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Comparison of the computed tomography COVID-19 Pneumonia Severity Scores in vaccinated and unvaccinated individuals without comorbidities

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ABSTRACT

Aims: The aim of this study to investigate the effect of vaccines on pneumonia severity by comparing the computed tomography pneumonia scores of vaccinated and unvaccinated individuals with COVID-19 without known comorbidities.

Methods: Between January 2021 and January 2022 a total of 270 patients, 133 vaccinated and 137 unvaccinated, with positive polymerase chain reaction tests and without any significant co-morbidity were included in the study. Computed tomography pneumonia scores, demographic characteristics, and vaccination information were evaluated through the hospital's electronic registry system.

Results: Mean pneumonia scores of individuals vaccinated for 1 dose were higher than individuals vaccinated for 2 or more doses. The shortest duration of infection after vaccination was determined in the group with 1 dose of vaccine and the longest in the group with 2 doses of vaccine. There was no significant difference between the total mean pneumonia scores of vaccinated (8.36∓3.97) and unvaccinated (7.88∓3.67) individuals (p >0.05). When the comparison was made in age groups, pneumonia scores of vaccinated individuals over 70 years of age were found to be significantly lower than unvaccinated individuals (p=0.003). A statistically significant positive correlation was found between the age of the patients and pneumonia scores in the entire study group (Rho=0.293).

Conclusion: There is no significant difference in the pneumonia scores of vaccinated and unvaccinated COVID 19 pneumonia patients without comorbidities, except for patients over 70 years of age.

Keywords: COVID-19, vaccines, multidetector computed tomography, pneumonia, comorbidity

INTRODUCTION

COVID-19, a member of the coronavirus family, spread rapidly and became a pandemic.[1] Many countries around the world began implementing vaccination programs to protect their citizens against the pandemic.[1] Breakthrough COVID-19 infections seen after vaccination have led to debate about the effectiveness of vaccines against variants.[1] Vaccines very rarely provide 100% protection. The protection of the Covid 19 vaccine has also been reported to be around 90 per cent.[1] Infections that develop as a result of inadequate immunity in vaccinated individuals are called breakthrough infections.[2] Breakthrough infections occur due to personal biological factors that affect the individual's immune system, or due to loss of vaccine efficacy as a result of mutations in viruses, as well as improper administration or storage of vaccines.[2]

COVID-19 pneumonia is more severe in patients with comorbidities that compromise the immune system.[3,4] Previous studies investigating the effects of vaccines on computed tomography (CT) pneumonia scores in vaccinated and unvaccinated individuals with comorbidities have not differentiated. In addition, the types of vaccines and vaccination procedures vary.[5-9] For these reasons, we aimed to investigate the effects of vaccines on the severity of COVID-19 pneumonia in patients without known comorbidities.

METHODS

Ethics

The study was approved by the Kırşehir Ahi Evran University Clinical Researches Ethics Committee (Date: 21.06.2022, Decision No: 2022-12/117). Because the study was designed retrospectively, no written informed consent form was obtained from patients. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Inclusion Criteria

Patients over 18 years of age with positive PCR tests and CT findings of viral pneumonia were included in the study. In the vaccinated group, single or more vaccinated individuals were included in the study.

Exclusion Criteria

Patients with co-morbidities (diabetes mellitus, malignancy, etc.) affecting the immune system were excluded from the study.

Vaccination Status

Vaccinated patients were categorized as having received a single dose (incomplete) or 2 or more doses (complete) of vaccine. Assuming that a single dose of vaccine did not provide sufficient immunity, the pneumonia scores of single-dose vaccinated individuals were compared with those of individuals who received 2 or more doses of vaccine, and the pneumonia scores of unvaccinated individuals were compared with those of individuals who received two or more doses of vaccine.

Image Analysis

Patients were scanned using Toshiba Alexion 16-slice and General Electric (GE) Lightspeed 128-slice CT scanners scanner using standard acquisition protocols. CT images were evaluated by using the hospital's picture archiving and communication system.

COVID-19 pneumonia can be divided into four stages based on the timeline of symptom progression: the early stage, which typically occurs within the first 0-4 days; the progressive stage, which typically occurs between days 5-8 days; the peak stage, which is typically observed between days 10-13 days ; and the resolution stage, which typically begins on 14th day or later. Although it varied according to the time of admission of each patient, a CT scan was performed at our hospital between 5-8 days. A second and, if necessary, a third CT scan can be done for patients who become clinically severe and develop respiratory distress. If a patient had multiple scans, the scan with the highest pneumonia score was used. All CT scans were interpreted by the same radiologist with more than 20 years of experience.

