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Factors affecting the serologic response to SARS-CoV-2 vaccination in patients with solid tumors: A prospective study

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ABSTRACT

Objective: To evaluate the factors affecting seropositivity and antibody levels after SARS-CoV-2 vaccines in patients with cancer because they were excluded from clinical studies of SARS-CoV-2 vaccines.

Methods: This prospective, observational, single-center study included 290 patients with solid tumors followed up in our medical oncology clinic between March 2021 and August 2021. SARS-CoV-2 antibody status was determined before the first dose of vaccine. Fifty-one patients with positive prevaccine baseline antibody tests were excluded from the study, regardless of whether they had previously confirmed SARS-CoV-2 PCR positivity. To determine the quantitative IgG antibody response of the vaccines, blood samples were collected at least 28 days after each dose of vaccine. Quantitative IgG levels against virus spike protein receptor binding domain (RBD) were measured using chemiluminescent enzyme immunoassay (CLIA). Demographic and clinical features affecting seropositivity were analyzed.

Results: One hundred and fifty-one (69.3%) patients were vaccinated with two doses of CoronaVac followed by one dose of BNT162b2 (Biontech) (group 1). Sixty-seven (30.7%) patients were vaccinated with three doses of BNT162b2 (group 2). The proportion of patients who developed seropositivity was significantly higher in group 2 (78.6% vs. 54.9%, \( p < 0.012 \)). Antibody response increased significantly after the second dose of vaccine in both groups. Female sex, being younger than 65 years, and chemotherapy status were significantly related to higher anti-SARS-CoV-2 S antibody levels (\( p = 0.033 \), \( p = 0.036 \), and \( p = 0.047 \), respectively). Antibody levels were significantly higher in patients who had previously received chemotherapy than in patients receiving active chemotherapy (\( p = 0.042 \)).

Conclusions: Our study is the first to evaluate basal SARS-CoV-2 IgG levels before the first dose of vaccine and after three doses in patients with solid tumors. The rate of development of seropositivity with two doses of mRNA vaccine was found to be higher than with two doses of inactivated SARS-CoV-2 vaccine. More attention should be paid to preventive measures in addition to vaccination in patients aged over 65 years and men with cancer diagnoses.

1. Introduction

Patients with cancer are in the high-risk group in terms of contracting coronavirus 2019 (COVID-19) infection and the severe course of the disease [1]. On the other hand, there are also concerns that this group of patients may not produce an adequate immune response after COVID-19 infection or vaccination, depending on the cancer type or the treatment process [2]. Although there are data in the literature showing that 90% antibody positivity occurs after two doses of vaccination in patients with solid tumors, there are also studies indicating that antibody levels in patients with cancer are lower than in the normal population [3].

According to the results of the CoronaVac vaccine, 99% of neutralizing antibodies develop in two doses at 0 and 28 days, and there is a correlation between neutralization tests and receptor-binding domain (RBD)-specific immunoglobulin (Ig)-G tests [4]. In the phase 3 study of the BNT162b2 vaccine, an efficacy of 95% was reported after two doses [5]. Preliminary results suggest that both vaccines currently used are effective and safe. However, because patients with cancer were not included in the clinical phase studies of these vaccines, data on

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laboratory and clinical long-term follow-up of the protection of vaccines in these patients are limited [6].

Even if the antibody response does not fully demonstrate the protection of the vaccine, it is considered an important indicator of the immune response [7]. In this study, RBD-specific IgG antibodies formed against the S (spike) RBD after vaccination were followed to evaluate the early period antibody response developed after vaccination and the persistence of the antibody response in vaccinated patients with cancer.

To the best of our knowledge, this prospectively designed study is the first in the literature to evaluate the serologic response to severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) vaccines in patients with cancer, measuring baseline antibody levels before vaccination, and including antibody follow-up after three doses of vaccine.

2. Methods

This prospective, observational, single-center study included 290 patients with solid tumors who were followed in our medical oncology clinic between March 2021 and August 2021. The study was conducted with the approval of Manisa Celal Bayar University Faculty of Medicine Clinical Research Ethics Committee (Date: July 05, 2021 and Decision No: 194). An informed consent form was obtained from all patients. Patients with a survival expectation of fewer than 3 months, a history of autoimmune disease, any active infectious disease, and a previous SARS-CoV-2 polymerase chain reaction (PCR) test positivity were excluded. Demographic information and the clinical and treatment characteristics of the patients were obtained from the medical record files.

