

# Correlation of important prognostic factors and CT scores in invasive and non-invasive ventilation of COVID-19 patients

✉ Ayfer Kaya Gök, M.D.,<sup>1</sup> ✉ Aygen Turkmen, M.D.,<sup>1</sup> ✉ Emine Köse, M.D.,<sup>1</sup>  
✉ Ferhat Çengel, M.D.,<sup>2</sup> ✉ Serpil Şehirlioglu, M.D.<sup>1</sup>

<sup>1</sup>Department of Anesthesia and Reanimation, University of Health Sciences Gaziosmanpaşa Training and Research Hospital, İstanbul-Türkiye

<sup>2</sup>Department of Radiology, University of Health Sciences Gaziosmanpaşa Training and Research Hospital, İstanbul-Türkiye

## ABSTRACT

**BACKGROUND:** Intensive care workers received the largest share of the COVID-19 pandemic, which caused nightmares to the whole world. In COVID-19 pneumonia cases which had high mortality rates, many prognostic factors and laboratory examinations were tried to evaluate the clinical severity quickly and accurately. This study was planned to investigate a correlation between the initially ventilation strategy and major prognostic parameters and CT scores in patients admitted to intensive care unit (ICU).

**METHODS:** In our study, we reviewed 50 consecutive non-invasive mv and 50 consecutive invasive mv treatment of COVID-19 pneumonia patients between March 23, 2020, and May 23, 2020, in the ICUs of our hospital. Patients who were divided into two groups (non-invasive mechanical ventilation [NIMV] and invasive mechanical ventilation [IMV]) as an initial ventilation strategy according to clinical severity and P/F ratios were evaluated comparatively; demographic data, admission and lowest P/F ratios, admission and highest SOFA scores, comorbidity status, scores on CT at diagnosis, length of ICU stays, hospitalization periods, and mortality rates were examined.

**RESULTS:** About 85% of all patients were 46 years and older. No significant difference was found in terms of gender and comorbidity status. The lowest P/F ratio was significantly lower in IMV group. The admission and highest SOFA values were higher in the IMV group. There was no significant difference between the CT scores and the number of lobes involved. The mortality rate in the IMV group was significantly higher.

**CONCLUSION:** Patients who started treatment with NIMV had relatively low poor prognostic factors, their mortality was lower. However, the total CT score at diagnosis was expected to be higher in those who were performed IMV, no significant difference was found in our study. We concluded that the severity classification of the patients cannot be made according to CT scores. CT results should be evaluated as a whole according to the patient's clinic, predisposing factors, and response to treatment.

**Keywords:** Classification; COVID-19; CT scores; pneumonia.

## INTRODUCTION

Intensive care units (ICUs) received the largest share of the COVID-19 pandemic, which caused a nightmare for the whole world. In cases of COVID-19 pneumonia with high mortality rates, many prognostic factors and tests have been tried to be classified to evaluate clinical severity quickly and accurately. COVID-19, caused by severe acute respiratory

syndrome coronavirus-2 from the coronavirus family, started in Wuhan, China in December 2019 and spread all over the world, and was declared a pandemic by the World Health Organization in March 2020.<sup>[1]</sup> In 2021, we are still trying to treat our patients by adding new data to our knowledge about the disease which has various mutations. To date, no treatment has been definitively shown to be effective for either suspected or confirmed COVID-19 patients.

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Address for correspondence: Ayfer Kaya Gök, M.D.

SBÜ Gaziosmanpaşa Eğitim ve Araştırma Hastanesi, Anestezi ve Reanimasyon Kliniği, İstanbul, Türkiye

Tel: +90 212 - 945 30 00 E-mail: ayferkayagok@gmail.com

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COVID-19 clinic presents in different spectrums ranging from asymptomatic to severe pneumonia.<sup>[2]</sup> About 5% of diagnosed patients require critical care and among patients in intensive care mortality rates of 39–72% are reported. Comorbidities were advanced age, male gender, and coexisting diseases. Mortality was higher in patients with high d-dimer levels, high SOFA scores, and low P/F ratios.

