Turkish Journal of Clinics and Laboratory

To cite this article: Cinar HG, Memis KB. Does the incidence of post-COVID pulmonary complications in vaccinated individuals correlate with the types of vaccines they received?. Turk J Clin Lab 2024; 3: 463-472

Research Article

# Does the incidence of post-COVID pulmonary complications in vaccinated individuals correlate with the types of vaccines they received?

## *BioNTech veya Sinovac ile aşılanmış bireylerde COVİD-19 sonrası akciğer komplikasyonlarının karşılaştırılması*

Hasibe Gokce Cinar*[1], Kemal Bugra Memis[2]

1Department of Radiology, Ankara Etlik City Hospital, Ankara, Turkey,
2Department of Radiology, Erzincan Binali Yildirim University Faculty of Medicine, Erzincan, Turkey.

## Abstract

**Aim:** Although several research have been undertaken to investigate the impact of the vaccination on long Coronavirus Disease 2019 (COVID-19) syndrome or post-acute sequelae, there is a lack of published evidence on the long-term effects of vaccines on lung-sequelae-related disease. Considering the limited global COVID-19 vaccine distribution, it is essential to establish the impact of vaccination in reducing pulmonary complications. Turkey has been offering COVID-19 vaccines from two platforms, including BNT162b2 (Pfizer-BioNTech, mRNA vaccine) and CoronaVac (Sinovac, inactivated vaccine). This study aimed to evaluate the efficacy of BioNTech and Sinovac vaccines in reducing post-COVID-19 pulmonary complications in individuals.

**Material and Methods:** A total of 94 patients COVID-19 pneumonia patients who were categorized based on the quantity of BioNTech or Sinovac vaccines they received before their first COVID-19 infection were included. The inclusion criteria consisted of a confirmed diagnosis of COVID-19 pneumonia through polymerase chain reaction testing, availability of the mentioned before and follow-up computed tomography scans, and administration of at least one dose of vaccine.

**Results:** The number of complications in patients fully vaccinated with Sinovac and who experienced post-COVID lung complications was significantly greater than in those vaccinated with BioNTech. The C-reactive protein and D-Dimer measurements of individuals who experienced complications in the Sinovac vaccinated group were significantly elevated on the index date.

**Conclusion:** The quantity of lung sequelae after COVID and laboratory parameters indicating this result were found to be higher in inactivated virus vaccines than in mRNA vaccines. This suggests that the protection of inactivated vaccines may be insufficient in severe cases.

**Keywords:** lung sequelae, vaccination, coronavirus disease, chest CT, inactivated vaccines, mRNA vaccines

Corresponding Author*: Hasibe Gokce Cinar, Department of Radiology, Ankara Etlik City Hospital, Ankara, Turkey,
E-mail: hgecinar@yahoo.com
Orcid: 0000-0003-2687-1544
Doi: 10.18663/tjcl.1544956
Recevied: 06.09.2024 accepted: 25.09.2024

## Öz

**Amaç:** Uzun Koronavirüs Hastalığı 2019 (KOVİD-19) sendromu veya akut sonrası sekeller üzerinde aşının etkisini araştırmak için çeşitli araştırmalar yapılmış olsa da, aşıların akciğer sekeli ile ilişkili hastalıklar üzerindeki uzun vadeli etkilerine dair yayımlanmış kanıtlar sınırlıdır. Küresel KOVİD-19 aşı dağıtımının sınırlı olması göz önüne alındığında, aşının akciğer komplikasyonlarını azaltmadaki etkisini belirlemek hayati önem taşımaktadır. Türkiye'de, KOVİD-19 aşıları BNT162b2 (Pfizer-BioNTech, mRNA aşısı) ve CoronaVac (Sinovac, inaktif aşı) dahil olmak üzere iki platformdan sunulmaktadır. Bu çalışma, BioNTech ve Sinovac aşılarının KOVİD-19 sonrası akciğer komplikasyonlarını azaltmadaki etkinliğini değerlendirmeyi amaçladı.

**Gereç ve Yöntemler:** İlk KOVİD-19 enfeksiyonlarından önce aldıkları BioNTech veya Sinovac aşılarının miktarına göre kategorize edilen toplam 94 KOVİD-19 pnömonisi hastası çalışmaya dahil edildi. Dahil etme kriterleri, polimeraz zincir reaksiyonu (PCR) testi ile doğrulanmış KOVİD-19 pnömonisi tanısı, belirli takip ve başlangıç bilgisayarlı tomografi taramalarının mevcut olması ve en az bir doz aşı uygulanmış olmasını içeriyordu.

**Bulgular:** KOVİD-19 sonrası akciğer komplikasyonları yaşayan ve Sinovac ile tam aşılanan hastalardaki komplikasyon sayısı, BioNTech ile aşılananlara göre anlamlı derecede daha yüksekti. Komplikasyon yaşayan Sinovac grubundaki bireylerin C-reaktif protein ve D-Dimer ölçümleri başlangıç tarihinde önemli ölçüde yüksekti.

**Sonuç:** İnaktif virüs aşılarında KOVİD sonrası akciğer sekel miktarı ve bu sonucu gösteren laboratuvar parametreleri mRNA aşısına göre yüksek bulunmuştur. Bu durum ağır vakalarda inaktive aşıların korumasının yetersiz olabileceğini düşündürmektedir.

**Anahtar Kelimeler:** akciğer sekeli, aşılama, koronavirüs hastalığı, göğüs BT, inaktive aşılar, mRNA aşıları

## Introduction

Extensive research has been conducted since the emergence of the COVID-19 pandemic in late 2019, caused by the SARS-CoV-2 virus, to determine the clinical sequelae of COVID-19 infection. Because this pandemic has harmed millions of people [1–4].