The CT pneumonia severity score index is a scoring system that determines the severity of pneumonia according to the lung volume affected.[10] The severity of pneumonia is determined by assigning a score between 1 and 5 according to the percentage of volume retained in each of the five lung lobes, and then summing the scores of the five lobes. A total score of less than 8 indicates mild pneumonia, 8-15 moderate pneumonia and 16-25 severe pneumonia (**Figure 1**).

Statistical Analysis

Statistical analysis of the study was performed using the Statistical Package for Social Sciences for Windows software (IBM SPSS version 28.0, Armonk, NY, USA). The normality assumption of the variables was tested using the Kolmogorov-Smirnov and Shapiro-Wilk tests. Descriptive statistics of the variables are presented as mean±standard deviation, median (min-max) and frequency n (%). For univariate analysis of the variables in the study, Kruskal-Wallis and Chi-square tests were used, depending on the type of variable and the availability of assumptions.

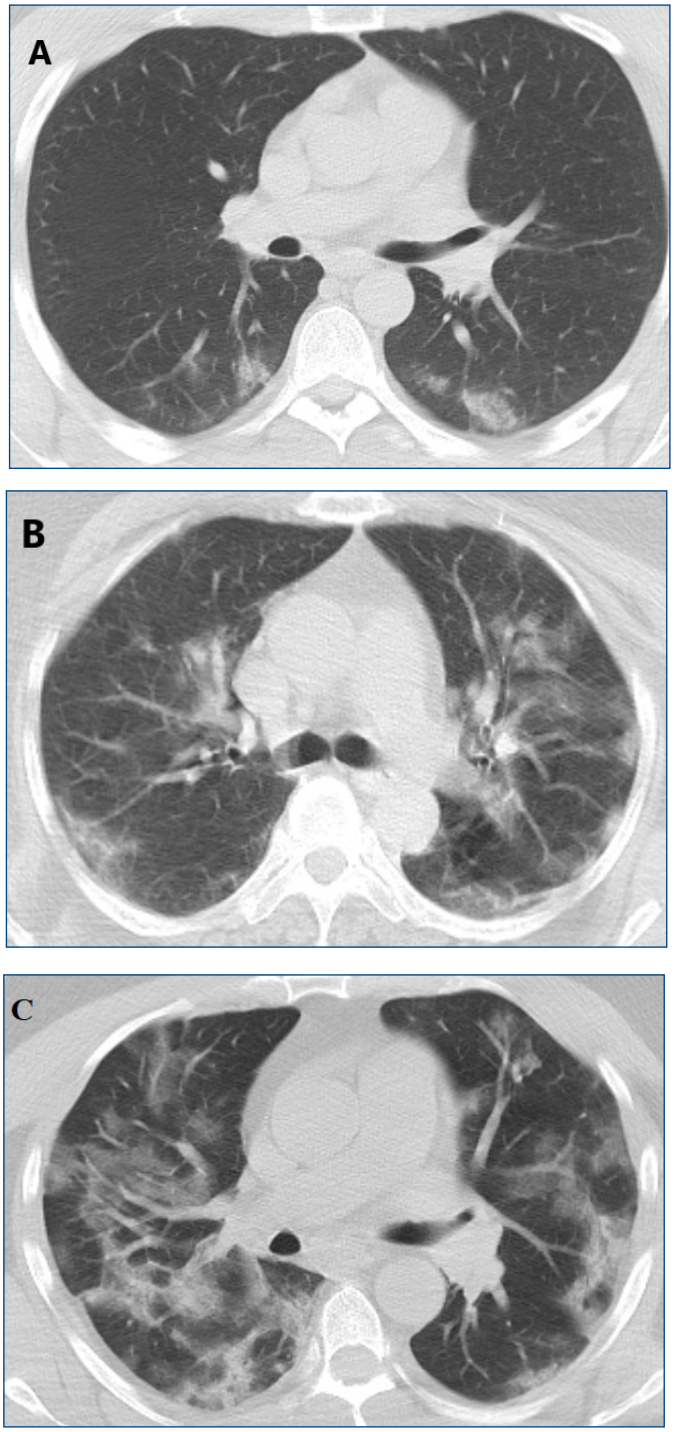

Figure 1. CT sections of different patients with mild (A), moderate (B), and severe (C) pneumonia

Pairwise comparisons of groups with significant differences between them obtained by the Kruskal-Wallis test were performed using the Mann-Whitney U test, with Bonferroni correction (0.05/number of groups). Relationships between variables were examined using Spearman's Rho correlation analysis.

RESULTS

In this study, CT images of 270 patients, 137 (50.7%) females and 133 (49.3%) males, who met fulfilling the inclusion criteria were examined. The mean age of the vaccinated group was 58.81∓14.31 years, whereas the mean age of the unvaccinated group was 56.36∓12.94 years.