Patients with cancer were vaccinated according to the recommendations of the national vaccination program. The vaccination program, which started with the inactivated virus vaccine CoronaVac in January 2021, continued with the use of two different vaccines according to patient preference after the BNT162b2 vaccine arrived in our country in April 2021. In line with the available scientific data, patients followed up in our clinic were recommended to administer the third dose of vaccine as BNT162b2, regardless of the type of the 1st two doses of vaccine.

2.1. Sample collection and storage

Approximately 10 mL of blood was collected from patients with cancer to determine the SARS-CoV-2 antibody status before the 1st dose of vaccination. Blood samples were centrifuged at 5000 rpm for 5 min within 2 h, and serum was separated, and an anti-SARS-CoV-2 IgG antibody test was performed. Patients with a positive pre-vaccine baseline antibody test, regardless of whether they had previously confirmed SARS-CoV-2 PCR positivity, were excluded from the study.

To determine the quantitative IgG antibody response of vaccines, blood samples were taken at least 28 days after the 1st dose, 2nd dose, and the 3rd dose of vaccines. An anti-SARS-CoV-2 IgG antibody test was performed on the same day.

2.2. Serologic tests

Quantitative IgG tests were performed using the chemiluminescent enzyme immunoassay (CLIA) method with ADVIA Centaur® SARS-CoV-2 IgG (Siemens, USA) kits. The test quantitatively detects IgG-type antibodies against virus S protein RBD. The detection range of the kit was 0.5–150 U/mL, and values above ≥1.00 U/mL were considered positive. In the user manual of the manufacturer, the sensitivity of the test is 96.4%, the specificity is 99.9%, and the common unit recommended by the World Health Organization (WHO) is 1 BAU/mL = 21.8 U/mL [8].

2.3. Statistical analysis

For descriptive statistics, mean ± standard deviation was used to give continuous data with normal distribution. For the variables without normal distribution, the Mann-Whitney U test was used to compare two independent groups. Pearson’s Chi-square and Fisher’s exact tests were used to compare the differences between categorical variables in 2 × 2 tables. The Kruskal-Wallis test was used to compare more than two independent groups where numerical variables had no normal distribution. The Wilcoxon test was used to examine the changes in the levels of anti–SARS-CoV-2 antibodies at baseline and after the 1st, 2nd, and 3rd doses of the vaccine program. Univariate and multivariate logistic regression analysis was used to analyze the factors impacting the rate of seropositivity after the second and third doses of the vaccination. The variables that were included in the multivariate analysis if they were significant in the multivariate analysis considering their clinical significance. For statistical analysis, “Jamovi project (2022), Jamovi (Version 2.2.5.0) [Computer Software] (Retrieved from https://www.jamovi.org)” and JASP (Version 0.16) (Retrieved from https://jasp-stats.org) were used. In all statistical analyses, the significance level (p-value) was determined at 0.05.

3. Results

Of the 290 patients whose consent was obtained initially, 12 refused to be vaccinated, nine withdrew their consent, and 51 patients with positive baseline antibody levels were excluded from the study. There were 218 patients with a mean age of 57.6 ± 11.5 years. Breast cancer was the most frequent type of cancer seen in 102 patients (46.8%). The demographic and clinical characteristics of the patients are given in Table 1.

One hundred fifty-one patients (69.3%) received two doses of CoronaVac followed by BNT162b2 (Group 1). In group 2, the patients (n = 67, 30.7%) were vaccinated with three doses of the BNT162b2 vaccine. The groups were similar in terms of demographic and clinical characteristics except for the age of the patients and the proportion of patients older than 65 years. The patients in group 1 were significantly older than those in group 2 (p < 0.001).