Research indicates that individuals with COVID-19 may face an increased likelihood of experiencing acute and post-acute sequelae that affect different organ systems. Additionally, there is a higher risk of mortality associated with COVID-19 infection. While the efficacy of COVID-19 vaccines in preventing severe COVID-19 disease and death has been extensively studied, it is currently unknown whether vaccination reduces the risk of pulmonary-extrapulmonary complications and mortality. This is the main area of focus in ongoing research [2, 5]. The clinical symptoms that occur within 30 days of initial infection are called acute sequelae of COVID-19. On the other hand, complications that arise or continue beyond the acute phase are referred to as post-acute sequelae of SARS-CoV-2 (PASC), which is also known as post-COVID syndrome or long COVID [6, 7]. Although most patients typically recover from COVID-19 infection within two to four weeks of experiencing symptoms, studies has shown that there is an elevated risk of cardiovascular, pulmonary, and neurological complications, as well as overall mortality, that can persist for up to two years [8, 9]. COVID-19 pneumonia can range in severity from asymptomatic to critical respiratory failure necessitating mechanical ventilator support. Patients with severe COVID-19 infection and those who are seriously ill have a heightened risk of developing long-term complications [10].

Following the 2003 SARS-CoV-2 outbreak, 67% of patients experienced long-lasting lung fibrosis within a month following being infected, and certain abnormalities remained evident even after a span of seven years [11]. Prior studies on the long-term effects of COVID-19 on the lungs have revealed that over 50% of recovered individuals exhibited abnormalities in their thoracic computed tomography (CT) for several weeks following being infected. Ground glass opacities (GGOs) and pleuroparenchymal bands were all commonly observed [10, 12].

As per Ministry of Health data, Turkey has been offering COVID-19 vaccines from two prominent vaccine platforms, including BNT162b2 from BioNTech/Fosun Pharma (Pfizer-BioNTech, mRNA vaccine) and CoronaVac from Sinovac Biotech Limited (inactivated vaccine), to people who are 18 years and above. CoronaVac has been available since 13 January 2021, while BNT162b2 has been available since 12 April 2021. COVID-19 booster shots became accessible starting on June 30, 2021. Individuals were able to choose between BNT162b2 or CoronaVac for the first and second dose. The study conducted by

Sonmezer et al. demonstrated that administering third booster injections with BNT162b2 or CoronaVac offers substantial defence against severe COVID-19 infection and completely eradicates the chances of being hospitalised, admittance to a critical care unit, or mortality [13, 14].

Long COVID is invariably accompanied with a significant economic burden. Within this entity, the spectrum of symptoms and is quite broad. In addition to long COVID terminology, various terminologies such as post-acute COVID-19 syndrome, chronic COVID syndrome and long-haul COVID are used in the literature [15]. While numerous studies have been carried out to examine the impact of the vaccine on long-COVID syndrome or post-acute sequelae, the available researched information for the long-term consequences of vaccination on lung-sequelae-related disease is currently limited. Gao et al. conducted a comprehensive analysis of 18 independent studies on a population that received predominantly mRNA vaccines. The review revealed that administering a double dose of the vaccine seemed to provide protection from long-term COVID [16]. There have been no studies to date that have explored this problem by evaluating thorax CT images.

Given the world's inadequate COVID-19 vaccine coverage, it is critical to determine whether vaccination reduces pulmonary sequelae. The current research aims to evaluate the efficacy of BNT162b2 and CoronaVac, two COVID-19 vaccines authorised in Turkey, in preventing post-COVID pulmonary complications in individuals aged 18 and above. Our goal is to fill the knowledge deficit regarding this topic, in order to ascertain whether to proceed with vaccination using a specific type of vaccine.

## Materials and Methods

This study obtained ethical approval from the Clinical Research Ethics Committee at Erzincan Binali Yildirim University (Protocol number: EBYU-KAEK-2023-11-002-EC-023567.003 / Date: 02 November 2023). Each patient gave written informed consent for the publication of this article using their data.

### Study design and population

The study was carried out at a tertiary university hospital. We aimed to comprise our study population of newly diagnosed patients with COVID-19 pneumonia, younger than 65 years of age, who had not previously had COVID-19, were vaccinated with a single type of vaccine, and did not have any high-risk comorbid diseases. We looked at 685 lung CTs from the hospital's PACS that were diagnosed with COVID-19 pneumonia between April 1, 2021 and February 1, 2022. Firstly, 143 of these 685 patients who have never been vaccinated against COVID-19 were excluded from the study. Because in most of these patients, widespread sequelae findings were observed in the lung parenchyma. Some patients had received one dose of booster BNT162b2 after being vaccinated with two doses of Coronavac. We excluded 68 patients who had previously received this type of hybrid vaccination in order to conduct an objective evaluation of the vaccines' specific effectiveness on pulmonary sequelae. Of the remaining 474 patients, 36 patients were excluded from the study because they had COVID-19 reinfection and 332 were excluded from the study because did not have a CT images within the specified time intervals. Ultimately, after assessing laboratory values and previous CT images, 12 patients were excluded from the study due to the presence of underlying interstitial lung disease, being over 65 years old, having high-risk comorbidities, or having an immunosuppressive status. The criteria for inclusion were as follows: a confirmed diagnosis of COVID-19 pneumonia through polymerase chain reaction (PCR) testing, presence of the aforementioned prior and follow-up CT scans, and receipt of at least one dose of vaccination. Therefore, our study included a total of 94 patients (Figure 1). All COVID-19 cases included in this study tested positive for the PCR test.

