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Immunity After Vaccination Against SARS-CoV-2 in Lung Transplant?

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ABSTRACT

Background. SARS-CoV2 infection causes high morbidity and mortality in lung transplant (LT) recipients. Vaccination with messenger RNA vaccines has been shown to play a key role in controlling the severity of infection in the general population. The aim of our study is to analyze whether vaccination with 2 doses of SARS-Cov2 provides immunity in LT recipients.

Methods. Retrospective descriptive and analytical study of LT recipients vaccinated with 2 doses of SARS-CoV2. We analyzed the vaccine received, if they had COVID-19, antibody levels (antispike and antinucleoprotein), anticalcineurin levels, infections in the last year, and presence of neoplasias.

Results. The most commonly administered vaccine was from Moderna, with 27% of patients showing immunity with a median antibody levels of 4.81 binding antibody units/mL, far from the values considered protective (> 34 binding antibody units/mL). Thirteen patients were infected with SARS-CoV2, 7 post vaccination (5 of them were antispike-positive). No relationship was demonstrated between generation of immunity and age and level of immunosuppression.

Conclusions. Vaccination against SARS-CoV2 in LT recipients generates limited and ineffective immunity with only 2 doses.

COVID-19 is the SARS-CoV-2 infection described in 2019 in China [1]. In immunosuppressed patients, the risk of developing COVID-19 is higher than in the general population [2], producing moderate-severe pneumonia in lung transplant (LT) recipients and requiring hospitalization in most cases (88%). This is because of higher levels of immunosuppression in LT recipients than in other solid-organ transplant recipients, as well as the existence, in some of them, of impaired lung function and the fact that the target organ of COVID-19 is the lung [1,3]. In addition, virus infections, such as SARS-CoV2, can also lead to chronic allograft dysfunction in these patients [4].

Vaccination plays an important role in slowing the spread of the virus and promoting the elimination of the virus from the host. The SARS-CoV-2 virus is made up of RNA containing proteins such as spike, which promotes binding between the host cell and the virus and between the infected cell and adjacent uninfected cells; it is also the main inducer of neutralizing antibodies in vaccines [4].

In immunocompetent patients, messenger RNA−based vaccines (Moderna, Pfizer/BioNTech) have shown high efficacy (> 90%) in preventing infection and, if it occurs, less severe infection [1,5]. Clinical trials initially conducted with these vaccines did not include LT recipients or other immunocompromised patients, so their efficacy in these patients was unknown, although it was suspected that the response was lower than in immunocompetent patients, as is the case with other vaccines. This lower immunogenicity is probably related to immunosuppressive treatment, which also has higher levels in LT compared with other solid-organ transplant [5,6].

Despite this, international societies recommend vaccination in LT recipients, as well as in patients with advanced lung disease who are on the waiting list, because it provides protection

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against severe COVID-19. Furthermore, the prevalence of allograft dysfunction and other adverse effects are low [5].

In Europe, a study has been conducted in Prague, with a small simple of LT recipients in which no immunity was found [5].

The aim of our study is to assess whether 2-dose vaccination against SARS-CoV-2 provides immunity in LT recipients and whether older age and/or a higher degree of immunosuppression influence the vaccine response.

MATERIALS AND METHODS

This is an observational, retrospective, descriptive, and analytical study. The inclusion criteria were be LT recipients at the Hospital Universitario 12 de Octubre in Madrid and to be vaccinated with 2 doses against SARS-CoV-2, the last of them during the period between January 2021 and September 2021. Patients who received 1 dose and those who were not vaccinated were excluded.

As an immunosuppressive regimen, all patients received basiliximab induction and then maintenance triple therapy based on a calcineurin inhibitor, a purine synthesis inhibitor, and steroids.

The variables collected were age, sex, underlying disease leading to transplant, time from transplant to analysis, type of transplant, type of vaccine received, whether they had SARS-CoV-2 infection and when it occurred (before or after vaccination and in this case how long after vaccination), number of infections in the last year, existence of neoplasia, levels of anticalcineurin in the last prevaccine sample (subtherapeutic, in adequate range, or supratherapeutic), levels of antibodies against SARS-CoV-2 (antispike and antinucleoprotein measured by DiaSorin RiS immunoglobulin [Ig] G), taking the measurements 4 months post vaccination and considering as positive levels > 34 binding antibody units/mL (BAU/mL).

Statistical analysis of qualitative variables was performed using χ^2 test. A P value < .05 was considered statistically significant. The analysis was performed using SPSS 25 (IBM, Armonk, NY).

RESULTS

We obtained a total sample of 93 patients, mostly male (59%) and with a mean (standard deviation) age of 56.99 (12.65) years. The mean time since transplant was 4.45 years, with the majority being bilateral (81.7%) and mostly because of chronic obstructive pulmonary disease (37.6%) and diffuse interstitial lung disease (29%). Baseline clinical data and sample information from our population are included in Table 1.