Anti–SARS-CoV-2 S antibodies and the frequencies of the serologic responses following the vaccination schedule in the groups are summarized in Table 2. The antibody response increased significantly after the 2nd dose of vaccination in both groups (Fig. 1). The proportion of the patients with positive serologic results was significantly higher in group 2 (78.6% vs. 54.9%, p = 0.012) (Table 3). The demographic and clinical parameters associated with the levels of anti–SARS-CoV-2 S antibodies and frequencies of serologic positivity in group 1. After the 1st dose, the antibody levels showed no significant differences based on the demographic and clinical parameters (p > 0.05). However, the patients with previous chemotherapy (patients who did not receive treatment in the last 3 months) were more frequently serologic positive than those with on-chemotherapy and patients who were chemotherapy-naive (p = 0.022). Female sex, being younger than 65 years, and type of chemotherapy were the significant factors for higher levels of anti–SARS-CoV-2 S antibodies following the 2nd dose (p = 0.033, p = 0.036, and p = 0.047, respectively). The antibody levels were significantly higher in patients with previous chemotherapy than in those with on-chemotherapy (p = 0.047). The proportion of serologic positivity was significantly higher in patients whose age was younger than 65 years (p = 0.006). (Table 4). The serologic positivity rate was significantly higher in younger patients (85.7%) than in the older patients (42.9%) (p = 0.028).

We detected 15 (7.3%) COVID-19 infections in the study groups. These cases were after the 1st, 2nd, and 3rd doses of the vaccines in five, three, and seven patients, respectively (Table 5).

A significant difference in the distribution of COVID-19 infections after the vaccine doses was seen between the groups (p = 0.007). There were seven cases after the 3rd dose of CoronaVac vaccine in group 1, in contrast to none in group 2. However, three patients developed the infection after the 2nd dose of the BNT162b2 vaccine in group 2.
Demographic and baseline clinical characteristics of the study groups.

| Table 1 | Overall (n = 218) | Group 1 (n = 151) | Group 2 (n = 67) | p |
| --- | --- | --- | --- | --- |
| Age in time of vaccination (year) | 57.6 ± 11.5 | 59.8 ± 10.8 | 52.6 ± 11.5 | <0.001d |
| <65 yearsb | 154 (70.6) | 96 (63.6) | 58 (86.6) | 0.001d |
| ≥65 yearsb | 64 (29.4) | 55 (36.4) | 9 (13.4) | |
| Sexb | | | |
| Male | 69 (31.7) | 53 (35.1) | 16 (23.9) | 0.137f |
| Female | 149 (68.3) | 98 (64.9) | 51 (76.1) | |
| Cancer type | | | |
| Head/neck | 6 (2.8) | 6 (4.0) | 0 (0.0) | 0.071f |
| Gastrointestinal | 46 (21.1) | 36 (23.8) | 10 (14.9) | |
| Genitourinary | 36 (16.5) | 25 (16.6) | 11 (16.4) | |
| Breast | 102 (48.6) | 61 (40.4) | 41 (61.2) | |
| Thoracic cavity | 13 (6.0) | 11 (7.3) | 2 (3.0) | |
| Rare tumors and others | 15 (6.9) | 12 (7.9) | 3 (4.5) | |
| Time from cancer diagnosis to vaccination (month) | 24.4 | 25.8 | 21.6 | 0.434f |
| Extent of disease (n = 146) | | | |
| Metastatic | 121 (82.9) | 90 (85.7) | 31 (75.6) | 0.225f |
| Locally advanced | 25 (17.1) | 15 (14.3) | 10 (24.4) | |
| Previous chemotherapyc | 190 (87.2) | 129 (85.4) | 61 (91.0) | 0.356f |
| Previous radiotherapyb | 79 (36.2) | 51 (33.8) | 28 (41.8) | 0.325f |
| Follow-up patientsb | 18 (8.3) | 11 (7.3) | 7 (10.4) | 0.616f |
| On-chemotherapye | 113 (51.8) | 81 (53.6) | 32 (47.8) | 0.513f |
| On-therapyc | 196 (89.9) | 138 (91.4) | 58 (86.6) | 0.397f |
| Type of therapy (n = 160) | | | |
| Adjuvant | 54 (27.6) | 34 (24.6) | 20 (34.5) | 0.174f |
| Neoadjuvant | 21 (10.7) | 13 (9.4) | 8 (13.8) | |
| Metastatic | 121 (61.7) | 91 (65.9) | 30 (51.7) | |
| On-targeted therapy | 119 (54.6) | 86 (57.0) | 33 (49.3) | 0.365f |
| Type of targeted therapy (n = 119) | | | |
| Monoclonal antibody | 57 (47.9) | 43 (50.0) | 14 (42.4) | 0.246f |
| Hormone therapy | 27 (22.7) | 17 (19.8) | 10 (30.3) | |
| Immunotherapy | 20 (16.8) | 17 (19.8) | 3 (9.1) | |
| Tyrosine kinase inhibitor therapy | 15 (12.6) | 9 (10.5) | 6 (18.2) | |