### Data collection

Age, gender, coexisting conditions (hypertension, diabetes, malignant disease, anemia, immunosuppressive diseases, and other disorders), and drugs used were all collect-ed. In addition, the individual's vaccination status, the quantity of doses received, dates of administration, and the producer of the vaccine were all documented. Furthermore, when diagnosed with COVID-19, at the onset of the disease, the hospital laboratory records included the collection of base-line measurements such as hemoglobin (Hb), white blood cell count (WBC), count of platelets (Plt), lymphocyte count, neutrophil count, neutrophil to lymphocyte ratio (NLR), C-reactive protein (CRP), D-dimer, and ferritin levels.

The study included 94 COVID-19 pneumonia patients who were categorized based on the quantity of BioNTech or Sinovac vaccines they received before their first COVID-19 infection. The patients were divided into two groups: those who were incompletely vaccinated (received 1 dose) and those who were completely vaccinated (received 2 doses), with or without additional booster doses (3 doses). The choices of vaccine type were made in our country according to people's preferences, not according to an indication deter-mined by the Turkish Ministry of Health.

### COVID-19 diagnosis and severity classification

PCR test results, with a specificity of over 99%, have been widely recognized as the most reliable diagnostic criterion for detecting COVID-19 infection [17]. The index date refers to the date when the initial diagnosis of COVID-19 patients was documented. In addition, we assessed patients based on the extent of their pulmonary COVID-19 infection.

The National Healthcare Commission's Recommendation for the Evaluation and Treatment Plan of COVID-19 Infection categorizes lung COVID-19 infection into three distinct types: Mild to moderate pneumonia characterized by fever, symptoms of respiration, and radiological manifestations. Severe pneumonia is defined by the presence of one or more of the signs that follow: Pulmonary distress is indicated by a respiratory rate (RR) exceeding 30 breaths per minute, a saturation level of oxygen of 93% while at rest, or a ratio of PaO2/FiO2 of 300 mmHg. The condition is considered extremely severe if one or more of the following criteria are met: A respiratory condition that requires the use of mechanical ventilation, shock, especially when combined with additional organ dysfunction, necessitates critical care in the intensive care unit.

### Chest CT protocol and image analysis - measurements

The chest CT images were acquired using a multislice-CT scanner (Somatom Force 64, Siemens Healthineers, Germany). After acquiring the scout image, imaging was con-ducted in a direction from the head to the tailbone while the person was supine position. The imaging was done with the following settings: 90/150 Sn kVp, 60 mAs, and a rotation time of 0.33 seconds. Imaging reconstruction was performed with a slice thickness of 1.5 mm in the axial plane. Two radiologists, with 9 and 11 years of experience respectively, collectively assessed the chest CT scans. The chest CT scans were evaluated using a workstation (Syngo.via, Siemens Healthineers, Erlangen, Germany) in order to determine the amount of pulmonary sequelae. The images were opened in the "MM Reading" applica-tion on the workstation, and the boundaries of the sequelae region were determined by selecting "Contour" from the "VOI freehand" tab, and then the data was obtained by calculating the volume with "Create VOI".

All patients in the research had previous chest CT scans acquired prior to the index date and stored in the PACS archive, which revealed no sequelae in the lung parenchymal areas. COVID-19 pneumonia was diagnosed based on the identification of certain abnormalities, such as ground glass opacity and consolidation, on the chest CT scan using the accepted terms for chest imaging established by the Fleischner Society [18]. Specific types of complications were evaluated as pleuroparenchymal linear atelectasis, tractional bronchiectasis, and ground-glass patches typically focused in the peripheral and basal regions of the lung parenchyma [12].

## Statistical analysis

The Shapiro-Wilk test was employed for assessing the normality of distributions of continuous variables. The median is the descriptive statistics for continuous data. Numbers and percentiles are used to represent categorical data. The Student's t-test will be employed for comparing normally distributed variables across both groups, whereas the Mann-Whitney U test will be utilized to analyses data that has an irregular distribution. The Chi-square test and, if needed, the Fisher exact test were used to do categorical evaluations. The data was analyzed using SPSS for Windows, version 24.0 (SPSS Inc., Chicago, IL, USA). P-value $< 0.05$ was considered statistically significant.

## Results

### Study population

This study includes a cohort of 94 patients diagnosed with COVID-19, consisting of 43 females and 51 males. The age distribution of females ranged from 24 to 63, with a median age of 55. The age distribution of males ranged from 26 to 64, with a median age of 57. The overall median age was found to be 57.

After undergoing inpatient therapy at the hospital, a total of 18 patients diagnosed with severe Covid-19 pneumonia successfully recovered. Additionally, out of the 76 patients diagnosed with mild to moderate COVID-19 pneumonia, 8 required hospitalization. The study population did not have any cases of critically severe COVID-19 pneumonia or fatalities. Table 1 provides an overview of the specific clinical and demographic aspects of the patients.

