DOI: 10.12923/cipms-2025-0007 Curr. Issues Pharm. Med. Sci.,

Current Issues in Pharmacy and Medical Sciences
Formerly ANNALES UNIVERSITATIS MARIAE CURIE-SKLODOWSKA, SECTIO DDD, PHARMACIA

journal homepage: https://czasopisma.umlub.pl/curipms

Dynamics of the level of anti-SARS antibodies within a year after three vaccinations of patients with prostate cancer

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ARTICLE INFO

Received 02 January 2024
Accepted 20 December 2024

Keywords:
anti-SARS-CoV-2 antibodies,
antibodies dynamics,
vaccination,
prostate cancer.

ABSTRACT

Cancer patients are a group particularly vulnerable to various infections, including SARS-CoV-2. Men are more susceptible to severe COVID-19, with a higher mortality rate. Many researchers have shown that immunity after two doses of the vaccine wanes over time, and a third booster dose is necessary to increase protection. Therefore, we undertook to assess the dynamics of anti-SARS-CoV-2 antibodies within a year after three doses of Pfizer-BioNTech vaccine in Polish men with prostate cancer. For this purpose, the titer of anti-SARS-CoV-2 antibodies was examined 3, 6, 9, and 12 months after the third dose of the vaccine. We also analyzed whether the decline in antibody titer depends on the tumor stage (Gleason Score, T stage). The obtained results indicate that the level of anti-SARS-CoV-2 antibody is significantly lower in PCa patients compared to the controls. Twelve months after the third vaccine dose, the seroprevalence among prostate cancer patients was 53.3% (50-59) and 29.8% (60-78), respectively. In the period from 3 to 6 months, as well as from 6 to 9 months after vaccination, a statistically significant decrease in antibody titer was observed in both analyzed age groups. Moreover, their levels were lower in more advanced clinical stages.

Conclusion: Due to the fact that in the following months the antibody titer decreased much faster in PCa patients than in people from the healthy control group, it seems reasonable to ask whether PCa patients should be vaccinated with a booster dose more often than once a year.

INTRODUCTION

SARS-CoV-2, the etiological agent of an acute infectious respiratory disease, the first cases of which were reported in late December 2019 in Wuhan, has quickly spread around the world, causing millions of illnesses and deaths [1,2]. As of November 3, 2024, 776,798,873 cases of COVID-19 and 7,074,400 deaths have been reported to WHO worldwide [3]. Some patients after COVID-19 may experience long-term systemic, neuropsychiatric, cardiopulmonary and gastrointestinal consequences [4-6]. SARS-CoV-2 variants of concern (VOCs) have emerged in the human population, such as Alpha, Beta, Gamma, Delta and Omicron. Currently, all circulating SARS-CoV-2 variants are Omicron lineages [7]. The Omicron variant is dominant worldwide due to its strong transmissibility [8,9].

Several COVID-19 vaccines produced by various pharmaceutical companies have been developed and deployed around the world. As many studies show, immunity after two doses of the vaccine decreases over time, and a third booster dose is necessary to increase protection [10-12]. Assessment of the humoral immune response to SARS-CoV-2 is essential for understanding breakthrough infections and immune protection, as well as developing a vaccination strategy [13].

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Cancer constitutes a serious challenge to public health on a global scale, both due to its incidence and mortality. According to the forecasts of the World Health Organization, the number of newly detected cancer cases is constantly increasing, and is projected to reach 30.2 million cases by 2040 [14]. Malignant tumors are the second cause of death in Poland. For every 100,000 people in the Polish population, there are 247 deaths due to malignant tumors [15]. Globally, the second most common cancer among men is prostate cancer (PCa), which is the fifth most common cause of cancer death [16]. In order to reduce the effects of SARS CoV-2 infection, many countries, including Poland, have implemented a vaccination program with particular emphasis on high-risk groups, which include cancer patients.

Our previous studies showed that prostate cancer patients had significantly lower levels of anti-SARS-CoV-2 IgG antibodies compared to controls [17]. Therefore, it seemed interesting to investigate the dynamics of antibodies developed after 3 doses of vaccine in this group of patients. For this purpose, the titer of anti-SARS CoV-2 antibodies was assessed 3, 6, 9 and 12 months after the last dose of the vaccine. To determine the dynamics of antibody levels over time, a comparison was made with a group of healthy people.