a mean ± standard deviation.
b n (%).
c median [min-max].
d Pearson Chi-Square, Fisher’s Exact or Fisher Freeman Halton test.
e Independent Samples T-Test.
f Mann-Whitney U test.

In Table 6, the demographic and clinical characteristics of the patients with COVID-19 infection are given after the 3rd dose of the vaccination program. All patients in group 1 who were vaccinated with the two doses of CoronaVac vaccine were initially followed by a single dose of BNT162b2.

In the multivariate analysis, age was found to be the only variable that showed a significant correlation with seropositivity (Table 7).

4. Discussion

In our study, the factors affecting seropositivity and antibody levels after SARS-CoV-2 vaccines were administered to patients with cancer were investigated. The development of seropositivity and the antibody levels were evaluated after the 1st, 2nd, and 3rd doses of vaccination in two patient groups who received two different vaccination regimens. In the group that received CoronaVac as the first two doses of vaccine, female sex, being younger than 65 years, and having completed chemotherapy were the factors that significantly affected high antibody levels (p = 0.033, p = 0.036, and p = 0.047, respectively). In this group, the difference disappeared with the administration of the 3rd dose of vaccine as BNT162b2. In the group vaccinated with the first two doses of BNT162b2, the only factor that significantly affected the serologic positivity rates was age younger than 65 years. The serologic positivity rate was significantly higher in younger patients (85.7%) than in older patients (42.9%) (p = 0.028).

Active disease for any malignancy significantly increases the risk of severe COVID-19 [9]. In the meta-analysis of Park et al., it was shown that patients receiving active cancer treatment had a higher mortality rate due to COVID-19 [10]. Cavanna et al. reported the mortality rate of
COVID-19 as 23.53% in a retrospective study in patients with cancer and this rate was found as 28% in another prospective study [11,12]. Due to the high mortality rates, patients with cancer are defined as a priority group in vaccination programs in our country and many countries. However, because clinical studies of SARS-CoV-2 vaccines did not include patients with immunosuppression, efficacy data in this risk population were limited. On the other hand, it is known that vaccination against viral agents is effective in patients with cancer, even if they receive immunosuppressive therapy [13]. In our study, in the multivariate analysis, the only factor that significantly affected seropositivity after two doses of vaccination was age under 65 years (p = 0.002) (OR: 3.17, 95% CI: [1.51–6.66]). There was no difference between the age groups after the 3rd dose of vaccine.

In a study including 346 patients with cancer, the rate of IgG S antibody development after two doses of inactivated SARS-CoV-2 vaccine was 84.1% in patients aged under 60 years; this rate was found to be significantly lower in patients aged over 60 years at 59.3% [14]. Similarly, in the study of Yasin et al., it was observed that the seropositivity rates were lower after the CoronaVac vaccine in patients with cancer aged over 60 years [15]. In a study evaluating the development of seropositivity in 102 patients with solid tumors receiving active cancer treatment after two doses of BNT162b2 vaccination seven of 10 patients who remained seronegative were found to be aged 60 years or older; however, pre-vaccination antibody levels were not measured in this study [16]. In our study, five of seven patients who had COVID-19 after completing three doses were aged over 60 years. It can be considered that at least three doses of vaccine should be given to patients with cancer, especially in the advanced age group, to obtain a similar immune response as in others.