Out of the total of 94 participants in the trial, 53 individuals were administered Sinovac vaccines while 41 individuals were given BioNTech vaccines. Table 2 shows the dose counts of patients vaccinated with Sinovac and BioNTech.

| **Table 1.** Data analysis of the general characteristics of the patients | |
|---|---|
| Variables | All population n = 94 |
| Gender, n (%) | |
| Female | 43 (45.7) |
| Male | 51 (54.3) |
| Age, years | 57 (24–64) |
| Hemoglobin, g/dL | 14.1 (10.8–16.7) |
| Leukocytes, ×103/µL | 6.9 (3.92–10.73) |
| Platelets, ×103/µL | 205 (175–304) |
| Lymphocytes, ×103/µL | 1.32 (0.76–1.75) |
| Neutrophils, ×103/µL | 5.04 (2.55–8.56) |
| NLR | 5.42 (2.61–7.78) |
| CRP, mg/L | 46.9 (16–110) |
| D-Dimer, µg/L) | 374 (185–823) |
| Ferritin, ng/mL | 314 (180–659) |
| Severity of disease, n (%) | |
| Severe | 18 (19.1) |
| Mild–moderate | 76 (80.9) |
| Data are median (IQR) or number (%). CRP, C-reactive protein; NLR, neutrophil to lymphocyte ratio. | |

| **Table 2**. Quantity of vaccine doses for each type | | |
|---|---|---|
| Vaccine types | Fully Vaccinated (≥ 2 doses) n = 83 | Incompletely Vaccinated (1 dose) n = 11 |
| Sinovac - CoronaVac | 47 (56.6) | 6 (54.5) |
| BioNTech - BNT162b2 | 36 (43.4) | 5 (45.5) |
| Data are number (%). | | |

### Relationship between vaccine type, blood parameters and sequelae status

There were no sequelae in 82 patients. The remaining 12 patients had sequelae found on the 1st year control chest CT. 7 of the patients with pulmonary sequelae were in the group vaccinated with Sinovac before the index date, and the other 5 were in the group vaccinated with BioNTech. There was no discernible correlation between the type of vaccine administered and the occurrence of post-COVID pulmonary sequelae ($p > 0.05$).

It was noted that no sequelae developed in any of the patients who received the booster dose (3rd dose) in both vaccine groups.

Table 3 compares the clinical and vaccination characteristics of the patients with either the existence or absence of sequelae. Patients in both groups shared similar age and gender distribution features ($p > 0.05$).

A significant relationship was found between the presence of sequelae and lympho-penia. Patients with pulmonary sequelae had considerably lower lymphocyte counts. Table 4 and Table 5 compare the clinical features of patients in the two groups based on the vaccine types and either the existence or absence of sequelae.

When the blood parameters of patients are investigated by vaccine type, it is clear that CRP and D-Dimer levels, in addition to lymphopenia, are significantly higher in patients having pulmonary sequelae vaccinated with Sinovac.

### Correlation with vaccine type and quantity of sequelae

A substantial relationship was discovered between the type of vaccine and the quan-tity of sequelae ($p = 0.005$). In the volume measurements of the sequelae areas observed in the lung parenchyma, the overall median volume value was found to be 136 cm3 (58.4-387.5). While the median volume value of the sequelae areas in the fully vaccinated Sinovac group was 208.4 cm3 (87.5-387.5), it was 85.7 cm3 (58.4-156.1) in the fully vaccinated BioNTech group.

Figure 2 shows chest CT images from a 49-year-old female who received two doses of the BioNTech vaccine.

Figure 3 shows chest CT images of a 55-year-old female who received two doses of the Sinovac vaccine.

## Discussion

This study assessed the incidence of lung sequelae following COVID-19 infection using CT imaging in patients previously vaccinated with BNT162b2 or CoronaVac. In addition, a quantitative sequelae evaluation was made between the two groups by measuring the volume of the pulmonary sequelae areas. The most important finding in our study was that the quantity of sequelae in patients who were fully vaccinated with Sinovac and had post-COVID pulmonary sequelae was significantly higher than in those vaccinated with BioNTech.

The Pfizer–BioNTech vaccine is an mRNA-based COVID-19 vaccine. Previous clinical trials have shown that the Pfizer/ BioNTech vaccine is 95% effective at preventing COVID-19 infection. Recent clinical research validates the effectiveness of the BioN-Tech vaccines in preventing infection and demonstrates their efficacy in reducing hospitalizations, admissions to intensive care units, and mortality rates [19, 20]. Furthermore, vaccination not only provides protection against initial infection but also appears to re-duce the occurrence of long-term COVID symptoms and complications in the lungs following reinfection. Multiple studies tend to corroborate this perspective [12, 21].

**Table 3.** The correlation between the clinical and vaccination characteristics of the patients and the existence or absence of sequelae

| Variables | Sequelae exist (n = 12) | No Sequelae (n = 82) | P-value |
|---|---|---|---|
| Gender, n (%) | | | 0.565 |
| Female | 5 (41.7) | 38 (46.3) | |
| Male | 7 (58.3) | 44 (53.7) | |
| Age, years | 55 (34–64) | 53 (24–62) | 0.349 |
| Hemoglobin, g/dL | 14.2 (10.8–15.8) | 13.9 (11.5–16.7) | 0.280 |
| Leukocytes, ×103/µL | 6.54 (3.92–10.73) | 7.1 (4.56–9.39) | 0.167 |
| Platelets, ×103/µL | 198.3 (185.4–304) | 214.7 (175–286) | 0.274 |
| Lymphocytes, ×103/µL | 1.08 (0.76–1.24) | 1.44 (1.16–1.75) | < 0.001* |
| Neutrophils, ×103/µL | 4.53 (3.39–8.56) | 5.37 (2.55–7.89) | 0.154 |
| NLR | 4.92 (2.61–6.76) | 5.86 (2.91–7.78) | 0.099 |
| CRP, mg/L | 56 (16–110) | 44 (29–103) | 0.483 |
| D-Dimer, µg/L | 473 (269–823) | 351 (185–704) | 0.415 |
| Ferritin, ng/mL | 396 (180–644) | 295 (167–659) | 0.269 |
| Severity of disease, n (%) | | | 0.320 |
| Severe | 7 (41.7) | 11 (13.4) | |
| Mild–moderate | 5 (58.3) | 71 (86.6) | |
| Sinovac, n (%) | | | < 0.001* |
| Single dose | 3 (42.9) | 3 (6.3) | |
| Two and above | 4 (57.1) | 43 (93.7) | |
| Biontech, n (%) | | | < 0.001* |
| Single dose | 2 (40) | 3 (8.3) | |
| Two and above | 3 (60) | 33 (91.7) | |

