BNT162b2 Vaccination Before Heart Transplantation: Kinetics of the Antibody Response

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Evidence of coronavirus disease 2019 (COVID-19) vaccination immune paresis in solid organ transplant (SOT) recipients is emerging[1,2]; however, little is known about the immune responses of SOT recipients vaccinated before transplant. This information is timely and of great value, especially considering a third booster dose vaccine for SOT recipients who have completed a 2-dose mRNA vaccine series before transplant.[3]

We prospectively assessed the kinetics of the receptor-binding domain (RBD) immunoglobulin G (IgG) and neutralizing antibody responses in heart transplant (HT) candidates vaccinated before transplant with the BNT162b2 vaccine (Pfizer, NY; BioNTech, Mainz, Germany) and subsequently underwent HT. Samples from HT patients were evaluated with enzyme-linked immunosorbent assay that detects IgG antibodies against the RBD of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). A SARS-CoV-2 pseudovirus neutralization assay was performed to detect SARS-CoV-2 neutralizing antibodies using a green fluorescent protein reporter-based pseudotyped virus with a vesicular stomatitis virus backbone coated with the SARS-CoV-2 spike protein.[4]

Eight HT candidates who had been vaccinated with the BNT162b2 vaccine underwent HT from February to May 2021; 7 had been fully vaccinated with 2 doses of vaccine 82 ± 35 d before the transplant, and 1 had received the first vaccine dose 6 d before the transplant. The patients ranged in age from 22 to 68 y; 1 was female. Comorbidities were frequent, with hypertension (50%), diabetes mellitus (38%), and dyslipidemia (50%) being the most common. Six patients were supported with the HeartMate 3 left ventricular assist device. Immunosuppression comprised tacrolimus, mycophenolate, and prednisone. Antithymocyte globulin induction therapy was not administered to 3 patients because of ongoing assist device-related infection. On the day of HT, all patients vaccinated with the second dose of the BNT162b2 vaccine 24 to 122 d before transplant and screened for antibodies on the day of HT had a highly positive anti-RBD IgG response with highly positive neutralization capacity. Vaccine-induced antibody response of the RBD IgG and neutralizing antibodies were persistently evident for all fully vaccinated HT recipients at 12 wk after HT; the antibody response declined slowly over time (Figure 1). One of 8 HT recipients received only the first dose of the vaccine 6 d before surgery and did not mount detectable immunity. No major rejection episodes were documented; ejection fraction was >55% for all patients, and all remained COVID-19 free during a 3-mo follow-up after transplant.

In light of the COVID-19 vaccination immune paresis in SOT recipients,[1] the medical transplant community is faced with new ethical questions about whether and under what conditions to perform transplants. This report demonstrates the persistence of vaccine-induced antibody response in HT recipients who had completed 2 doses of the BNT162b2 vaccine by 82 ± 35 d before transplantation, suggesting that vaccination of SOT candidates is a promising means of providing protection from COVID-19. At the time of vaccination, most of the reported patients were supported with the left ventricular assist device, thus contributing to the scarce literature.

Reports of donor-derived transmission of SARS-CoV-2 are starting to accumulate.[5] In parallel, the possibility of reactivation of donor-derived viral disease requires investigation. Given the increasing number of patients on the HT waitlist and the very limited resource of donors, the risk of viral transmission must be balanced against the risk to the recipient associated with not using an available organ and losing the opportunity for transplant. Pre-HT vaccination might increase the chance for vaccinated patients to be considered for COVID-19–infected donor organs.

Among the limitations of this study were the small number of patients and the lack of randomization. Nevertheless, our

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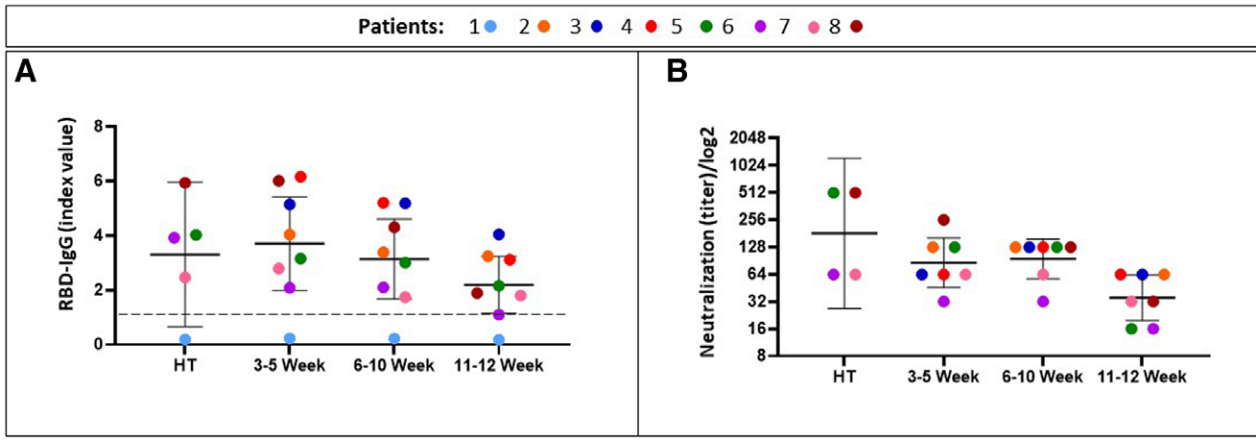

FIGURE 1. Quantitation of post–heart transplantation RBD IgG (A) and neutralizing (B) antibodies following BNT162b2 vaccination before transplant. The dashed line indicates the limit of positive antibodies level. Solid lines and numbers indicate the geometric mean titer. IgG, immunoglobulin G; RBD, receptor-binding domain.

findings challenge the concept of immune paresis in recipients of SOT. Although vaccine-induced antibody response is not yet been proven to be a surrogate marker of protection, data derived from trials in the general population demonstrate a correlation between the level of neutralizing antibodies to the SARS-CoV-2 spike protein and symptomatic disease.[4]

In summary, our experience strongly supports the recommendations for vaccination of all HT candidates (ideally with the completion of 2 doses of vaccine a minimum of 2 wk before transplant).[5] In the posttransplantation setting, the persistence of a highly positive antibody response and neutralization capacity at 3 mo point out that the timing of the third dose of mRNA vaccine is at least 3 mo from HT.

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