The diagnosis of COVID-19 is confirmed through laboratory testing with positive result of real-time reverse transcriptase polymerase chain reaction (PCR), or retrospectively by positive IgM and IgG. However, negative results have been obtained in some cases that strongly suggest the disease in terms of history and laboratory. Especially in patients with respiratory failure symptoms, typical COVID-19 pneumonia findings were observed in the CT examination of the lungs and the sensitivity was found to be 98%. Despite negative PCR results, overall lung involvement score on the 2<sup>nd</sup> week had predictive value for clinical severity and could be indicator for further treatment.<sup>[3–5]</sup>

In cases of COVID-19 pneumonia with high mortality rates, CT results were classified for rapid and accurate assessment of clinical severity, and higher CT scores were found in severe cases.<sup>[6]</sup>

This study was planned to investigate a correlation between the initial ventilation strategy and major prognostic parameters and CT scores in patients who admitted to ICU.

The primary endpoint of our study was to evaluate the correlation of ventilation support in COVID-19 ICU-patients with poor prognostic parameters and CT scores. The secondary endpoint was to investigate the effects of these parameters on the length of intensive care and hospital stays and mortality rates.

## MATERIALS AND METHODS

In our study, we reviewed 50 consecutive non-invasive mechanical ventilation (NIMV) and 50 consecutive invasive mechanical ventilation (IMV) treatment of COVID-19 pneumonia patients between March 23, 2020, and May 23, 2020, in the ICUs of our hospital. Files were scanned retrospectively. The approval of the Clinical Research Ethics Committee of our hospital, dated May 26, 2021, and numbered 265, was obtained for the study. In this period, the indications for admission to the ICU were fever, muscle/joint pains, cough and sore throat, dyspnea, respiratory frequency  $\geq 30$ /min, using extrarespiratory muscles, SpO<sub>2</sub> level below 90% in room air, and bilateral diffuse diffusion in lung tomography. Patients who were divided into two groups (NIMV and IMV) as an initial ventilation strategy according to clinical severity and P/F ratios were evaluated comparatively; demographic data, admission and lowest P/F ratios, admission and highest SOFA scores, comorbidity status, scores on CT at diagnosis, length

**Table 1.** Percentage of involvement of each lobe

Lobar involvement	Score
1–25%	1
26–50%	2
51–75%	3
76–100%	4

of ICU stays, hospitalization periods, and mortality rates were examined.

Group IMV: Patients who were intubated on admission to the ICU and whose treatment started with IMV.

Group NIMV: Patients whose treatment was started with non-invasive ventilation upon admission to the ICU.

The CT scans of the patients at the time of diagnosis were examined by the same radiologist, CT visual quantitative evaluation was based on summing up lesions involving each lobe, which was scored as 0 (0%), 1-minimal (1–25%), 2-mild (26–50%), 3-moderate (51–75%), or 4-severe (76–100%), respectively. The total severity score was reached by summing the five lobe scores (0–20) (Table 1).

Demographic data of both groups, admission and lowest P/F ratios, admission and highest SOFA scores, comorbidity status, the scores on CT taken at diagnosis, ICU, and hospital stay lengths were examined.

## Analysis of Data

The data were analyzed in computer environment with SPSS 22.0 program. First of all, the normality distribution of the data was examined (Kolmogorov–Smirnov test) and it was determined that they were not normally distributed. For this reason, non-parametric tests were applied. The data of the groups were tested in terms of number, percentage, mean, and standard deviation. Pearson's Chi-square and Mann–Whitney U-tests were used to compare the data of the groups. P<0.05 was considered significant.

## RESULTS

First of all, demographic data of patients age, gender, and additional comorbidities were examined (Table 2).

It was determined that 85% of all patients were aged 46 years or older, 92% of the patients in the IMV group and 78% of the patients in the NIMV group were over the age of 46. In NIMV group, min age was 23, max age was 98 and mean age was 60. In IMV group, min age was 32, max age was 88 and mean age was 65. There was a statistically significant difference between the groups in terms of age factor (p<0.05). It

**Table 2.** Comparison of descriptive characteristics between groups

	Total	IMV Group	NIMV Group	*p
Age, n (%)				
Age 45 and under	15 (15)	4 (8)	11 (22)	0.045
Ages 46 and over	85 (85)	46 (92)	39 (78)	
Gender, n (%)				
Male	66 (66)	31 (62)	35 (70)	0.263
Female	34 (34)	19 (38)	15 (30)	
Comorbidity, n (%)				
None	29 (29)	16 (32)	13 (26)	0.605
Comorbidities	71 (71)	35 (68)	36 (74)	

\*Chi-Square test. IMV: Invasive mechanical ventilation; NIMV: Noninvasive mechanical ventilation.

