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Serologic Status According Severe Acute Respiratory Syndrome Coronavirus 2 in Patients After Orthotopic Heart Transplantation

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ABSTRACT

Background. The SARS-CoV-2 pandemic is ongoing. In this context, patients after organ transplantation are especially endangered because of their increased susceptibility to infections. Real effectiveness of vaccinations against SARS-CoV-2 and exposition to the virus in populations after organ transplantation is still being assessed.

Methods. We investigated 371 adult patients (82.7% men, 17.3% women), aged 54 ± 14 years, with a median time from transplantation of 1296 days (interquartile range, 473-400 days) after orthotopic heart transplantation consecutively admitted to the transplant center between February and September 2021. SARS-CoV-2 spike protein antibodies were assessed quantitatively by Elecsys Anti-SARS-CoV-2 S. Data according to past COVID-19 infection and vaccination were compared with the test results.

Among the whole group, 59 patients were unvaccinated and had no past COVID-19 infection, 200 patients had a full course of vaccination (2 doses) with an mRNA vaccine, 1 patient had received a viral vector vaccine, 11 patients had had a single dose of an mRNA vaccine, and 99 patients had previously had a COVID-19 infection. Median time from vaccination to antibody assessment was 54 days (interquartile range, 30-76 days).

Aim. The aim of this study was to determine exposure to the virus among patients after heart transplantation before vaccination and humoral response to the vaccination and assess the role of antispike antibodies in the prevention of infection.

Results. After vaccination, 22.3% had no antibodies (45 patients), 47.3% had titers between 0.8 U/mL [0.82 binding antibody units (BAU)/mL] and 250 U/mL (257.25 BAU/mL; 95 patients), and 30.2% had titers above 250 U/mL (257.25 BAU/mL; 61 patients). After a single dose of vaccine, 63% patients had no antibodies. In the group of unvaccinated patients, 3 patients had titers above 250 U/mL (257.25 BAU/mL; 5.1%) and 12 patients had titers up to 250 U/mL (257.25 BAU/mL; 20.3%).

In patients after COVID-19 infection, only 2% did not show antispike antibodies, and in 61.4% the titers were above 250 U/mL (257.25 BAU/mL).

In the group of patients infected after the full course of vaccination (4 patients after a single dose and 2 after 2 doses), none of the patients developed antibodies after vaccination. Up to the end of September 2021, none of the patients with antibodies against SARS-CoV-2 developed COVID-19.

Conclusions. The presence of spike protein antibodies may be a relevant marker of effective vaccination. In patients after heart transplantation, exposure to SARS-CoV-2 is high.

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DUE to the wide spectrum of symptoms or even asymptomatic course [1] of SARS-CoV-2 infection in patients after orthotopic heart transplantation (HTx), the real exposure to the virus is not known. Both vaccination against the virus and the infection itself elicit antispike antibodies, known for their neutralizing potential to the virus [2]. Both vaccination and the infection may induce a cellular response that may also be present in the absence of a humoral response [3]. Efforts have been made to assess the effectiveness of vaccinations against COVID-19 in patients after solid organ transplantation.

AIM OF THE STUDY

The aim of this study was to determine antibody response to anti-SARS-CoV-2 vaccination in a cohort of patients after HTx, determine exposure to the virus among patients after HTx before vaccination, and assess the role of antispike antibodies in the prevention of infection.

METHODS AND MATERIALS

This study was a single-center prospective observational study. Consecutive adult patients admitted to the transplantation ward or transplantation ambulance between February 2021 and September 2021 were included. The whole analyzed group consisted of 371 patients (17.3% women) after HTx. Mean age of patients was 54 ± 14 years (median = 58; interquartile range [IQR], 44.8-65.6 years).

Median time from transplantation was 1296 days (IQR, 473-4001).

Data according to current and previous COVID-19 infection were compared with the test results. Among the whole group, 59 patients were unvaccinated and had no known past COVID-19 infection, 201 patients had the full course of vaccination (2 doses) with mRNA vaccine, and 1 patient received viral vector vaccine. Among the investigated group, 11 patients had a single dose of vaccine (partially vaccinated) and 99 patients had previously had a COVID-19 infection. Median time from vaccination to antibody assessment was 54 days (IQR, 30-76).

Anti-SARS-CoV-2 antibodies determined by a quantitative method (Elecsys Anti SARS-CoV-2 S, Cobas, Roche) were assessed. The sensitivity and specificity of the test are 84% and 100%, respectively [4]. The positive cutoff was at least 0.8 U/mL.

The study was performed in accordance with the Declaration of Helsinki. The Bioethics Committee of the Medical University of Silesia gave permission to perform the study (Decision No. PCN/CMN/0022/KB1/30/21).

Statistical Analysis

Categorical variables are presented as counts and percentages. Continuous variables are presented as means and standard deviations or medians with lower and upper quartiles.

RESULTS

Among fully vaccinated patients, 45 did not produce antibodies (22.3%). Among seropositive patients, 61 had titers above 250 U/mL [257.25 binding antibody units (BAU)/mL; 30.2%]. Among partially vaccinated patients (a single dose of vaccine), 63% of patients did not produce antibodies. In the group of unvaccinated patients, 3 patients had titers above 250 U/mL (257.25 BAU/mL; 5.1%) and 12 patients had titers up to 250 U/mL (257.25 BAU/mL; 20.3%).

In patients after COVID-19 infection, only 2% did not show antispike antibodies, and in 61.6% titers were above 250 U/mL (257.25 BAU/mL).

