was $86 \pm 0\%$ at the time of admission to intensive care, while it was $96 \pm 1\%$ at discharge.

It was observed that 64 (97%) of 66 patients who underwent invasive mechanical ventilation died in the intensive care unit. It was observed that two patients were discharged after leaving the mechanical ventilator. Advanced age, hypertension, and presence of diabetes mellitus are considered as independent risk factors for patients with covid 19 [14]. Patients in group 1 were found to have a higher mean age and two or more systemic diseases compared to the other group ($p > 0.05$). This may be because the elderly and comorbid patients cannot tolerate hypoxia well and therefore need IMV support more than other patients. When invasive mechanical ventilation was initiated, these patients, who were already prone to severe hypoxemia and had high comorbidities, were evaluated together with studies with similar mortality rates [3,18]. However, in this study these patients were not due to IMV support; It should be noted that it is the last method implemented after HFNO and NIMV support.

Conclusion

Advanced age and additional systemic diseases increase mortality in patients infected with Covid19 treated in intensive care. We believe that patients of advanced age and 2 and above with additional systemic diseases need more IMV support and that adequate clinical improvement cannot always be achieved with HFNO and IMV support applications in these patients.

In this study conducted in our intensive care units, we think that the results were influenced by the age of the patients, comorbid characteristics, as well as the criteria for admission to the intensive care unit, criteria for switching to mechanical ventilation. We think that there is a long-term follow-up that includes discharged patients and that further studies are needed.

Conflict of interests

The authors declare that they have no competing interests.

Financial Disclosure

All authors declare no financial support.

Ethical approval

Ethics committee approval was obtained from the army university ethics committee and the material was added to the method section. (2020/257)

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