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Research Article / Araştırma

COVID-19 Could Be More Severe and Fatal in the Octogenarian and Nonagenarian Population in Intensive Care Unit

COVID-19, Yoğun Bakım Ünitesindeki Octogenarian ve Nonagenerian Popülasyonda Daha Şiddetli ve Ölümcül Olabilir

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ABSTRACT

Objectives: In this study, it was aimed to determine demographic and clinical characteristics, supportive treatments in intensive care unit (ICU), mortality rates and factors affecting mortality by grouping COVID-19 intensive care patients as octogenarian and nonagenarian groups, and patients younger than 80-years-old.

Methods: The patients aged ≥18 years diagnosed with COVID-19 with PCR positivity in ICUs between March 19, 2020 and March 31, 2021 were included in this retrospective observational study.

Results: Of the 1004 PCR positive patients, 58.7% were male. The youngest patient was 20, the oldest patient was 100-years-old. There were 738 patients in Group 1 (20-79 years) and 266 patients in Group 2 (≥80 years). Between the two groups, gender, APACHE II score, need for intubation, need for vasopressor/inotrope, and patients in need of care were higher in Group 2 (p<0.001 for all). Only the patients in Group 1 were established ECMO. Hypertension (HT), cardiovascular, respiratory and neurological diseases, number of comorbidity, and mortality rate were higher significantly in Group 2 (p<0.001, p=0.001, p=0.006, p<0.001, p<0.001, and p<0.001; respectively). Age, male gender, HT, intubation, and vasopressor/inotrope requirement were found to be predictors of mortality.

Conclusion: COVID-19 may have a more severe and fatal course in the octogenerian and nonagenerian age group with high comorbidity in the ICU.

Keywords: COVID-19, intensive care unit, mortality rate, nonagenarian, octogenarian

ÖZ

Amaç: Bu çalışmada, "Coronavirus Disease-2019 (COVID-19)"a yakalanan yoğun bakım hastalarını octogenarian ve nonagenarian grup ve 80 yaşından genç hastalar olarak gruplandırarak demografik ve klinik özelliklerinin, yoğun bakımdaki destek tedavilerinin, mortalite oranlarının ve mortaliteye etkili faktörlerin belirlenmesi hedeflendi.

Yöntem: Retrospektif gözlemsel bu çalışmaya, 19 Mart 2020-31 Mart 2021 tarihleri arasında COVID-19 yoğun bakım ünitelerinde yatan polimeraz zincir reaksiyonu pozitifliği ile COVID-19 tanısı alan ≥18 yaş hastalar dahil edildi.

Bulgular: Polimeraz zincir reaksiyonu pozitif 1004 hastanın %58,7'si erkek, en genç hasta 20, en yaşlı hasta 100 yaşındaydı. Grup 1'de (20-79 yaş) 738, grup 2'de (≥80 yaş) 266 hasta vardı. Cinsiyet, akut fizyoloji ve kronik sağlık değerlendirmesi II (APACHE II) skoru, entübasyon ihtiyacı, vazopresör/inotrop ihtiyacı ve bakım ihtiyacı olan hastalar grup 2'de daha fazlaydı (hepsi için p<0,001). Sadece grup 1'deki hastalara ekstrakorporeal membran oksijenasyonu uygulandı. Hipertansiyon, kardiyovasküler sistem, solunum sistemi ve nörolojik hastalıklar, komorbidite sayısı ve mortalite oranı grup 2'de anlamlı olarak yüksekti (sırasıyla; p<0,001, p=0,001, p=0,006, p<0,001, p<0,001, p<0,001). Yaş, erkek cinsiyet, hipertansiyon, entübasyon ve vazopresör/inotrop ihtiyacı mortalite prediktörleri olarak belirlendi.

Sonuç: COVID-19, yoğun bakım ünitesindeki octogenarian ve nonagenarian popülasyonda daha şiddetli ve ölümcül olabilir.