The distribution of pneumonia scores and percentages of the patients in both groups is summarized in **Table 1**.

There was no significant difference in pneumonia scores between the groups in comparisons based on gender (**Table 2**).

In the vaccinated group, 43 people received 1 dose (39 Sinovac, 4 BioNTech), 66 people (60 Sinovac, 6 BioNTech) received 2 doses, 16 people (14 Sinovac, 2 BioNTech) received 3 doses and 6 people (2 Sinovac, 4 BioNTech) received 4 doses. 44 patients who received 1 dose of vaccine were considered insufficiently vaccinated. When comparing the pneumonia scores of vaccinated and unvaccinated individuals, comparisons were made with individuals who had two or more vaccinations.

When the mean pneumonia scores were compared according to the vaccine dose numbers in the vaccinated group, the difference between the pneumonia scores was not significant (p= 0.118). However, the pneumonia score of those who received 1 dose of incomplete vaccine was found to be the highest, and those who received 4 doses of vaccine had the lowest mean pneumonia scores (**Table 3**).

The difference was found to be statistically significant (p = 0.000) when the time elapsed until the infection appeared in the patients after vaccination according to the number of vaccine doses. The shortest duration of infection after vaccination was determined in the group with 1 dose of vaccine and the longest in the group with 2 doses of vaccine (**Table 3**). No significant relationship was found between the duration of disease onset and the severity of pneumonia after vaccination (Rho=-0.086, p=0.244).

When the mean pneumonia scores of vaccinated (8.36∓3.97) and unvaccinated (7.88∓3.67) individuals were compared the difference between the total mean pneumonia scores of both groups was not statistically significant (p > 0.05). When pneumonia scores were compared according to age groups, there was no significant difference between pneumonia scores in the 19–39 and 40–49 age groups. The mean pneumonia scores of the vaccinated patients were higher in the 50–59 and 60–69 age groups. Mean pneumonia scores of unvaccinated patients in the 70–80 age group were found to be higher than vaccinated patients (**Table 4**).

There was no significant difference in the frequency of CT findings such as consolidation, air bronchogram and ground-glass opacities in the comparison of all patients in the vaccinated and unvaccinated groups (p=0.569). Since the number of individuals vaccinated with BioNTech was low in the vaccinated patient group, a statistical comparison could not be made between the two vaccines. When the age of the patients and pneumonia scores were compared in all patient groups, a statistically significant positive correlation was found between age and pneumonia scores (Rho=0.293, p < 0.001). Pneumonia scores increased with age.

DISCUSSION

In this study, we aimed to evaluate the effect of the vaccine on the severity of pneumonia by comparing the CT severity scores of vaccinated and unvaccinated individuals without known comorbidity. We thought that the effect of vaccines on breakthrough pneumonia could be more objectively assessed in a study group in which comorbidities did not have a

Table 1. Pneumonia scores and percentages of vaccinated and unvaccinated patients

Severity Score		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	20	23	Total	p*
G1	N	2	11	11	11	15	5	9	10	10	14	7	14	6	2	1	2	-	1	1	1	133	0.000
	%	1.5	8.3	8.3	8.3	11.3	3.8	6.8	7.5	7.5	10.5	5.3	10.5	4.5	1.5	0.8	1.5	-	0.8	0.8	0.8	100	
G2	N	4	7	4	11	13	5	9	8	21	9	8	9	8	7	2	5	3	3	1	-	137	0.000
	%	2.9	5.1	2.9	8.0	9.5	3.7	6.6	5.8	15.3	6.6	5.8	6.6	5.8	5.1	1.5	3.7	2.2	2.2	0.7	-	100	

*: Chi-Square Test. G1: vaccinated group, G2 Unvaccinated group.

Table 2. Comparison of of mean pneumonia scores groups by gender

Gender	Males	Females	p*
G1	7.90±4.41 8 (1–20)	7.85±4.40 8 (1–23)	0.796
G2	9.03±4.79 9 (1–20)	8.65±4.07 9 (1–18)	0.723
G1+G2	8.41±4.47 9 (1–20)	8.32±4.21 8,5 (1–23)	0.860

*Mann-Whitney U test. G1: vaccinated group, G2 Unvaccinated group.