In the group of patients infected after the full course of vaccination (4 patients after a single dose, 2 patients after 2 doses), none of the patients developed antibodies after the vaccination. Up to end of September 2021, none of the patients with the presence of antibodies against SARS-CoV-2 spike protein developed COVID-19. Detailed clinical characteristics are presented in Table 1.

Table 1. Clinical Characteristics of the Investigated Group

		Unvaccinated/No Past COVID-19	Vaccinated (2 Doses)	Vaccinated Partially (1 Dose)	Past COVID-19 Infection	Total *n*
No. of patients		59	202	11	99	371
Age, median (IQR)		52.5 (38.9-63)	61.2 (48.1-66.4)	57.1 (48.6-62.7)	55.8 (43.1-64.6)	54 (44.8-65.6)
Sex, female, *n* (%)		8 (13.6)	36 (17.8)	1 (9.1)	19 (19.2)	64 (17.3)
Time posttransplant, median (IQR)		1951 (925-3733)	1620 (591-4766)	927 (144-1506)	1443 (369-4367)	1296 (473-4001)
Original cardiovascular disease/ cardiomyopathy, *n* (%)	Ischemic	17 (28.8)	77 (38.1)	7 (63.6)	33 (33.3)	134 (36.1)
	Hypertrophic	4 (6.8)	9 (4.5)	0	3 (3)	16 (4.3)
	Dilated	33 (55.9)	90 (44.6)	3 (27.3)	48 (48.5)	174 (46.9)
	Valvular	1 (1.7)	4 (2)	0	2 (2)	7 (1.9)
	Arrhythmic	0	3 (1.5)	0	2 (2)	5 (1.3)
	Restrictive	0	7 (3.5)	1 (9.1)	4 (4)	12 (3.2)
	Congenital heart disease	0	5 (2.5)	0	2 (2)	7 (1.9)
	Other	4 (6.8)	7 (2.5)	0	5 (5.1)	16 (4.3)
Antibody status, *n* (%)	<0.8 U/mL	44 (74.6)	45 (22.3)	7 (63.6)	2 (2)	98 (26.4)
	0.8-250 U/mL	12 (20.3)	96 (47.5)	4 (36.4)	36 (36.4)	148 (39.9)
	>250 U/mL	3 (5.1)	61 (30.2)	0 (0)	61 (61.6)	125 (33.7)

IQR, interquartile range.

DISCUSSION

Patients receiving immunosuppression are an especially vulnerable group, and achieving adequate response to the vaccination against SARS-CoV-2 is pivotal. General population studies showed high efficacy of vaccines against SARS-CoV-2 infection [5], but in immunocompromised patients the response is impaired. Among patients after renal transplantation the antibody response was low (only 36.4% showed antibody response to the vaccination) [6]. In a small group of patients after heart transplantation (26 patients) the rate of seroconversion was only 34.8% [7]. In an inhomogeneous group of solid organ transplant recipients, Boyarsky et al [8] showed lowered seroconversion rates after a single dose (17%) and 2 doses (54%) of mRNA vaccine [9]. In this context, our group showed surprisingly high seroconversion rates. The observation is particularly interesting because our group was vaccinated with an mRNA vaccine (as in previously cited studies) and for antibody assessment we used 1 of the 2 assays applied in their studies. The main difference was that our group comprised only patients after heart transplantation.

It is worth mentioning that some patients in the unvaccinated group with no previous COVID-19 infection had positive antibodies. We suggest that they had prior asymptomatic infection. Furthermore, none of the patients who developed antibodies after vaccination had SARS-CoV-2 infection. However, this observation was made during waning of the virus in our population. Long-term observations are needed.

It is suggested that the level of antispike (neutralizing) antibodies we assessed is connected to the degree of protection against the infection [10,11].

The protective level is still to be estimated, but it is suggested that antibody titers higher than 100 BAU/mL may be protective [12]. Other authors suggested that the protective value against severe COVID-19 exceeds 265 BAU/mL [2].

There is also a possibility of existence of cell-mediated (T cells and natural killer T cells) response to the vaccine even in the absence of a humoral response [10]. Additionally, innate immunity may play an important role independent of vaccination status.

Routine estimation of antibody titers is currently not recommended by the Food and Drug Administration and other organizations [10].

Due to weakened response to the vaccination, many strategies to improve vaccination efficacy are proposed, including a third dose of the vaccine [13]; decreasing immunosuppression prior to vaccination, especially cessation of antimetabolites; immunization with different types of the vaccine [14] and immunization based on antibody response [15].

Due to impaired access to medical resources in the pandemic, we suggest that the safest option is double strength vaccination of solid organ transplant recipients rather than modification of immunosuppressive regimen, which may potentially lead to graft rejection. Assessment of antibodies may be beneficial but requires additional medical visits. Investigations of these 2 strategies should be performed.

Limitation of the Study

Observations were made before the fourth wave of pandemic. During the observation period, the number of infections in the general population was low. Furthermore, we did not assess response of B and T lymphocytes.

CONCLUSIONS

Exposure to SARS-CoV-2 virus in the population of patients after HTx is high, and it is likely that some infections were asymptomatic. The reaction to vaccination was surprisingly high (when compared to other solid organ transplant recipients) but the titers were low. It is not certain whether high titers of antispike antibodies prevent infection or COVID-19 in this group of patients, but the lack of antibodies should prompt greater vigilance in case of exposure.

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