Data are median (IQR) or number (%). * p<0.05 indicates statistical significance. CRP, C-reactive protein; NLR, neutrophil to lymphocyte ratio.

**Table 4.** The relationship between clinical features of patients vaccinated with Sinovac and the possibility of sequelae

| Variables | Sequelae exist n = 7 | No Sequelae n = 46 | P-value |
|---|---|---|---|
| Gender, n (%) | | | 0.328 |
| Female | 3 (42.8) | 18 (39.1) | |
| Male | 4 (57.2) | 28 (60.9) | |
| Age, years | 58 (34–63) | 54 (24–62) | 0.305 |
| Hemoglobin, g/dL | 14.2 (11.5–15.8) | 14.3 (11.5–16.1) | 0.430 |
| Leukocytes, ×103/µL | 6.91 (4.63–10.73) | 7.06 (4.81–9.01) | 0.372 |
| Platelets, ×103/µL | 210.3 (185.4–304) | 214.7 (186–280) | 0.350 |
| Lymphocytes, ×103/µL | 0.91 (0.76–1.05) | 1.52 (1.16–1.71) | 0.001* |
| Neutrophils, ×103/µL | 4.63 (3.39–8.29) | 5.35 (2.55–7.62) | 0.115 |
| NLR | 5.08 (3.45–6.76) | 5.91 (2.91–7.78) | 0.109 |
| CRP, mg/L | 74 (58–110) | 40 (29–90) | < 0.001* |
| D-Dimer, µg/L | 515 (376–823) | 326 (195–652) | 0.001* |
| Ferritin, ng/mL | 431 (270–644) | 315 (167–531) | 0.095 |
| Severity of disease, n (%) | | | 0.220 |
| Severe | 4 (57.2) | 7 (15.2) | |
| Mild–moderate | 3 (42.8) | 39 (84.8) | |

Data are median (IQR) or number (%). * p<0.05 indicates statistical significance. CRP, C-reactive protein; NLR, neutrophil to lymphocyte ratio.

**Table 5.** The relationship between clinical features of patients vaccinated with BioNTech and the possibility of sequelae

| Variables | Sequelae exist n = 5 | No Sequelae n = 36 | P-value |
|---|---|---|---|
| Gender, n (%) | | | 0.415 |
| Female | 2 (40) | 20 (55.6) | |
| Male | 3 (60) | 16 (44.4) | |
| Age, years | 51 (42–64) | 52 (24–62) | 0.526 |
| Hemoglobin, g/dL | 13.5 (10.8–14.6) | 14 (12.1–16.7) | 0.175 |
| Leukocytes, ×103/µL | 6.54 (3.92–9.51) | 6.86 (4.56–9.39) | 0.215 |
| Platelets, ×103/µL | 198.3 (185.4–240) | 223 (175–286) | 0.167 |
| Lymphocytes, ×103/µL | 1.08 (0.85–1.24) | 1.40 (1.21–1.75) | < 0.001* |
| Neutrophils, ×103/µL | 4.76 (3.75–8.56) | 5.17 (2.96–7.89) | 0.140 |
| NLR | 4.81 (2.61–5.54) | 5.56 (3.5–7.41) | 0.115 |
| CRP, mg/L | 45 (16–81) | 52 (36–103) | 0.650 |
| D-Dimer, µg/L | 384 (269–655) | 351 (185–704) | 0.635 |
| Ferritin, ng/mL | 431 (270–644) | 315 (167–531) | 0.244 |
| Severity of disease, n (%) | | | 0.195 |
| Severe | 3 (60) | 4 (11.1) | |
| Mild–moderate | 2 (40) | 32 (88.9) | |

Data are median (IQR) or number (%). * p<0.05 indicates statistical significance. CRP, C-reactive protein; NLR, neutrophil to lymphocyte ratio.

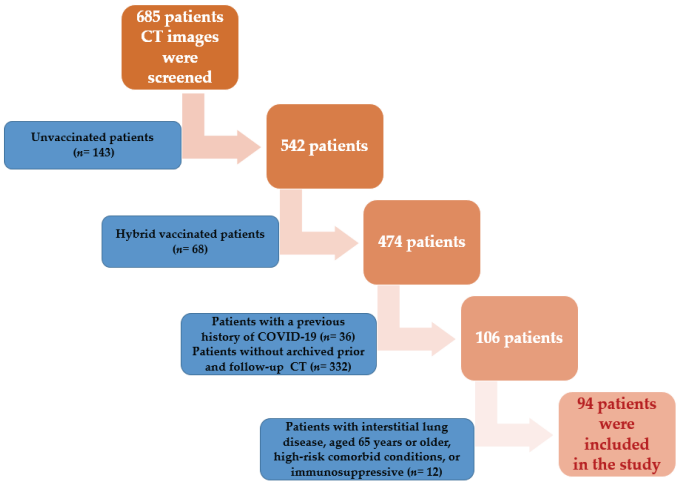


**Figure 1.** Diagram showing the study population.

CoronaVac is a COVID-19 vaccine that uses an entirely inactive virus. Although it is the most widely utilized COVID-19 vaccine globally, CoronaVac has received little re-search when compared to other vaccines [14]. In previous studies, its effectiveness against SARS-CoV-2 is approaching 95%. Moreover, these vaccines have demonstrated a high level of efficacy in diminishing hospitalizations, admissions to intensive care units, and mortality rates caused by COVID-19. Additionally, they are highly effective in preventing and minimizing long-term complications after infection [2, 13, 22].