**Table 3.** Comparison of groups in terms of various parameters

	IMV Group	NIMV Group	*p
Total CT score	10.17±4.43	9.47±4.6	0.61
Number of lobes involved in CT	4.67±0.73	4.51±1.07	0.955
P/F ratio (ICU admission)	147.02±77.72	149.14±68.96	0.539
Lowest P/F ratio	91.91±40.22	127.98±69.04	0.001
SOFA admission	5.44±2.49	3.74±1.02	<0.001
SOFA highest	9.36±2.46	6.38±2.99	<0.001
ICU length of stay	13.04±11.74	12.5±7.87	0.433
Length of hospital stay I6	16.98±13.08	19.94±11.67	0.1

\*Mann-Whitney U test. CT: Computed tomography; SOFA: Sequential organ failure assessment score; ICU: Intensive care unit; IMV: Invasive mechanical ventilation; NIMV: Noninvasive mechanical ventilation. P/F: Ratio of arterial oxygen partial pressure (PaO<sub>2</sub>) to fractional inspired oxygen (FiO<sub>2</sub>).

was determined that the group aged 46 years and over in the IMV group was proportionally higher than the NIMV group and the significant difference was due to this group.

There was no statistically significant difference between the groups in terms of gender and comorbidity status of the patients (p>0.05).

Among the poor prognostic factors of the patients in the ICU, the distribution of P/F ratio (admission and lowest), SOFA score (admission and highest), admission CT scores and number of lobes involved, ICU, and hospitalization length of stays between two groups are presented in Table 3.

In the comparison of various parameters of the groups, statistically significant difference was found between the lowest P/F ratio, SOFA admission, and highest mean values of SOFA (p<0.05). It was determined that the mean value of the lowest P/F ratio of the IMV group was lower than NIMV group. The highest mean values of SOFA were higher in the IMV group. There was no significant difference between CT scores and the number of lobes involved.

**Table 4.** Comparison of groups in terms of mortality rates

Mortality	Total	IMV Group	NIMV Group	*p
Yes	65 (65%)	42 (84%)	23 (46%)	<0.001
No	35 (35%)	8 (16%)	27 (54%)	

\*Chi-Square test. IMV: Invasive mechanical ventilation; NIMV: Noninvasive mechanical ventilation.

Mortality rates among the patient groups are analyzed in Table 4.

A statistically significant difference of mortality rates was found in the IMV group (p<0.05).

## DISCUSSION

Different clinical situations can be observed in COVID-19 disease, ranging from asymptomatic situation to severe pneumonia.

In a study in China, it was reported that mild cases were

81% and these patients were treated as outpatients.<sup>[7]</sup> In this study, mortality was 28% in hospitalized patients, 62% in the ICU, and 81% in those receiving IMV.<sup>[8]</sup> In Italy retrospective case series that involved 1591 critically ill patients, 99% required respiratory support, including endotracheal intubation in 88% and non-invasive ventilation in 11%; ICU mortality was 26%.<sup>[9]</sup> In our study, we also found statistically significant difference of mortality rates in the IMV group.

A systematic review and meta-analysis was done by Fang et al.,<sup>[10]</sup> to collect and evaluate the associations of epidemiological, comorbidity factors with the severity, and prognosis of COVID-19, 69 publications were examined. They found that the males and comorbidities, including any comorbidities, were significantly associated with the severe disease. Most problematic comorbidities were chronic obstructive pulmonary disease, respiratory system disease, and cerebrovascular disease. In another study, it was reported that advanced age, additional comorbidities (hypertension, diabetes, cardiovascular diseases, chronic lung disease, and cancer), high-risk scores, high d-dimer and C-reactive protein levels, and low lymphocyte counts are effective in the increase in mortality rates.<sup>[11]</sup> Alharthy et al.<sup>[12]</sup> found old age, active smoking, pulmonary embolism, decreased SpO<sub>2</sub>/FiO<sub>2</sub> ratio, and increased lactate and D-dimers were predictors of 28-day mortality in critically ill COVID-19 patients. Furthermore, in a recent report of 1590 hospitalized COVID-19 patients in China, the male rate was 57.3%, there might be a sex predisposition to COVID-19 that men are prone to the infection.<sup>[13]</sup> In our study, interestingly, we found that there was no statistically significant difference between the groups in terms of gender and comorbidity status of the patients. Our most common comorbidity was hypertension.