In our study, the rate of development of quantitative IgG antibody response after three doses of vaccination in patients with cancer was found as 88.2%. Monin et al. stated that vaccination with a single dose of BNT162b2 in patients with cancer did not provide sufficient efficacy and that the 2nd vaccination should be administered 21 days after the 1st dose [17]. In a study evaluating patients with cancer after vaccination with two doses of mRNA-based mRNA-1273 (Moderna) or two doses of
Table 4  
Association of demographic and clinical parameters with the levels of anti-SARS-CoV-2 S antibodies and frequencies of serologic positivity in Group 2 (n = 67).

| 1st dose | 2nd dose | 3rd dose |
|-----------------|-----------------|-----------------|
| **Age in time of vaccination** | **Age in time of vaccination** | **Age in time of vaccination** |
| <65 year | >65 year | <65 year | >65 year | <65 year | >65 year |
| 0.3 [0.0–100.0] | 0.1 [0.0–100.0] | 0.3 [0.0–100.0] | 0.1 [0.0–100.0] | 0.3 [0.0–100.0] | 0.1 [0.0–100.0] |
| 13.0 (34.2) | 3.0 (37.5) | 11.2 [0.0–100.0] | 0.1 [0.0–100.0] | 30.0 (85.7) | 3.0 (42.9) |
| 0.592** | 0.999* | 0.082* | 0.028* | 0.021** | 0.091* |
| **Sex** | **Sex** | **Sex** |
| Male | Female | Male | Female | Male | Female |
| 0.3 [0.0–100.0] | 0.3 [0.0–100.0] | 12.0 (34.3) | 18.8 [0.0–100.0] | 20.0 (76.9) | 13.0 (81.3) |
| 0.661** | 0.999* | 0.080** | 0.336* | 0.500** | 0.999* |
| **Disease status** | **Disease status** | **Disease status** |
| Progression | Remission | Progression | Remission | Progression | Remission |
| 0.3 [0.0–100.0] | 0.2 [0.78–4.0] | 12.0 (38.7) | 4.0 (26.7) | 9.0 [0.0–100.0] | 19.3 [0.0–100.0] |
| 0.140** | 0.421* | 0.744* | 0.922** | 0.999* | – |
| **Extent of disease** | **Extent of disease** | **Extent of disease** |
| Metastatic | Locally advanced | Metastatic | Locally advanced | Metastatic | Locally advanced |
| 0.4 [0.0–100.0] | 0.2 [0.0–100.0] | 10.0 (41.7) | 2.0 (28.6) | 7.2 [0.0–100.0] | 11.2 [0.1–56.0] |
| 0.887** | 0.676* | 0.922** | 0.999* | – | – |
| **Type of therapy** | **Type of therapy** | **Type of therapy** |
| Adjuvant | Neoadjuvant | Metastatic | Neoadjuvant | Metastatic | Neoadjuvant |
| 0.1 [0.0–78.4] | 0.2 [0.0–78.4] | 0.4 [0.0–78.4] | 0.313*** | 0.744* | 0.922** |
| 3.0 (25.0) | 2.0 (28.6) | 9.0 (39.1) | 0.744* | 0.922** | 0.999* |
| 0.808** | 0.850* | 0.305** | 0.999* | 0.600** | 0.455* |
| **Type of targeted therapy** | **Type of targeted therapy** | **Type of targeted therapy** |
| Monoclonal antibody | Hormon therapy | Immunotherapy | Tyrosine kinase inhibitors | Monoclonal antibody | Hormon therapy | Immunotherapy |
| 0.5 [0.0–100.0] | 1.4 [0.1–78.4] | 0.1 [0.0–0.2] | 1.9 [0.1–9.7] | 0.5 [0.0–100.0] | 3.0 [0.0–50.0] | 0.2 [0.0–50.0] |
| 5.0 (41.7) | 3.0 (50.0) | 0.0 (0.0) | 2.0 (50.0) | 37.0 [0.0–100.0] | 34.8 [0.4–78.6] | 19.1 [0.0–80.9] |
| 0.328*** | 0.624* | 0.313*** | 0.262* | 0.331*** | 0.501* |
| **Treatment groups** | **Treatment groups** | **Treatment groups** |
| On-chemotherapy only | On-chemotherapy and targeted therapy | Follow-up | On-targeted therapy only | On-chemotherapy only | On-chemotherapy and targeted therapy |
| 0.2 [0.0–82.0] | 2.5 [0.4–100.0] | 0.2 [0.0–78.4] | 0.2 [0.0–100.0] | 0.2 [0.0–100.0] | 2.5 [0.4–100.0] |
| 4.0 (23.5) | 3.0 (75.0) | 7.0 (33.3) | 7.0 (33.3) | 7.0 [0.0–100.0] | 7.0 (33.3) |
| 0.808** | 0.305** | 0.305** | 0.305** | 0.305** | 0.305** |
| **Chemotherapy groups** | **Chemotherapy groups** | **Chemotherapy groups** |
| On-chemotherapy | Previous chemotherapy | Chemotherapy-naive | On-chemotherapy | Previous chemotherapy | Chemotherapy-naive |
| 0.3 [0.0–100.0] | 0.3 [0.3–2.4] | 0.3 [0.3–2.4] | 0.3 [0.0–100.0] | 0.3 [0.0–100.0] | 0.3 [0.0–100.0] |
| 7.0 (33.3) | 1.0 (33.3) | 69.8 [29.8–80.9] | 7.0 [0.0–100.0] | 7.0 [0.0–100.0] | 7.0 [0.0–100.0] |
| 0.835*** | 0.999* | 0.498*** | 0.999* | 0.518** | 0.455* |