After vaccination, cellular and humoral immune responses are established in the body. In the cellular response, the formation of cytotoxic T-lymphocytes occurs, and in the humoral response, B cell maturation takes place in the germinal centers of the lymph nodes [23, 24]. The pathogenic memory B-cell response in SARS-CoV-2, which can be triggered by prolonged autoantibody production in long-term COVID patients, has been held responsible [25, 26]. BNT162b2 significantly enhances SARS-CoV-2-specific binding and neutralizing antibody responses. On the other hand, CoronaVac induces stronger responses from CD4+ and CD8+ T cells compared to BNT162b2 [27, 28]. By inducing the described immune responses, vaccination can prevent organ damage by enabling faster clearance of SARS-CoV-2 and may contribute to the effective clearance of post-acute viral reservoirs [29].

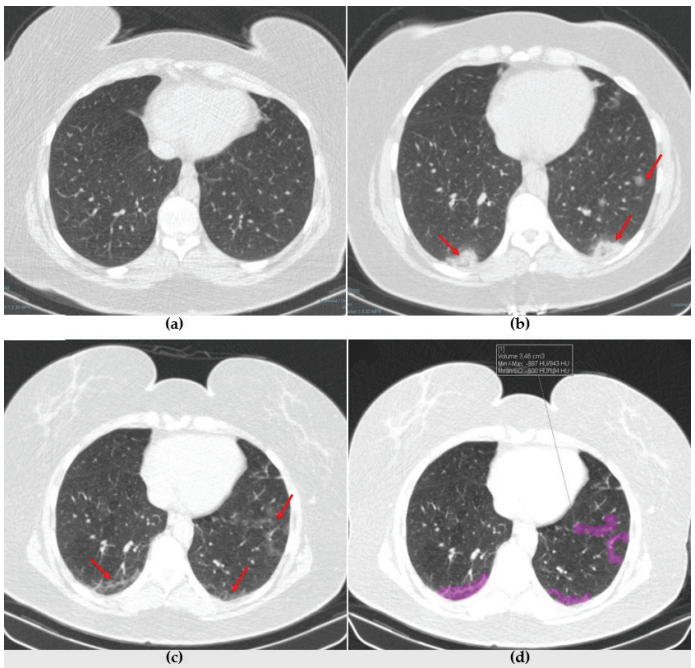


**Figure 2. A** 49-year-old female COVID-19 patient, vaccinated with two doses of BioNTech vaccine, presenting with dry cough for 1 week. (a) In the axial thorax CT images acquired 6 months before the index date, no infiltration is seen in either lung parenchyma. **(b)** The axial thorax CT

images acquired the index date shows a patchy ground glass opacity (GGO) appearance in the bilateral lower lobes and left upper lobe (red arrows). **(c)** 1 year follow-up axial thorax CT images show that GGO appearance of the bilateral lower lobes is lesser compared to the previous CT scan. Multiple fibrotic parenchymal bands and patchy opacities (red arrows) were found, especially in the anterior basal segment of the left lower lobe. **(d)** The parenchymal volume of this patient with sequelae was computed as 85.7 cm3 based on volume measurements taken in all parts where the sequelae areas were observed.

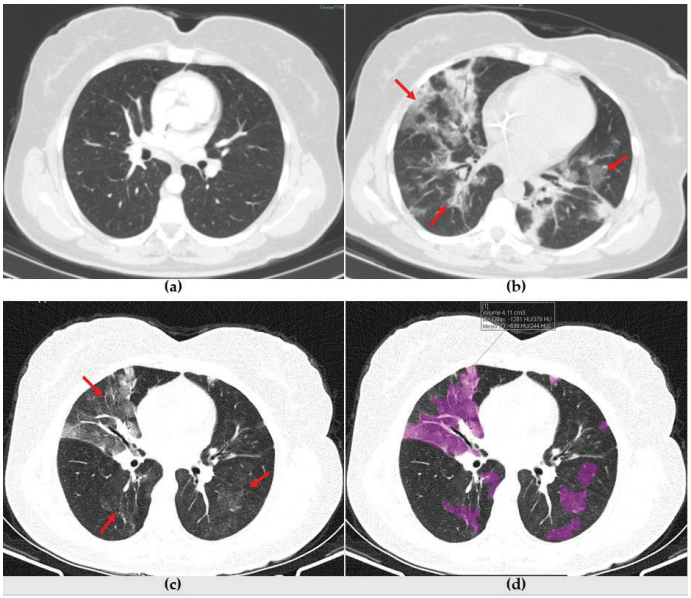


**Figure 3. A** 55-year-old female COVID-19 patient, vaccinated with two doses of Sinovac vaccine, presenting with fever and dry cough for 4 days. (a) In the axial thorax CT images acquired 8 months before the index date, no infiltration is seen in either lung parenchyma. **(b)** The axial thorax CT images acquired the index date shows a patchy ground glass opacity (GGO) appearance in the bilateral lower lobes, right middle lobe and left upper lobe (red arrows). **(c)** 1-year follow-up axial thorax CT images show that GGO appearance of the bilateral lower lobes and left upper lobe is lesser compared to the previous CT scan. Multiple fibrotic parenchymal bands and patchy opacities (red arrows) were found, especially in the right middle lobe. **(d)** The parenchymal volume of this patient with sequelae was computed as 387.5 cm3 based on volume measurements taken in all parts where the sequelae areas were observed.

