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COVID-19 Infection in Heart Transplants in Pre- and Postvaccination Periods

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ABSTRACT

Background. Heart transplant (HTx) recipients constitute a group vulnerable to COVID-19 infection. Vaccination has been a turning point in the evolution of the pandemic. The objective was to analyze a series of HTx recipients with COVID-19 prior to vaccination and post vaccination.

Methods. Inclusion: All HTx recipients diagnosed with COVID-19 (February 2020 to April 2022). Exclusion: HTx younger than 16 years. They were subdivided into prevaccination period (February 2020 to February 2021) and postvaccination period (March 2021 to April 2022). They were classified into 3 groups according to severity. Group 1: mild symptoms without admission. Group 2: admission for nonsevere pneumonia. Group 3: severe pneumonia according to American Thoracic Society/Infectious Diseases Society of America criteria. The general therapeutic attitude before and after vaccination was similar in both groups.

Results. A total of 65 HTx recipients have had COVID-19 to date (10.7% of the 374 HTx recipients alive).

In the prevaccination period, 22 HTx recipients presented the disease (Fig 1A): 27% in group 1; 59% were admitted for nonsevere pneumonia (group 2), with favorable evolution and a mean stay of 16 days; and 14% in group 3 (criteria for severe pneumonia), with 2 HTx recipients dying in this group.

In the postvaccination period, 43 HTx recipients have presented COVID-19 (Fig 1B), 49% in group 1, 42% in group 2, and 9% in group 3. The hospital stay is slightly reduced to 15 days and 3 of the 4 patients in group 3 have died (mortality rate 7%).

Conclusions. A significant number of HTx recipients have been affected by COVID-19, associating high mortality in severe forms both in the pre- and postvaccination period. In our series of patients, vaccination has reduced the percentage of hospitalization for nonsevere pneumonia slightly below the average hospitalization and mortality.

BACKGROUND

The COVID-19 pandemic has had a strong effect on health systems, causing millions of deaths around the world. Heart transplant (HTx) recipients are a population at risk of developing severe forms and, therefore, of mortality. The management of these patients is a challenge in which there is a delicate balance between avoiding rejection with immunosuppression and trying to control the infection.

Vaccination has marked a turning point in the evolution of the pandemic, reducing serious forms of infection, hospitalization, and mortality in the general population.

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The objective of this study was to analyze a series of HTx recipients with COVID-19 prior to vaccination and post vaccination.

MATERIALS AND METHODS

HTx recipients diagnosed with COVID-19 were consecutively recruited from February 2020 to April 2022 in a Spanish transplant hospital. HTx recipients younger than 16 years were excluded. They were subdivided into prevaccination period (February 2020 to February 2021) and post-vaccination period (March 2021 to April 2022). At the beginning of the pandemic the center’s heart transplant team drew up a protocol for therapeutic action according to the patient’s infectious situation [1]. They were classified into 3 groups according to severity. Group 1: mild symptoms without admission. Group 2: admission for nonsevere pneumonia. Group 3: severe pneumonia according to American Thoracic Society/Infectious Diseases Society of America criteria [2,3].

The general therapeutic attitude before and after vaccination was similar in both groups.

RESULTS

The prevalence of COVID-19 infection in the series was 10.7% (65 patients of the 374 HTx recipients alive). The baseline characteristics of the patients in each group and period are shown in Table 1. In all groups (pre- and postvaccination) the prevalence was higher in male recipients. Most of the transplant recipients’ baseline treatment included tacrolimus, mycophenolate mofetil (MMF), and deflazacort.

In the prevaccination period, 22 HTx recipients presented the disease (Fig 1A). The first group included 6 patients (27%) with mild symptoms. The second group included most of the patients (13, 59%) and they were admitted for nonsevere pneumonia. MMF use was suspended and everolimus use was started by extrapolation because it has shown a protective effect against viral infection due to cytomegalovirus. The evolution of the patients was favorable with a mean stay of 16 days (no deaths in this group). The third group, composed of 3 patients (14%) includes those with severe pneumonia criteria. Immunosuppressants were discontinued and 2 HTx recipients died. The mortality rate in this period was 9%.

In the postvaccination period, 43 HTx recipients presented COVID-19 (Fig 1B). The general therapeutic attitude was similar to that in the prevaccination groups (Table 1). Group 1 was the majority (49%). A total of 18 patients (42%) were admitted for nonsevere pneumonia (group 2) with a mean stay of 15 days and none died. Group 3 was reduced to 9% (4 patients, 3 died). The mortality rate was 7%.

In both periods no acute rejection was detected with the changes made in immunosuppression.

Regarding vaccination status, all had a complete schedule (the corresponding 2-3 doses at the time of infection) except for 1 patient who had only 1 dose and 5 patients who did not have the third dose (Table 1). None of the patients has presented reinfection.

DISCUSSION

Since the pandemic began, it has become a worldwide problem. Among the groups most vulnerable to infection are immunosuppressed patients such as HTx recipients, adding an extra level of difficulty by requiring to avoid rejection with the treatment.