BNT162b2 (Pfizer/BioNTech) or a single dose of adenovirus-based Ad26.COV2.S (Johnson & Johnson), the rate of seroconversion with BNT162b2 was 95%, and the seropositivity rate was found to be significantly lower (92%) in hematologic malignancies and those receiving active cytotoxic chemotherapy, and there was no difference between antibody titers [18]. Compared with the literature, the slightly lower level of antibody development in our general study population may be associated with the higher number of patients vaccinated with the inactivated vaccine and the older patients in this group.

In our country, the vaccination program, which started in high-risk groups with the inactivated virus vaccine CoronaVac in January 2021, continued with the use of two different vaccines based on patient preference after the BNT162b2-mRNA vaccine became available in April 2021. Considering the rapidly emerging scientific data at that time, it was recommended that patients who were vaccinated with the 1st two doses of CoronaVac should be vaccinated with the 3rd dose of BNT162b2 (group 1). Patients who started the vaccination program with BNT162b2 completed the program with three doses of the same vaccine (group 2). In our study, the antibody responses of these different vaccination groups were also compared. As a result of the 1st two vaccinations, anti-SARS-CoV-2 S antibodies were higher in group 2 than in group 1 (p < 0.001). Similar to our study, a recent article showed that vaccination with BNT162b2 induced a significantly higher SARS-CoV-
antibody levels and seropositivity rates after the 3rd dose between the groups with two doses of CoronaVac followed by a single dose of inactivated virus vaccines [21]. In our study, the proportion of patients with positive serologic results was significantly higher in group 2 (78.6% vs. 54.9%, p < 0.012). Patients receiving immunosuppressive therapy or in the risk group for different reasons may be encouraged to prefer mRNA vaccines.

The limitations of our study included the inclusion of patients from a single center, the relatively short follow-up period considering that antibody titers might increase over time, and the lack of evaluation of SARS-CoV-2–specific T cell responses.

5. Conclusion

It is vital to determine the most effective types of SARS-CoV-2 vaccines in patients with cancer and their dosage schedules, which are increasing in numbers worldwide. To our knowledge, our study is the first to measure basal SARS-CoV-2 IgG levels before the 1st dose of vaccine and evaluate three doses of vaccine. The rate of development of seropositivity with two doses of mRNA vaccine was found to be higher than with two doses of inactivated SARS-CoV-2 vaccine. In addition, it was revealed that more attention should be paid to preventive measures in addition to vaccination in patients aged over 65 years with cancer. In the diagnosis, treatment, and follow-up of patients with cancer, interventions to prevent COVID-19 and studying their effectiveness are valuable in terms of providing adequate protection for patients.

Table 6
Characteristics of the patients with COVID_19 infection after the 3rd dose of the vaccination program.

| Age | Sex | Cancer type | Extent of disease | Type of treatment | Vaccine Group | Hospitalization | Prognosis |
|-----|-----|-------------|------------------|------------------|---------------|----------------|-----------|
| 63  | Male| Gastrointestinal | On-therapy       | Adjuvant         | Group 1       | No             | Survived |
| 48  | Female| Breast      | Metastatic       | Metastatic       | Group 1       | No             | Survived |
| 67  | Female| Genitourinary | Metastatic       | Metastatic       | Group 1       | Yes            | Non-survived |
| 62  | Male| Gastrointestinal | Metastatic       | Metastatic       | Group 1       | Yes            | Survived |
| 64  | Female| Genitourinary | Metastatic       | Metastatic       | Group 1       | Yes            | Non-survived |
| 40  | Female| Rare tumors and others | Metastatic | Metastatic       | Group 1       | Yes            | Survived |