Anahtar sözcükler: COVID-19, mortalite oranı, nonagenarian, octogenarian, yoğun bakım ünitesi

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Introduction

Severe acute respiratory syndrome coronavirus-2, which emerged in the Wuhan region of China in December 2019 and caused a pandemic, caused disease in all age groups, from newborns to older people.[1,2] Furthermore, there were patients in all age groups who needed to be hospitalized in the intensive care unit (ICU) with the diagnosis of coronavirus disease 2019 (COVID-19).

COVID-19 basically causes COVID-19 pneumonia and/or respiratory failure in the respiratory system. In addition, it carries with systemic problems by affecting all systems such as cardiac, neurological, and immune systems.[3] Therefore, COVID-19 patients may need ICU admission and different supportive treatments in ICU. In addition to the medical treatment of COVID-19 in the ICU, various supportive treatments and systems from nasal oxygen to invasive mechanical ventilator (IMV) and even extracorporeal life support systems (such as extracorporeal membrane oxygenator (ECMO), dialysis) are applied according to the needs of COVID-19 patients.

In this study, it was aimed to compare the demographic and clinical characteristics of octogenarian and nonagenarian COVID-19 patients followed in the ICU with the diagnosis of COVID-19 and COVID-19 patients younger than 80 years of age, supportive treatments in the ICU, mortality rates, and to determine the factors that may affect mortality.

Methods

The data of patients aged 18 years and older, diagnosed with COVID-19 by PCR positivity, hospitalized in ICU between March 19, 2020 and December 31, 2020, were included in the study by retrospectively scanning after the approval of the Ethics Committee. PCR negative patients younger than 18 years of age were excluded from the study. The data of 1004 patients included in the study were reviewed retrospectively. The patients' demographics (age and gender), clinical as comorbidities (diabetes mellitus (DM), hypertension (HT), cardiovascular system disease (CVD), respiratory system disease, renal failure, malignancies, neurological disease, rheumatological diseases, psychiatric ilnesses, liver disease, thyroid diseases and others and, number of comorbidities (up to seven with no comorbidities [0-7]), acute physiologic, and Chronic Health Evaluation (APACHE II) score, supportive treatments such as (nasal/mask oxygen), high flow nasal cannula (HFO), non-IMV, IMV, need for intubation, hemodiafiltration, continuous renal replacement therapy and ECMO requirement), duration of IMV, and length of stay in ICU were recorded. Mortality rate and factors affecting mortality were determined.

The patients were separated into two groups as Group 1 (20-79-years-old) and Group 2 (80-100-years-old) according to their age and the findings were compared.

Statistical Analysis

Quantitative data were summarized as mean±standard deviation, while qualitative data were summarized as frequency and percentage, n (%). Comparisons between groups were made by choosing the appropriate t-test or one-way analysis of variance methods in independent groups in terms of quantitative data. When a statistically significant p value was obtained as a result of one-way analysis of variance, pairwise group comparisons were analyzed with the post hoc Tukey test. In terms of qualitative data, Chi-square or Fisher's exact test was used appropriately for comparisons between groups. Bonferroni corrected z-test was used for post hoc pair-wise comparisons between groups in terms of ratios. As a result of univariate analysis in determining the factors affecting mortality, significant variables at the $p<0.20$ level were determined as potential risk factors for the multiple logistic regression models. The final multiple logistic regression model was determined by the backward likelihood ratio method (Backward LR). Odds ratios (OR) and 95% confidence intervals (95% CI) from multiple logistic regression were reported. For model fit, the correct classification ratio of the deceased to the survivors was given by the Hoshmer Lemeshow test. Analyzes were performed using the R programming v.3.6.3 (R Foundation for Statistical Computing, Vienna, Austria). $P<0.05$ was considered statistically significant.

Results

Of a total of 1004 patients, 589 (58.7%) were male. The mean age of all patients was 69.5 years, the youngest patient was 20-years-old, and the oldest patient was 100-years-old. The APACHE II score average was 17.6 and, the patients most common needed nasal/mask oxygen support in ICU. Intubation requirement of all patients was 55.8%, duration of IMV 8.54 days, and length of stay in ICU 12.62 days. The most common comorbidity in all patients was HT (54.6%) and the least detected comorbidity was psychiatric diseases (0.9%). The rate of those with no comorbidity was 16% and the rate of those with 7% comorbidity was 0.4%. The mortality rate of 1004 patients was 54.2% (Table 1).