In our study, while there was no significant difference in the presence of post-COVID lung sequelae between the two patient groups vaccinated with BioNTech mRNA and Sinovac inactivated virus vaccines, it was observed that the quantity of sequelae in the Sinovac group was significantly higher than the BioNTech group. Moreover, both the basal CRP and D-Dimer values of patients with sequelae in the Sinovac vaccinated group were considerably higher. This situation implies that the protection of the Sinovac vaccine may be insufficient in severe cases.

When we examined the effect of blood parameters on the presence of pulmonary sequelae in the total population, we discovered that only lymphocyte counts could have a predictive effect. Multiple studies have indicated that the lymphocyte count can serve as an indicator of the seriousness of COVID-19 and can be used to predict the occurrence of lung sequelae. According to reports, when the number of lymphocytes decreases, the disease gets more severe and the possibility of sequelae increases [30, 31]. Supporting the literature, we observed lower lymphocyte counts in patients with pulmonary sequelae.

In addition, when the blood parameters of the subgroups according to vaccine types are examined, more significant results are noted on the index date in patients with sequelae in the Sinovac group. Furthermore, elevated levels of CRP and D-Dimer were observed in this group, in addition to lymphopenia. Therefore, blood parameters should be examined more closely when following these cases.

This research examined COVID-19 patients who had different vaccination status and became the first to provide current information about the relationship between the mRNA and inactive viral vaccines as well as the likelihood of developing pulmonary sequelae. An additional benefit of this study is its contribution to the limited body of research comparing these two vaccine types in the literature. Last but not least, this study represents the initial assessment of quantitative sequelae data with CT imaging in addition to sequelae rates following lung infection. Furthermore, the combination of blood tests and imaging findings resulted in a more comprehensive and reliable evaluation.

This study had multiple constraints. To begin with, it is a single-center trial with a small patient population. To corroborate our findings, larger cohort studies from multiple centers are needed. Another issue is that there are studies stating that Hemoglobin and Hematocrit values are effective in predicting the possibility of post-COVID lung sequelae. Unfortunately, we were unable to acquire results on this subject because we could not access these blood parameters of all cases. Similarly, since we did not have access the medical history of all cases, we could not evaluate the effect of comorbidities such as diabetes, hypertension, hyperlipidemia, and coronary artery disease on the sequelae. Furthermore, it is important to note that this study does not provide a comprehensive analysis of symptomatic COVID-19 pneumonia caused by variant virus. This limitation arises from

the fact that not all variants of COVID-19 have been thoroughly characterized, and we lack information regarding the timing of vaccination in relation to the index date for the patients. Future research should concentrate on vaccination prophylaxis against sequalae rates as well as sequalae pathogenesis in various organ systems. Targeted treatment approaches can thus be devised to assure long-term protection.

## Conclusion

Our study demonstrated that the type of vaccine has no effect on the prevalence of sequelae. However, the amount of quantitative sequelae is significantly higher in inactivated virus vaccines, and the effect of laboratory parameters on the development of sequelae is more evident in this group.

## Funding

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

## Conflicts of Interest

The authors declare they have no conflicts of interest.

## Ethics Approval

The study was approved by the the Clinical Research Ethics Committee at Erzincan Binali Yildirim University (Protocol number: EBYU-KAEK-2023-11-002-EC-023567.003 / Date: 02 November 2023).

## Informed Consent

Each patient gave written informed consent for the publication of this article using their data.

## Availability of Data and Material

The data that support the findings of this study are available on request from the corresponding author.

## Authors' contribution

Concept – G.Ç., Design- G.Ç., and K.B.M., Data collection and/or processing - G.Ç., and K.B.M., Analysis and/or interpretation - G.Ç., and K.B.M., Writing – G.Ç., Critical review – K.B.M.. All authors read and approved the final version of the manuscript.