The most important intensive care hospitalization indication is COVID-19-related acute respiratory failure (ARDS), the main problem is in the respiratory system, other organ damage is not significant. In the respiratory system, alveolo-epithelial cells are damaged, and because endothelial cells are less affected, less exudate is formed compared to other ARDS forms.<sup>[14]</sup> According to the ARDS Berlin definition, the onset time should be <1 week, but the onset time in ARDS associated with COVID-19 is 8–12 days. There are different stages according to the severity of the disease. As Gattinoni<sup>[15]</sup> said, although most of the patients had severe hypoxemia, respiratory mechanics were not affected. Gattinoni et al.<sup>[15]</sup> mention two phenotypes based on disease severity, host response, host physiological reserve, and comorbidities and response of hypoxia to respiratory support: L-type (with low elastance, low ventilation/perfusion ratio, low lung weight, and low recruitability lung) and type H (lung with high elastance, high lung weight, and high recruitability). We know the importance of knowing the stage of our patient's lung at the diagnosis to treat appropriately. In L-type patients, hypoxia may improve with increasing oxygen concentrations, and patients whose dyspnea persists may benefit from non-invasive

ventilation strategies. When they are intubated, ventilation with high tidal volumes and low PEEP is appropriate due to lung mechanics (with low elastance, high compliance, and low recruiting). On the contrary, type H patients should be treated such as ARDS, high PEEP, and prone position which should be used frequently. With the right decisions at the diagnosis, we can reduce mortality with the appropriate ventilation strategy and treatment guidance for our patient. In our study, the group whose P/F ratio was <300 were non-invasively ventilated and the treatments were mostly beneficial since lung mechanics were better. In patients with P/F ratios below 100 and more severe respiratory failure symptoms, invasive ventilation was started and our current ARDS ventilation strategies were utilized. Mortality was found to be higher in the IMV group.

CT examination is the most direct and rapid examination method, which can quickly confirm the diagnosis and by the scoring system, it can help early attention to the tendency to severity.<sup>[16]</sup> The common CT manifestation of COVID-19 includes multiple segmental ground glass opacities (GGOs) distributed dominantly in extrapulmonary/subpleural zones and along bronchovascular bundles with crazy paving sign and interlobular septal thickening and consolidation. Pleural effusion or mediastinal lymphadenopathy is rarely seen.<sup>[17]</sup> CT scores can predict the severity of the disease by showing the percentage of lung involvement. In the early stages, localized inflammatory infiltrates appear as patchy or segmental ground-glass opacities in one or both lungs, subpleural or peribronchovascular spaces. In the later stages, GGOs are seen at increasing rates and in many lobes. Higher CT severity score is positively correlated with male gender and older age group patients which may be attributed to the coexisting morbidities and related factors of aging.<sup>[18]</sup> In a study by Li et al.,<sup>[6]</sup> CT images were classified by the same radiologists in accordance with the Fleischner Society Nomenclature recommendations and found that the overall CT score was higher in severe pneumonia. Our patients were divided into two groups as NIMV and IMV patients. In the IMV group, the poor prognostic values such as low P/F ratio and high SOFA value were found to be significantly different as expected. Mortality rates were also found to be statistically significantly higher. While a more serious pneumonia was expected according to these findings, no significant difference was found between the two groups in terms of CT scores and the number of lobes involved. We think that this difference is due to the CT timing, we had only CT scores at the time of admission to the ICUs.

As for the treatment, there are no specific drugs and many therapies are being tested in clinical trials. We hope to find the solution.

## Conclusion

Patients with relatively low poor prognostic values were those who were started on NIMV and their mortality was

lower than the IMV group. However, we concluded that the severity classification of the patients cannot be made according to the admission CT scores. CT results should be evaluated as a whole according to the patient's clinic, predisposing factors, and response to the treatment.

### Limitation

This is a retrospective observational study. Prospective controlled studies are needed.

Our patients had only CT scores at the time of admission to the ICU, two different (mild-moderate and severe) acute respiratory failure treatment started according to P/F ratios, we did not have information about CT scores in the earlier stages, and we could not evaluate CT during the follow-up of the treatment. Further studies are needed.

**Ethics Committee Approval:** This study was approved by the Gaziosmanpaşa Training and Research Hospital Clinical Research Ethics Committee (Date: 26.05.2021, Decision No: 265).