Of the 1004 patients, 738 were in Group 1 and 266 were in Group 2. When the groups were compared, there was a difference between the genders ($p<0.001$). The rate of men (64.6%) in Group 1 and the rate of women (57.9%) in Group 2 were high. APACHE II score was significantly higher in Group 2 ($p<0.001$). The rate of patients followed in the ICU

Table 1. Total, Group 1, and Group 2 patients' charactheristics of demographic and clinical

Variables	Total (n=1004)	Group 1 (n=738)	Group 2 (n=266)	p
Gender, n (%)				
Female	415 (41.3)	261 (35.4)	154 (57.9)	<0.001[¥]
Male	589 (58.7)	477 (64.6)	112 (42.1)	
Age (mean±SD)	69.51±13.96	63.84±11.71	85.23±4.31	<0.001[c]
APACHE II (mean±SD)	17.67±11.76	16.38±11.49	21.27±11.76	<0.001[c]
Nasal/mask oxygen, n (%)	806 (80.3)	595 (80.6)	211(79.3)	0.648[¥]
High flow nasal cannula, (%)	441 (43.9)	338 (45.8)	103 (38.7)	0.046[¥]
Non-invasive mechanical ventilation, n (%)	192 (19.1)	142 (19.2)	50 (18.8)	0.875[¥]
Intubation, n (%)	560 (55.8)	373 (50.5)	187 (70.3)	<0.001[¥]
Vasopressor/inotrop, n (%)	435 (43.3)	277 (37.5)	158 (59.4)	<0.001[¥]
Hemodiafiltration, n (%)	167 (16.6)	115 (15.6)	52 (19.6)	0.136[¥]
Continuous renal replacement therapy, n (%)	10 (1)	8 (1.1)	2 (0.8)	0.740[f]
Nursing care, n (%)	156 (15.5)	69 (9.4)	87 (32.7)	<0.001[¥]
ECMO, n (%)	7 (0.7)	7 (1)	0 (0)	0.200[f]
Duration of mechanical ventilation (day)	8.54±11.98	7.95±10.41	9.71±14.59	0.141[c]
Length of stay in ICU (day)	12.62±10.34	11.98±9.63	14.4±11.93	0.003[c]
Diabetes mellitus, n (%)	368 (36.7)	263 (35.6)	105 (39.5)	0.266[¥]
Hypertension, n (%)	548 (54.6)	368 (49.9)	180 (67.7)	<0.001[¥]
Cardiovascular system diseases, n (%)	325 (32.4)	218 (29.5)	107 (40.2)	0.001[¥]
Respiratory system diseases, n (%)	165 (16.4)	107 (14.5)	58 (21.8)	0.006[¥]
Renal failure, n (%)	96 (9.6)	65 (8.8)	31 (11.7)	0.176[¥]
Malignancies, n (%)	86 (8.6)	66 (8.9)	20 (7.5)	0.477[¥]
Neurological diseases, n (%)	178 (17.7)	92 (12.5)	86 (32.3)	<0.001[¥]
Rheumatological diseases, n (%)	18 (1.8)	13 (1.8)	5 (1.9)	1.000[f]
Psychiatric diseases, n (%)	9 (0.9)	8 (1.1)	1 (0.4)	0.458[¥]
Liver disease, n (%)	13 (1.3)	10 (1.4)	3 (1.1)	1.000[f]
Thyroid disease, n (%)	50 (5)	43 (5.8)	7 (2.6)	0.040[¥]
Other, n (%)	75 (7.5)	62 (8.4)	13 (4.9)	0.062[¥]
Number of comorbidities, n (%)				
0	161 (16)	139 (18.8)	22 (8.3)[a]	<0.001[¥]
1	234 (23.3)	184 (24.9)	50 (18.8)[a]	
2	233 (23.2)	166 (22.5)	67 (25.2)	
3	219 (21.8)	163 (22.1)	56 (21.1)	
4	115 (11.5)	64 (8.7)	51 (19.2)[a]	
5	31 (3.1)	17 (2.3)	14 (5.3)[a]	
6	7 (0.7)	3 (0.4)	4 (1.5)	
7	4 (0.4)	2 (0.3)	2 (0.8)	
Mortality, n (%)	544 (54.2)	363 (49.2)	181 (68.1)	<0.001[¥]