MATERIALS AND METHODS

Subjects

The study included men with diagnosed and histopathologically confirmed prostate cancer. Patients were hospitalized at the Department of General and Oncological Urology of the 1st Military Clinical Hospital with Outpatient Clinic in Lublin. All patients underwent radical prostatectomy. Only patients who did not require additional therapy (chemotherapy or radiotherapy) were qualified for the study. Two age groups were distinguished, i.e., 50-59 ($\bar{x}$ = 56.3±2.2) and 60-78 ($\bar{x}$ = 68.9±5.3). In order to compare the results, a control group similar in terms of age structure was selected. This group included volunteers treated in hospital outpatient clinics in whom any cancer had been ruled out. Both people from the study and control groups had to meet the following criteria: 1) inclusion criteria: three doses of the Pfizer vaccine, no history of infection; 2) exclusion criteria from the study: partial vaccination (one or two doses), history of infection, vaccination with two different vaccines. The schedule for administering subsequent doses of the vaccine and the dates of blood sample collection are shown in Figure 1.

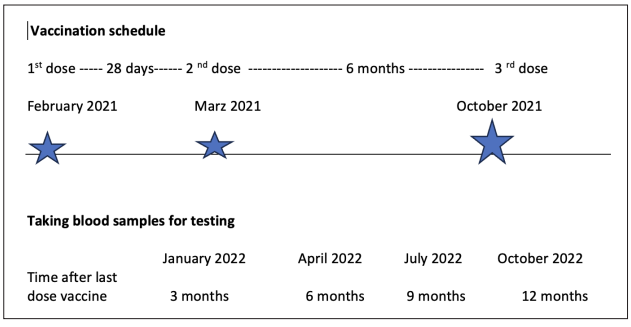

Figure 1. Vaccination schedule and deadline for collecting blood samples for testing

The antibody diagnostic test detects several different antibodies. To maintain the homogeneity of the research group, people who had only anti-SARS-CoV-2 RBD IgG antibodies in their serum were included in the analysis. In this way, people whose infection could have been asymptomatic were excluded. Additionally, all respondents had to meet the age criterion indicated above. Due to the above-mentioned criteria, the initial study group of 400 prostate cancer patients and the control group of 390 people were significantly reduced. Ultimately, 97 patients with prostate cancer in the research group and 82 men in the control group were included in the analysis. The characteristics of both groups are presented in Table 1.

Table 1. Baseline characteristics of studied groups

		Patients			
		PCa patients		Control group	
		n	%	n	%
Total		97		82	
Age	54–59	30	30.9	35	42.7
	60–70	67	69.1	47	57.3
p		0.1199			
Place of residence	Urban	67	69.1	56	68.3
	Rural	30	30.9	26	31.7
p		0.9999			
Gleason score	6	44	45.4		
	7	30	30.9		
	8	13	13.4		
	9	10	10.3		
T	T1	54	55.7		
	T2	43	44.3		
	T3	0	0		
	T4	0	0		
N	N0	97	100.0		
M	M0	97	100.0		

Serum samples collection

Venous blood collected from all subjects was centrifuged at 1500 rpm for 15 minutes at room temperature, and the serum was divided into several portions and frozen at -80°C.

Detection of SARS-CoV-2 antibodies

The presence and level of antibodies were assessed in serum collected from all study participants using a commercially available Microblot Array COVID-19 IgG test (TestLine Clinical Diagnostics, Brno, Czech Republic) according to the manufacturer's instructions. Results are given in units of U/ml, as described previously [17].

Statistical Analysis

GraphPad Prism version 10.4.0 was used for statistical analysis (San Diego, CA, USA). Categorical variables were expressed as numbers and percentages. The normality of the distribution of continuous variables was checked using the Shapiro-Wilk test. Descriptive statistics were used to present patient baseline characteristics. Seroprevalence is

presented as a percentage. The chi-square test was used to compare the prevalence of antibodies in both groups. Means and standard deviations (SD) were calculated. Antibody levels were analyzed using the Mann–Whitney U test and the Kruskal-Wallis test. If the p-value <0.05, the result was considered statistically significant.

Ethics

The research was approved by the Medical University of Lublin Ethics Committee and is in accordance with the GCP regulations (No. KE-0254/295/2019, 26 September 2019 and no. KE-0254/194/10/2022, 6 October 2022). Written informed consent was obtained from each participant.

RESULTS

In the group of prostate cancer patients, the decline in antibody titer was faster compared to the control group (Figure 2). This is especially noticeable in the group of older patients, i.e., those aged 60-78.

The exact values of antibody titers at each stage of the study are presented in Table 2 (among PCa patients) and in Table 3 (in the control group). In the period from 3 to 6 months, and also from 6 to 9 months after vaccination, a statistically significant decrease in antibody titer was observed in both the 50-59 and 60-78 age groups (p <0.0001).