Table 7
Univariate and multivariate logistic regression analysis of the variables impacting the seropositivity rate after the second dose.

| Age: <65 vs. ≥65 | OR [95%CI] | p | OR [95%CI] | p |
|-----------------|------------|---|------------|---|
| 4.01            | [1.98-8.13]| < 3.17      | < 0.002   |
| Sex: Female vs. male | 2.39       | 0.014 | 1.68       | 0.276 |
| Type of cancer: Breast vs. Others | 2.00 | 0.040 | 0.99       | 0.985 |
| Vaccine groups: Group 2 vs. Group 1 | 3.02 | 0.009 | 2.26       | 0.069 |
| Extent of disease: Locally advanced vs. Metastatic | 0.66 | 0.461 |

OR: Odds ratio, CI: confidence interval.

2–specific binding and neutralizing antibody response than CoronaVac [19].

During our study, 15 (7.3%) of 218 patients had COVID-19. All seven patients with COVID-19 after three doses of vaccine were in the group with two doses of CoronaVac followed by a single dose of BNT162b2. Five of these patients, all of whom were on active therapy, required hospitalization, and two patients with metastatic disease died of COVID-19. Although there was no significant difference in terms of antibody levels and seropositivity rates after the 3rd dose between the vaccine groups, as mentioned above, the course of COVID-19 might have been affected in our study group due to factors related to cellular immunity. In the study of Ariamaneh et al., COVID-19 was detected in five patients after two doses of inactive SARS-CoV-2 vaccine, and none of these patients, three of whom did not receive active oncologic treatment, and two of whom had stage 3 disease, had no hospitalization or mortality [14]. According to the newly announced Chinese government data, the case/death rates of those vaccinated with BNT162b2 and those vaccinated with CoronaVac were as follows: 0.21% vs. 1.28% after the 1st dose of vaccine, 0.04% vs. 0.31% after the 2nd dose of vaccine, and 0.02% vs. 0.04% after three doses of vaccine, respectively. It was emphasized that the protection of the BNT162b2 vaccine was better, especially in two-dose vaccinations [20].

In our study, antibody levels were also evaluated according to the type of cancer treatment. Monin et al. showed that the antibody response was weak in patients with solid tumors receiving active chemotherapy, and it was emphasized that the steroids administered during chemotherapy could affect the immune response [17]. In our study, in group 1, the patients with previous chemotherapy were more frequently serologically positive than those with on-chemotherapy and patients who were chemotherapy-naive (p = 0.022). There was no significant difference between the antibody levels of the patients who were followed up without treatment and those receiving targeted therapy, after the 1st, 2nd, and 3rd doses of vaccines (p = 0.699, p = 0.953, and p = 0.650, respectively). Considering the targeted agent subgroups, although there was a trend of an increase in the antibody levels after the 2nd and 3rd doses of vaccine in those receiving monoclonal antibodies and hormone therapy in group 1, no statistically significant difference was found (p = 0.162, p = 0.800, and p = 0.696, respectively). In the study of Thakkar et al., seroconversion rates were reported to be higher in patients who received hormone therapy and immunotherapy [18].

It is known that the efficacy of mRNA vaccines is higher than that of inactivated virus vaccines [21]. In our study, the proportion of patients with positive serologic results was significantly higher in group 2 (78.6% vs. 54.9%, p < 0.012). Patients receiving immunosuppressive therapy or in the risk group for different reasons may be encouraged to prefer mRNA vaccines.

The limitations of our study included the inclusion of patients from a single center, the relatively short follow-up period considering that antibody titers might increase over time, and the lack of evaluation of SARS-CoV-2–specific T cell responses.

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Authorship

APE, FE contributed to the study design, data collection, statistical analysis and interpretation, and drafting of the manuscript. FE, SA, GG contributed to the study design, statistical analysis and interpretation, and critically revised the manuscript for important intellectual content. All authors approved the final version of the manuscript for publication and met the ICMJE authorship criteria.
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