Quantitative data were summarized as mean±standard deviation, and qualitative data were summarized as frequency and percentage, n (%). [¥]: Chi-square test; [f]: Fisher's exact test; [c]: t-test in independent groups; [a]: Statistically significant different from Group 1. APACHE: Acute Physiology and Chronic Health Evaluation; ECMO: Extracorporeal membrane oxygenator.

due to the need for intubation, need for vasopressor/inotrope, and need for care, among the supportive treatments applied in the ICU, was significantly higher in Group 2 (p value p<0.001 for all). ECMO was not applied to any patient in Group 2. Length of stay in ICU was significantly longer in Group 2 (p=0.003). When the comorbidities of the two groups were compared, rate of HT, CVS, respiratory system, and neurological diseases was higher significantly in Group 2 (p<0.001, p=0.001, p=0.006, and p<0.001; respectively). There was also a significant difference between the two groups in the number of comorbidities (p<0.001). The mortality rate was significantly higher in Group 2 (68.1%) than Group 1 (49.2%) (p<0.001) (Table 1).

In the multiple logistic regression analysis of the factors affecting mortality; the evaluation of risk factors in the model is given as adjusted for gender and age variables. Accordingly, the need for intubation, the need for vasopressor/inotrope, and HT were found to be predictors that increase mortality (Table 2).

Table 2. Factors affecting mortality and multiple logistic regression model results

Variables	OR (CI 95%)	p
Gender (Male)	1.01 (0.53-1.91)	0.973
Age (1 year increase)	1.01 (0.98-1.03)	0.719
Intubation (yes)	9.19 (1.4-60.26)	0.021
Vasopressor/Inotrope (yes)	8.58 (4.34-6.95)	<0.001
Hypertension (yes)	1.89 (1.01-3.56)	0.047

Accurate classification rate: 91%, Hoshmer Lemeshow Test model fit (χ^2 [df: 8]=6.62) p=0.578. OR: Odds ratio; CI: 95% confidence interval.

Discussion

After the declaration of the pandemic, articles were shared by many researchers in the literature, dealing with different aspects of the pandemic and the virus, including the pathogenesis and treatment principles of COVID-19, and showing that the course of the disease may be related to genetic differences.[4-6] Although many features of COVID-19 have been discovered, there are still unknown features. With all these features, COVID-19 continues to cause disease in all age groups since the beginning of the pandemic. During the period of quarantine, lock down, and isolation, as well as during the normalization period, patients from all age groups were admitted to the ICU. In many studies in the literature, it has been reported that the elderly population is more affected by the disease.[7]

In this study, we examined the demographic characteristics of COVID-19 patients in the tertiary ICU, as well as how COVID-19 progresses in the octogenarian and nonagenarian population, which supportive treatments are needed in the ICU and its outcomes.

The octogenarian and nonagenarian groups comprised 26.5% of the 1004 patients. Although the life expectancy of this age group has increased in Turkey today, according to the 2020 data, the age of ≥80 years constitutes 1.83% of the entire population in Turkey.[8] Therefore, in this study, which included all adult age groups, it was an expected result that there were fewer patients in Group 2 than Group 1. There is an inverse ratio in the male-female ratio between the two groups. Studies showing that the male gender is more affected by COVID-19 that is similar to the gender distribution in Group 1.[9,10] In this study, unlike the literature data, female gender was higher than male gender in the octogenarian and nonagenarian groups.[11] The APACHE II score, which is an important predictor of mortality in ICU, was higher in the octogenerian and nonagenarian groups with higher mortality.[12] Nasal/mask oxygen support was the most common supportive treatment in both groups. Considering that COVID-19 has lung involvement at different rates from person to person, and hypoxemia and respiratory failure are the most common causes of hospitalization in the ICU, oxygen support was the highest need for supportive treatment in both groups. The need for HFO was higher in Group 1 and the need for intubation was higher in Group 2. It has been reported as methods that delay or reduce the need for prone position intubation with HFO.[13,14] This result indicates that young and mobile patients adapt better to HFO. Prone position is not possible in patients with advanced age and care needs. Therefore, in older patients, the intubation rate may have increased with the severity of the disease being more severe. The need for vasopressor/inotrope was higher in Group 2. In this group, which can cause mortality and have a high mortality rate, there may be evidence of septic shock or multiorgan failure. Gupta et al.[15] reported that the need for IMV and the need for vasopressors were 67.4% and 48.3%, respectively. Both rates were higher than the results for all patients in the present study.