The most commonly administered vaccine was Spikevax from Moderna (93%), with antispike IgG in 27% of patients and a median antibody levels of 4.81 BAU/mL (range, 4.81-71.60).

Thirteen patients (14%) were infected with SARS-CoV-2, without generating natural immunity (antinucleoprotein IgG) in 38%. Of these, 7 became infected post vaccination (5 of them despite having antispike IgG), with a median time from second dose to infection of 2.6 months. Neither older age (comparing the 75th percentile with the rest) nor higher immunosuppression (analyzed by anticalcineurin levels in the most recent sample before vaccination, number of infections in the last year and the presence of neoplasias) influenced the generation of immunity (Table 2).

Table 1. Sample Characteristics

Variable	Sample Results
Sex, No. (%)	• Women: 37 (40.9) • Men: 56 (59.1)
Age, mean (SD), y	56.99 (12.65)
Time since transplant, mean (SD), y	4.45 (3.71)
Type of transplant, No. (%)	• Unilateral: 17 (18.3) • Bilateral: 76 (81.7)
Disease leading to transplant, No. (%)	• Chronic obstructive pulmonary disease: 35 (37.6) • Diffuse interstitial lung disease: 27 (29) • Pulmonary hypertension: 18 (19.4) • Cystic fibrosis: 10 (10.8) • Other: 3 (3.2)

SD, standard deviation.

DISCUSSION

Our study demonstrates greater humoral immunity in LT recipients than in previous studies, using the Moderna vaccine vs Pfizer. It is also the first to analyze whether the degree of immunosuppression and age in LT recipients influence the vaccine response, indicating that there is no such relationship.

In our LT recipient sample, the majority of patients received a messenger RNA vaccine (Moderna), with immunity being achieved 4 months after administration of the second dose in 27% of the patients. The median antibody title was 4.81 BAU/mL, far from the values considered protective (> 34 BAU/mL).

Despite vaccination, 7 patients became infected with SARS-CoV-2, 2.6 months after the second dose, including 5 of them with protective levels of antispike antibodies, demonstrating suboptimal efficacy of the vaccine antibodies.

Because of a lower response to other vaccines reported in elderly people [7], we compared the antibody levels at the 75th percentile of the sample with the rest, without finding significant differences. We also assessed whether greater immunosuppression, as measured by supratherapeutic levels of anticalcineurin before vaccine, the presence of neoplasias, or more than 1 infection in the last year, influenced the vaccine response, without finding any differences.

Table 2. Analysis of Immunity With Respect to Degree of Immunosuppression and Age

	Immunity(Antibodies Yes vs No)	
Variable	χ^2 Square	P Value
Anticalcineurin levels (adequate vs elevated)*	1.184	.553
Infections in the last year (none vs > 1)	0.019	.891
Existence of neoplasias (no vs yes)	0.431	.512
Age (in quartiles)	2.920	.404

* Adequate levels of anticalcineurin drugs are 15-18 ng/mL for the first 6 mo, 10-15 ng/mL from 6-12 mo, and 7-8 ng/mL from 12 mo onward.

Studies of the SARS-CoV-2 vaccine in LT recipients have so far only taken into account the results after administration of 2 doses, as in our study. In an Austrian study, with a small sample (12 LT recipients), no humoral immunity was observed after the administration of 2 doses of the Pfizer vaccine in any patient [5], while in an Israeli study of 168 LT recipients, also carried out with Pfizer, humoral immunity was observed in 18% [6]. In our sample, we observed a higher immunity, 27%, although our sample was intermediate between the 2 studies, and the vaccine administered in most of them was another, that of Moderna. There are studies in immunocompetent patients, such as one by Klein [7], one by Boyarsky [8], and another by Narasimhan [9], which show greater humoral immunity in patients who received the Moderna vaccine than the Pfizer vaccine, which could explain our better results compared with previous studies in LT recipients.

In the previously mentioned studies in LT recipients [5,6], it was not analyzed whether high immunosuppression or older age influenced the vaccine response. However, studies in immunocompetent [7] patients have shown that older patients develop low humoral immunity. This relationship was not demonstrated in our study either. On the other hand, it has the limitations of being a small simple study and having been conducted with only 2 doses of vaccine.

To confirm the greater efficacy of the vaccine from Moderna, it would be interesting to analyze several groups of LT recipients in which the different types of existing vaccines against SARS-CoV-2, as well as to analyze cellular immunity and not only humoral immunity.

CONCLUSIONS

We conclude that vaccination against SARS-CoV-2 in LT recipients generates limited and ineffective immunity with only 2 doses. It is possible that these patients may require periodic doses to ensure better immunity; in fact, 4 doses have already been administered in these patients in Spain. It would be important to conduct studies after administration of more doses to verify this.

DATA AVAILABILITY

The data that has been used is confidential.

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