## References

1. Bull-Otterson L, Baca S, Saydah S, et al. Post–COVID conditions among adult COVID-19 survivors aged 18–64 and ≥65 years—United States, March 2020–November 2021. MMWR Morb Mortal Wkly Rep. 2022; 71(21): 713-717.
2. Lam ICH, Zhang R, Man KKC, et al. Persistence in risk and effect of COVID-19 vaccination on long-term health consequences after SARS-CoV-2 infection. Nat Commun. 2024; 15: 1716.
3. Cohen K, Ren S, Heath K, et al. Risk of persistent and new clinical sequelae among adults aged 65 years and older during the post-acute phase of SARS-CoV-2 infection: Retrospective cohort study. BMJ. 2022; 376: e068414
4. WHO Coronavirus (COVID-19) Dashboard. Available online: https://covid19.who.int (accessed on 18 October 2023).
5. Al-Aly Z, Xie Y, Bowe B. High-dimensional characterization of post-acute sequelae of COVID-19. Nature. 2021; 594(7862): 259-264.
6. Thaweethai T, Jolley SE, Karlson EW, et al. Development of a definition of postacute sequelae of SARS-CoV-2 infection. JAMA. 2023; 329(22): 1934-1946.
7. Daugherty SE, Guo Y, Heath K, et al. Risk of clinical sequelae after the acute phase of SARS-CoV-2 infection: Retrospective cohort study. BMJ. 2021; 373: n1098
8. Wan EYF, Mathur S, Zhang R, et al. Association of COVID-19 with short- and long-term risk of cardiovascular disease and mortality: A prospective cohort in UK Biobank. Cardiovasc Res. 2023; 119(8): 718-1727.
9. Bowe B, Xie Y, Al-Aly Z. Acute and postacute sequelae associated with SARS-CoV-2 reinfection. Nat Med. 2022; 28: 2398-2405.
10. Watanabe A, So M, Iwagami M, et al. One-year follow-up CT findings in COVID-19 patients: A systematic review and meta-analysis. Respirology. 2022; 27: 605-616.
11. Wu X, Dong D, Ma D. Thin-section computed tomography manifestations during convalescence and long-term follow-up of patients with severe acute respiratory syndrome (SARS). Med Sci Monit. 2016; 22: 2793-2799.
12. Bahadir S, Kabacaoglu E, Memis KB, et al. The effects of vaccines on the sequelae rates of recurrent infections and the severity of pulmonary COVID-19 infection by imaging. Vaccines. 2023; 11: 1321.
13. Sonmezer MC, Dizman GT, Erul E, et al. Relative vaccine effectiveness of the third dose of CoronaVac or BNT162b2 following a two-dose CoronaVac regimen: A prospective observational cohort study from an adult vaccine center in Turkey. Vaccines. 2022; 10: 1140.
14. Yan VKC, Wan EYF, Ye X, et al. Waning effectiveness against COVID-19-related hospitalization, severe complications, and mortality with two to three doses of CoronaVac and BNT162b2: A case-control study. Emerg Microbes Infect. 2023; 12(1): 2209201.
15. Aydin S, Unver E, Karavas E, et al. Computed tomography at every step: Long coronavirus disease. Respir Investig. 2021; 59(5): 622-627.
16. Gao P, Liu J, Liu M. Effect of COVID-19 vaccines on reducing the risk of long COVID in the real world: A systematic review and meta-analysis. Int J Environ Res Public Health. 2022; 19: 12422.

17. Miller TE, Garcia Beltran WF, Bard AZ, et al. Clinical sensitivity and interpretation of PCR and serological COVID-19 diagnostics for patients presenting to the hospital. FASEB J. 2020; 34(10): 13877-13884.
18. Hansell DM, Bankier AA, MacMahon H, et al. Fleischner Society: Glossary of terms for thoracic imaging. Radiology. 2008; 246: 697-722.
19. Prasad NK, Lake R, Englum BR, et al. COVID-19 vaccination associated with reduced postoperative SARS-CoV-2 infection and morbidity. Ann Surg. 2022; 275(1): 31-36.
20. Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine. N Engl J Med. 2020; 383(27): 2603-2615.
21. Ayoubkhani D, Bermingham C, Pouwels KB, et al. Trajectory of long COVID symptoms after COVID-19 vaccination: Community based cohort study. BMJ. 2022; 377: e069676.
22. Jara A, Undurraga EA, González C, et al. Effectiveness of an inactivated SARS-CoV-2 vaccine in Chile. N Engl J Med. 2021; 385(10): 875-884.
23. Geisen UM, Berner DK, Tran F, et al. Immunogenicity and safety of anti-SARS-CoV-2 mRNA vaccines in patients with chronic inflammatory conditions and immunosuppressive therapy in a monocentric cohort. Ann Rheum Dis. 2021; 80(10): 1306-1311.
24. Haberman RH, Herati R, Simon D, et al. Methotrexate hampers immunogenicity to BNT162b2 mRNA COVID-19 vaccine in immune-mediated inflammatory disease. Ann Rheum Dis. 2021; 80(10): 1339-1344.
25. Woodruff MC, Ramonell RP, Nguyen DC, et al. Extrafollicular B cell responses correlate with neutralizing antibodies and morbidity in COVID-19. Nat Immunol. 2020; 21(12): 1506-1516.
26. Kaneko N, Kuo HH, Boucau J, et al. Loss of Bcl-6-Expressing T Follicular Helper Cells and Germinal Centers in COVID-19. Cell. 2020; 183(1): 143-157.e13.
27. Furer V, Eviatar T, Zisman D, et al. Immunogenicity and safety of the BNT162b2 mRNA COVID-19 vaccine in adult patients with autoimmune inflammatory rheumatic diseases and in the general population: A multicentre study. Ann Rheum Dis. 2021; 80(10): 1330-1338.
28. Seyahi E, Bakhdiyarli G, Oztas M, et al. Antibody response to inactivated COVID-19 vaccine (CoronaVac) in immune-mediated diseases: A controlled study among hospital workers and elderly. Rheumatol Int. 2021; 41(8): 1429-1440.
29. Jena A, Mishra S, Deepak P, et al. Response to SARS-CoV-2 vaccination in immune-mediated inflammatory diseases: Systematic review and meta-analysis. Autoimmun Rev. 2022; 21(1): 102927.
30. Tarraso J, Safont B, Carbonell-Asins JA, et al. Lung function and radiological findings 1 year after COVID-19: A prospective follow-up. Respir Res. 2022; 23(1): 242.
31. Abdel-Hamid HM, Rizk HI, Magdy S. Occurrence of pulmonary residuals as one of the sequelae of COVID-19 and its predictors among moderate and severe cases. Indian J Tuberc. 2021; 68(4): 450-456.