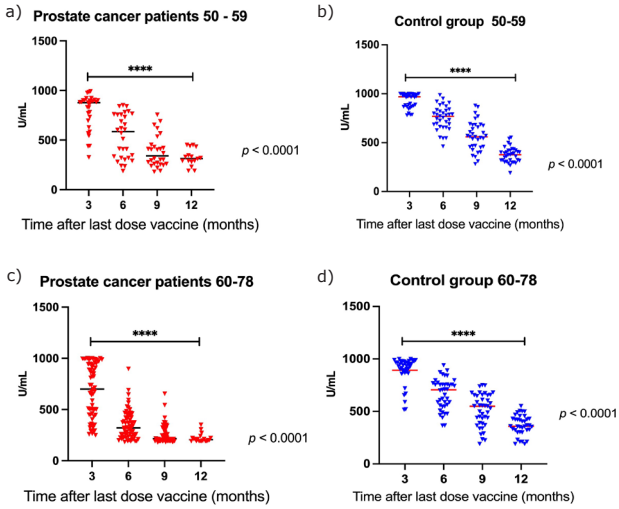

Figure 2. Anti-SARS CoV-2 antibody titer 3, 6, 9 and 12 months after the last (third) vaccine dose in PCa patients (red color) and control group (blue color) by age. a) PCa patients aged 50-69; b) Control group aged 50-69; c) PCa patients aged 60-78; d) Controls 60-78; Kruskal-Wallis Test; **** p <0.0001

Table 2. Comparison of the dynamics of anti-SARS CoV-2 antibodies in PCa patients according to age

Age of patients	50-59				60-78			
Time of last dose vaccine (months)	3	6	9	12	3	6	9	12
Antibody levels	783.3 ± 178.0	540.5 ± 219.6	383.4 ± 187.7	323.5 ± 84.8	682.4 ± 260.5	347.2 ± 138.3	258.6 ± 91.6	218.9 ± 43.1
p value	0.0001*				0.0001*			
		0.0049*				0.0001*		
			0.5704					
							0.1094	

*statistically significant, chi-square test

It is clear that the humoral response in PCa patients was much weaker than in the control group, especially in the older age group. Twelve months after administration of the third dose of the vaccine, the antibody titer was low and amounted to 323.5 U/mL in the group of PCa patients aged 50-59 years and 218.9 U/mL in the group aged 60-78 years, respectively; in principle, it did not differ significantly from the antibody titer 9 months after the last dose of vaccine. However, in men from the control group, the decline in antibody titer was slower. A significant decrease in titer was observed 12 months after the third dose of vaccine.

Table 3. Comparison of the dynamics of anti-SARS CoV-2 antibodies in the control group according to age

Age	50-59				60-78			
Time of last dose vaccine (months)	3	6	9	12	3	6	9	12
Antibody levels	931.0 ± 73.8	752.0 ± 123.0	655.0 ± 150.6	374.2 ± 78.2	892.3 ± 127.5	666.0 ± 147.1	511.6 ± 153.0	366.9 ± 95.5
p value	0.0001*				0.0001*			
		0.0001*				0.0001*		
			0.0001*					
							0.0001*	

*statistically significant, chi-square test

Next, we wanted to check whether the dynamics of antibodies after vaccination depends on the stage of cancer advancement. We included Gleason Score (Figure 3a) and T stage (Figure 3b). As the analysis showed, 3 months after vaccination, the level of anti-SARS-CoV-2 antibodies was similar in the GS 8-9 and GS 6-7 groups. However, in the following months, the antibody titer decreased much faster in the group of patients with a Gleason score of 8-9, reaching values significantly lower than in the group of patients with a GS of 6-7. This difference was statistically significant (p < 0.0001).

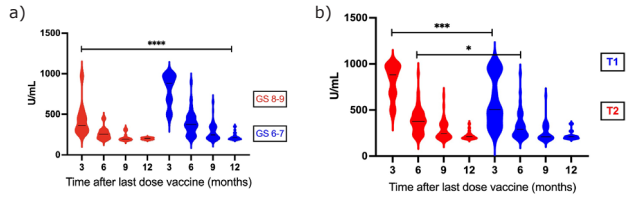

Figure 3. Anti-SARS CoV-2 antibody titer 3, 6, 9 and 12 months after the last (third) vaccine dose: a) in relation to Gleason Score (GS) Kruskal-Wallis Test; **** p <0.0001; b) in relation to T stage. Mann-Whitney test; red color – T2 stage, blue color – T1 stage; *** p=0.0001; * p=0.01

Among the examined patients, the majority of patients, 55.7%, were diagnosed with stage T1, and 44.3% – T2. Three months after the last dose of vaccine, the level of anti-SARS-CoV-2 antibodies was lower in the T2 phase (p=0.0001). Six months after vaccination, antibody levels were also lower in the T2 group (p=0.0103). However, after 9 and 12 months, the antibody titer was only slightly lower, and this difference was no longer statistically significant. We then compared whether there was a difference in the level of antibodies between the GS 6/7 and GS 8/9 groups as well as between the T1 and T2 groups subsequent months after the third dose of vaccine (Table 4).