Table 3. Comparisons of mean pneumonia scores according to vaccine dose and time to infection after vaccination

	1 Dose	2 Doses	3 Doses	4 Doses	p value*	Comparison Group	Post Hoc p value#
Severity Score	9.79±5.04 9 (1–20)	8.40±4.08 9 (1–17)	9.44±3.95 9 (1–18)	7.42±3.64 7 (4–14)	0.118	-	-
Time to infection after vaccination (day)	44.67±80.18 22 (3–370)	109.15±84.29 93 (2–335)	95.72±81.65 82 (7–271)	60.85±76.06 26 (5–216)	0.000	1 vs. 2 1 vs. 3 1 vs. 4 2 vs. 3 2 vs. 4 3 vs. 4	0.000 0.010 0.653 0.383 0.070 0.224

*: Kruskal–Wallis, #: Mann–Whitney U

Table 4. Comparisons of mean pneumonia scores according to age

Age	19-39	40-49	50-59	60-69	70+	Total	p#
G1	7.52±3.79 7 (3–16)	7.00±4.42 6 (2–23)	7.02±4.07 7,5 (1–18)	7.53±3.67 7 (1–13)	11.26±3.89 12 (1–16)	7.88±3.67 8 (1–23)	0.000
G2	6.75±4.53 6 (1–16)	8.02±5.22 7 (2–17)	10.38±3.38 11 (1–17)	8.51±3.87 9 (2–18)	7.62±3.28 9 (3–16)	8.36±3.97 9 (1–18)	0.000
p*	0.518	0.963	0.002	0.041	0.003	0.056	

*Mann Whitney U # Kruskal Wallis. G1: vaccinated group, G2 Unvaccinated group.

negative impact. The mean pneumonia scores of those in the study group who received one dose were higher than those who received two or more doses. The time to development of infection after one dose of vaccine is lower than that of individuals vaccinated two or more times. Studies show that serum neutralization and IgG or IgA binding levels are lower after the first dose of vaccine, especially in older individuals.[11]

Some studies have reported that pneumonia occurring less than 2 weeks after vaccination has a lower pneumonia score than pneumonia occurring more than 19 weeks after vaccination.[5] In this study, no statistically significant difference was found between the severity of pneumonia occurring shortly or long after vaccination.

Previous similar studies reported that age was an important factor influencing the pneumonia score, with patients over 50 years of age having higher pneumonia scores.[11,12] In this study, when patients in both groups were evaluated together, the pneumonia scores of patients over 50 years of age were found to be higher than the other age groups. Over the age of 70, this difference became more pronounced. Changes in the immune system with age and changes in the immune system after the age of 50 have been the subject of many studies. This situation, known as immune ageing, paves the way for many diseases .[12]

When we compared the pneumonia scores of two or more vaccinated patients in our study group with those of unvaccinated patients, we found that the pneumonia scores were close in individuals under 50 years of age. Mean pneumonia scores were found to be significantly lower in the vaccinated group (8.84±3.72) than in the unvaccinated group (11.26±3.89) in individuals older than 70 years. This finding may indicate that vaccinated individuals over 70 years of age had milder pneumonia than unvaccinated individuals. However, all these findings may only be specific to the individuals in our study group.

The pneumonia scores of vaccinated people aged 50-70 years were higher than those of unvaccinated people. This finding suggests that the vaccinated individuals in the study group did not develop an adequate protective immune response against the virus. If an effective vaccine, given under the right conditions, does not provide sufficient immunity, there may be a problem with the individual's immune system. Even if they are vaccinated, pneumonia may be more severe in people with an immune deficiency than in unvaccinated people. This finding could also be due to loss of vaccine effectiveness against the virus and new highly virulent variants. The main reason for breakthrough infections after vaccination is the emergence of different variants. These new variants cause both natural and vaccine-induced immunity to lose effectiveness.[14] As all patients in our region were not tested for variants, we could not detect variants in our study. However, this study was conducted during the period of the Delta and Omicron variants.

Most of the studies that evaluated the effectiveness of vaccines using CT pneumonia scores showed that pneumonia was milder in vaccinated individuals.[5-8] Fewer studies have reported that vaccines do not change pneumonia scores.[9] However, all these studies did not distinguish patients with comorbidities.[5-9] Differences between studies may be due to differences in the virus variants and vaccines used. The immune system is very complex and can be influenced positively or negatively by many regional and personal factors. However, it is not possible to determine a definite cause with the data from our study or similar studies. More detailed multidisciplinary studies are needed.

Limitations

There are several limitations to this study. Firstly, viral variants could not be detected. Therefore, the study results cannot be generalized to all variants and vaccines.

CONCLUSION

There is no significant difference in pneumonia scores between vaccinated and unvaccinated COVID 19 pneumonia patients without comorbidities, except for patients over 70 years of age. There is a significant correlation between pneumonia score and age.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was approved by the Kırşehir Ahi Evran University Clinical Researches Ethics Committee (Date: 21.06.2022, Decision No: 2022-12/117).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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