Table 1. Baseline Characteristics

| Characteristic                  | Group 1 (n = 6) | Group 2 (n = 13) | Group 3 (n = 3) | Group 1 (n = 21) | Group 2 (n = 18) | Group 3 (n = 4) |
|--------------------------------|----------------|-----------------|----------------|-----------------|-----------------|----------------|
| Age, mean (SD), y              | 51.2 (17.5)    | 61.2 (12.5)     | 64.7 (9.1)     | 48.8 (18.5)     | 57.7 (12.5)     | 53.2 (15.2)    |
| Sex, No. (%), male             | 5 (83.3)       | 11 (84.6)       | 3 (100)        | 12 (57.1)       | 13 (72.2)       | 3 (75)         |
| Time since HTx, mean (SD), d   | 2028 (2373)    | 4221 (2220)     | 5313 (1308)    | 3493 (2546)     | 2496 (1708)     | 2915 (2181)    |
| Basal treatment, No. (%)       |                |                 |                |                 |                 |                |
| Cyclosporine                   | 2 (33.3)       | 5 (38.5)        | 1 (33.3)       | 6 (28.6)        | 3 (16.7)        | 0              |
| Tacrolimus                     | 4 (66.7)       | 8 (61.5)        | 2 (66.7)       | 15 (71.4)       | 15 (83.3)       | 4 (100)        |
| Mycophenolate mofetil          | 5 (83.3)       | 11 (84.6)       | 2 (66.7)       | 17 (81)         | 15 (83.3)       | 3 (75)         |
| Everolimus                     | 1 (16.7)       | 2 (15.4)        | 1 (33.3)       | 4 (19)          | 3 (16.7)        | 1 (25)         |
| Deflazacort                    | 6 (100)        | 13 (100)        | 3 (100)        | 21 (100)        | 18 (100)        | 4 (100)        |
| Reduction/suppression, No. (%) |                |                 |                |                 |                 |                |
| Cyclosporine                   | 0              | 2 (40)          | 1 (100)        | 0               | 1 (33.3)        | 0 (100)        |
| Tacrolimus                     | 0              | 2 (25)          | 2 (100)        | 0               | 3 (20)          | 4 (100)        |
| Mycophenolate mofetil          | 0              | 11 (100)        | 2 (100)        | 0               | 15 (100)        | 3 (100)        |
| Everolimus                     | 0              | 0               | 1 (100)        | 0               | 0               | 1 (100)        |
| Deflazacort                    | 0              | 0               | 0              | 0               | 0               | 0              |
| Graft rejection, No. (%)       | 0              | 0               | 0              | 0               | 0               | 0              |
| Vaccination status, No. (%)    |                |                 |                | 19 (90.5)       | 15 (83.3)       | 3 (75)         |
| Complete                       | -              | -               |                | -               | -               | -              |
| 1 Dose left                    | -              | -               |                | 2 (9.5)         | 2 (11.1)        | 1 (25)         |
| 2 Doses left                   | -              | -               |                | 0               | 1 (5.6)         | 0              |
| 3 Doses left                   | -              | -               |                | 0               | 0               | 0              |

HTx, heart transplant.
After the appearance of the vaccine for COVID-19 and the vaccination of the population, the pandemic took a radical turn. In this series, 3 HTx risk groups were considered pre- and postvaccination periods.

In this series, the prevalence of COVID-19 infection in HTx recipients was 10.7%. There are no data available on the prevalence in other published series. There are data published by a seroprevalence study in Spain after the first wave of the pandemic in which the seroprevalence of the reference area of our hospital was 5.7% [4], which was similar to that presented in that time period for infection in transplant recipients with a prevalence of 5.2% [1]. No further seroprevalence studies were done. The mean age was between 48 and 69 years, and most of the patients were men, which was very similar to the rest of the published series [5–7].

The treatment in most of the patients both pre- and post vaccination included calcineurin inhibitors, MMF, and corticosteroids. The strategy followed in both periods was also similar; in group 2 MMF was changed to everolimus and in group 3 the dose of all immunosuppressants was reduced, even withdrawing them in the most severe cases [1]. In most published series, the trend is to reduce or suppress immunosuppression in hospitalized patients and in severe forms [5–8]. An important problem that can occur after this reduction is the appearance of acute rejection. In our series, no case of rejection was reported, as well as in most published series [5–7] except Marcondes-Braga et al who reported a 10% rejection rate [8].

Vaccination is recommended in HTx recipients, as stated in the position paper of the European Society of Cardiology [9]. In this series, nearly all completed vaccination as recommended (90.5% group 1, 83.3 group 2, 75% group 3). Data on the vaccination status of other series are not available. In the prevaccination period, the percentage of hospitalized patients rose to 86%. This percentage decreased after vaccination to 51%. In the series with the largest number of published patients, this percentage is between 62% and 82% (without data on vaccination status) [5–8]. The mean stay in our series was slightly reduced from 16 to 15 days.

Mortality in the prevaccination period of our series was 9%. This was reduced to 7% after vaccination. There is great variability in mortality reported in published series. The data reported in these series did not specify vaccination status. The multicenter series with the largest number of patients (n = 99) by Genuardi et al reported a 15% mortality rate [6]. Bottio et al (n = 47) reported a mortality rate of 30% [5]. However, Duran et al (n = 28) reported a mortality rate of 7% [10]. This variability in mortality may be because of the retrospective nature of data collection, the different time periods in which the series are collected, and the nonreporting of milder cases.

Limitations of our study include its retrospective nature and the possibility that some case of mild COVID-19 that has not been tested has not been registered. However, because it is a single-center study, the methodology followed for data collection has been common and very strict since the start of the pandemic, considering it to be the longest currently published single-center series with pre- and postvaccination data.

**Fig 1.** (A) Distribution of prevaccination patients. (B) Distribution of postvaccination patients.
CONCLUSIONS

A significant number of HTx recipients have been affected by COVID-19, associating high mortality in severe forms both in the pre- and postvaccination period. In our series of patients, vaccination has reduced the percentage of hospitalization for nonsevere pneumonia slightly below the average hospitalization and mortality.

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