Table 4. Differences in antibody levels between: GS 8/9 *vs* GS 6/7 and T1 *vs* T2 - Statistical significance analysis

Time of last dose vaccine (months)	Gleason Score (GS) 6/7 *vs* 8/9 p value	T stage T1 *vs* T2 p value
3	<0.0001*	<0.0001*
6	0.0001*	0.0103 *
9	0.0004*	0.0569
12	0.5827	0.8827

*statistically significant; Mann-Whitney Test

DISCUSSION

After the introduction of vaccinations against COVID-19 on a global scale, many independent scientific centers conducted studies aimed at examining the humoral response to vaccination of selected subpopulations [18,19]. Some studies have shown that both the innate and adaptive immune responses are weaker in men [20,21]. Weakened immunity of cancer patients increases the risk of exposure to infections, including SARS-CoV-2 [22-24]. Moreover, observations conducted in various countries have shown that men are more susceptible to severe COVID-19 than women, require ICU treatment twice as often, and the risk of death is 30% higher than in a comparative group of women [25,26]. Therefore, cancer patients became eligible for COVID-19 vaccination as soon as vaccines became available. The first vaccinations against COVID-19 began in Poland at the end of December 2020 as part of the National Vaccination Program with the Comirnaty vaccine.

The immune response after vaccination against SARS-CoV-2 in patients with solid tumors has been described by many researchers, noting the relatively low titer of antibodies in cancer patients compared to a healthy, age-matched control group [27,28]. The humoral response increases with the number of doses administered [29-31]. There are not many studies in the scientific medical literature on the dynamics of anti-SARS-CoV-2 antibodies, however, after vaccination in cancer patients. To the best of our knowledge, these are the first studies assessing the dynamics of anti-SARS-CoV-2 antibodies within a year after administering three doses of the COVID-19 vaccine in Polish cancer patients.

A similar study was undertaken by Swadźba et al. [32], who conducted research among Polish health care workers vaccinated against COVID-19. Two years after administration of the first dose of the vaccine, the presence of anti-SARS-CoV-2 antibodies was detected in 100% of the subjects; their level was high then decreased slightly. In turn, interesting observations were made by Harrache et al. [33], who stated that the kinetics of anti-SARS-CoV-2 antibodies is influenced by the type and number of vaccine doses, as well as clinical and demographic factors, such as age.

Administration of the third dose of the mRNA vaccine was found to significantly increase antibody titers and extended their half-life. Similarly, all patients we studied were vaccinated with three doses of the Pfizer-BioNTech vaccine. Yorsaeng et al. [12], examining the Thai population, showed that people who received only two doses of the vaccine had lower levels of anti-RBD IgG antibodies, which decreased rapidly over time. Similiarly, the study by Naaber et al. [34] showed a strong initial vaccine response after two doses of the Pfizer-BioNTech Comirnaty vaccine, which declined six months after vaccination.

Our observations showed that in PCa patients, the decrease in antibody titer was faster than in the control group, which is particularly visible among older patients, i.e., aged 60-78. Twelve months after administration of the third dose of the vaccine, the level of antibodies was low in both age groups. Moreover, our results indicate a relationship between antibody dynamics and cancer stage. As the analysis showed, 3 months after vaccination, the level of anti-SARS-CoV-2 antibodies was similar in the GS 8-9 and GS 6-7 groups. However, in the following months, the antibody titer decreased much faster in the group of patients with a Gleason score of 8-9, reaching values significantly lower than in the group of patients with a GS of 6-7. Therefore, it seems that PCa patients should be vaccinated with a booster dose more often than once a year.

The limitation of our study was the relatively small number of patients, which resulted from the adopted criteria for qualifying people for the study. We did not assess antibody levels after each dose of vaccine or before administering subsequent doses. This was dictated by the research goals, which were to answer the question: how long does humoral immunity last after three doses of the COVID-19 vaccine? We only analyzed humoral immunity. In the future, it would be worth assessing the cellular response as well. Therefore, further research is also needed to develop the best preventive strategy for patients with solid organ cancer.

CONCLUSIONS

According to our findings that in the following months, the antibody titer decreased much faster in PCa patients than in people from the healthy control group, it seems reasonable to ask whether PCa patients should be vaccinated with a booster dose more often than once a year.

INFORMED CONSENT STATEMENT

Written informed consent has been obtained from the patients to publish this paper.

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