**Peer-review:** Externally peer-reviewed.

**Authorship Contributions:** Concept: A.K.G.; Design: A.K.G.; Supervision: A.K.G., A.T.; Resource: A.K.G.; Materials: A.K.G., E.K.; Data: A.K.G., E.K., S.Ş., F.Ç.; Analysis: A.K.G.; Literature search: A.K.G.; Writing: A.K.G.; Critical revision: A.K.G., A.T.

**Conflict of Interest:** None declared.

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## ORJİNAL ÇALIŞMA - ÖZ

**COVID-19 hastalarında invaziv ve non-invaziv ventilasyon uygulamalarında önemli prognostik faktörlerin ve BT skorlarının korelasyonu****Dr. Ayfer Kaya Gök,<sup>1</sup> Dr. Aygen Turkmen,<sup>1</sup> Dr. Emine Köse,<sup>1</sup> Dr. Ferhat Çengel,<sup>2</sup> Dr. Serpil Şehirlioglu<sup>1</sup>**<sup>1</sup>Sağlık Bilimleri Üniversitesi Gaziosmanpaşa Eğitim ve Araştırma Hastanesi, Anestezi ve Reanimasyon Kliniği, İstanbul<sup>2</sup>Sağlık Bilimleri Üniversitesi Gaziosmanpaşa Eğitim ve Araştırma Hastanesi, Radyoloji Kliniği, İstanbul

**AMAÇ:** Tüm dünyaya kabus yaşatan COVID-19 pandemisinden en büyük payı yoğun bakımlar aldı. Mortalite oranlarının yüksek olduğu COVID-19 pnömonisi olgularında, klinik şiddetin hızlı ve doğru bir şekilde değerlendirilmesi için pek çok prognostik faktör ve tetkik sınıflandırılmaya çalışıldı. Yoğun bakıma kabul edilen hastalarda başlangıçta öngörülen ventilasyon stratejisi ile başlıca kötü prognostik parametreler ve BT skorları arasında korelasyon olup olmadığını araştırmak amacı ile bu çalışma planlandı.

**GEREÇ VE YÖNTEM:** Çalışmamızda, hastanemiz anestezi ve reanimasyon kliniği kohort yoğun bakım ünitelerine 23.03.2020–23.05.2020 tarihleri arasında COVID-19 tanısı ile tedavi edilen ardışık 50 noninvaziv mv ve ardışık 50 invaziv mv tedavisi yapılan hasta üzerinden geriye dönük olarak dosya taraması yapıldı. Klinik ciddiyetine ve P/F oranına göre başlangıç ventilasyon stratejisi olarak iki gruba ayrılmış olan hastalar (NIMV ve IMV yapılanlar) karşılaştırmalı olarak değerlendirildi. Gruplar arasında demografik veriler, kötü prognostik değer olan giriş ve en düşük P/F oranları, giriş ve en yüksek SOFA skorları, komorbidite durumu ve tanıda çekilen BT'deki skorlar, yoğun bakım ve hastane yatış süreleri arasında korelasyon olup olmaması incelendi, mortalite oranlarına bakıldı.

**BULGULAR:** Gruplar arasında yaş faktörü açısından tüm hastaların %85'inin 46 yaş ve üstünde olduğu saptandı. Hastaların cinsiyetleri ve komorbidite durumları açısından anlamlı fark saptanmadı. Hasta gruplarının mortalite ile karşılaştırılmasında, IMV grubundaki eksitus oranının NIMV grubundan belirgin bir şekilde yüksek olduğu saptandı. IMV grubunun en düşük P/F oranı ortalama değerinin NIMV grubundan daha düşük olduğu, SOFA giriş ve en yüksek ortalama değerlerinin IMV grubunda daha yüksek olduğu saptandı. BT skorları ve tutulan lob sayısı arasında anlamlı fark saptanmadı.

**TARTIŞMA:** Çalışmamızda, kötü prognostik değerleri nispeten az olan hastalar noninvaziv ventilasyonla tedavisine başlanan hastalardı ve mortalite-leri invaziv ventilasyon grubuna göre azdı. Ancak tanı aşamasında çekilen BT'nin skorlamasına göre hastaların ciddiyet sınıflamasının yapılamayacağı sonucuna vardık, IMV yapılanlarda toplam BT skorunun daha yüksek olması beklenirken anlamlı fark bulunmadı. BT sonuçları hastanın kliniği, pre-dispozan faktörleri, yapılan tedaviye verdiği cevaba göre bir bütün olarak değerlendirilmelidir.

**Anahtar sözcükler:** BT skorları; COVID-19; pnömonisi; sınıflandırması.

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