The need for care was a predicted outcome in Group 2 with advanced age patients. When adequate oxygenation cannot be achieved despite conventional treatments and lung protective ventilation strategies in ARDS, the next step is veno-venous ECMO. The treatment approaches are similar in COVID-19 ARDS, too. During the pandemic, the Extracorporeal Life Support Organization has created a guideline that determines relative and absolute contraindications along with ECMO indications in COVID-19 patients. In this guideline, it is stated as one of the advance aged absolute contraindications. Therefore, ECMO was applied only to patients in Group 1.[16]

The most common comorbidities in both groups were, in order, similar to the literature data; HT, DM, CVD, and respiratory system diseases. Among these comorbidities, the rates of HT, CVDs and respiratory system diseases were significantly higher in Group 2. These three comorbidities increase with increasing age.[17,18] Therefore, the excess of these comorbidities in the octogenerian and nonagenarian groups was consistent with the results of other previous studies.[11] Again, neurological diseases such as Alzheimer's, dementia, Parkinson's, and cerebrovascular event were more common in Group 2. Neurological comorbidity rate of all patients (17.7%) was lower than the rate in the study of Romagnolo et al.,[19] but higher in the octogenerian and nonagenarian groups (32.3%). Neurological diseases are also comorbidities that increase with age. Therefore, it may have accompanied more frequently in Group 2. García-Azorín et al.[20] reported that both the mean age and the presence of neurological diseases were reported as a predictor of mortality in the patient group with neurological disease comorbidity. Romagnolo et al.[19] also showed that, in addition to age and male gender, neurological comor-

bidities are one of the factors affecting mortality. In the present study, although neurological diseases were not among the factors affecting mortality, it was found to be a more common comorbidity in older patients with higher mortality.

A linear relationship between the number of comorbidities and mortality was also demonstrated in a previous study.[21] A study emphasizing mortality, multimorbidity, and age was also reported in the Journal of the American Heart Association.[22] A similar relationship was obtained in the present study as well. While the rate of those with no comorbidities in Group 1 was higher than Group 2, the rate of those with 2, 4, 5, 6, and 7 comorbidities was higher in Group 2. In addition, the mortality rate was higher in Group 2 and the results were similar to other studies.

The mortality rate for all patients (54.2%) was higher than the ICU mortality rate (35%) in a reported meta-analysis data. In the meta-analysis, the mortality rates of the subgroups by region were reported as 39% in China, 48% in Asia, 34% in Europe, 15% in the USA, and 39% in the middle east.[23]

In the multiple logistic regression analysis, male gender and age were among the demographic characteristics; the need for intubation and vasopressor/inotrope as supportive therapies; among the comorbidities, HT was determined as the factors affecting mortality. In Kokturk et al.[24] study, which was also reported from Turkey, male gender, age ≥65 years, sepsis, and multiorgan dysfunction were determined as mortality predictors, similar to the results of the present study. In this study, the need for vasopressor/inotrope, which is one of the indicators of sepsis and multiorgan dysfunction, is also one of the predictors of mortality.

The limitations of the study are that it is single-center and retrospective, and the absence of symptoms and laboratory data that could be predictors of mortality.

Conclusion

As a result, COVID-19 continues to cause serious illness and death in all age groups. However, COVID-19 has a more severe and fatal course in the ≥80 age group, which has high comorbidities and needs more supportive treatments in the ICU.

Disclosures

Ethics Committee Approval: The study was approved by The Ankara City Hospital No 1 Clinical Research Ethics Committee (Date: 15/12/2021, No: E1-21-2025).

Informed Consent: Written informed consent was obtained from all patients.

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