SARS-CoV-2 mRNA Vaccination Is Not Associated With the Risk of Allosensitization in Patients Awaiting Kidney Transplantation

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Potential proinflammatory events such as vaccination may be associated with an increased risk of allosensitization,1 which for waitlisted candidates becomes an obstacle for successful kidney transplantation. Potential vaccine-induced antibody-mediated alloresponse resulting in sensitization should be detectable by an increasing trend in values of panel-reactive antibody (PRA) measurements and by increases in anti-HLA antibodies.

To assess the potential link between severe acute respiratory syndrome coronavirus 2 mRNA vaccination and an increased humoral allosensitization in kidney transplant candidates, we conducted this retrospective observational study. The final analysis included the results of 146 waitlisted candidates who received 2 doses of mRNA vaccine and 121 unvaccinated candidates, all from the period between January 2020 and October 2021. PRAs were measured every 3 mo using the standard technique.2,3 PRA categories were defined as low (PRA < 21%), medium (PRA 21%–50%), and high (PRA > 51%) according to the mean PRA. Anti-HLA antibodies were analyzed in the subgroup of 21 highly sensitized candidates (peak PRA > 50%) using the single antigen bead technology. Screening was performed using the LabScreen

Mixed, and, in the case of a positive result, single antibodies were tested using the LabScreen Single Antigen Luminex technique (both from One Lambda, Inc). The laboratory cutoff of 500 mean fluorescent intensity (MFI) was set as a threshold for anti-HLA antibody positivity. One-sided paired Wilcoxon test was used to compare the difference between the PRA/MFI before and after vaccination. Institutional review board approval is not required for anonymous retrospective observational studies under the local legislation.

An increase in sensitization (defined as an increase in PRA above 26%, see below) was observed in 4 out of 146 candidates after vaccination. This rate (2.74%) is similar to the sensitization rate observed during the study period before vaccination (2.87%; P > 0.999). The threshold of 26% was derived as 2 SDs from all the differences between two consecutive PRA measurements during the study period excluding those following vaccination (n = 557). Furthermore, there was no increase in measured PRA after vaccination in the whole cohort (P = 0.996; Figure 1A) or in any subgroups classified by the PRA levels (P = 0.995 for high, P = 0.625 for medium, and P = 0.964 for low PRA groups; Figure 1B–D). For visualization, we plotted the development of the PRA levels over time in the PRA subgroups (Figure 1E).

In highly sensitized candidates, we observed no increase in averaged MFI of anti-HLA antibodies (P = 0.659 overall, P = 0.622 for class I, and P = 0.689 for class II; Figure 1F–H), MFI of up to 2 immunodominant anti-HLA antibodies (P = 0.307 for class I, and P = 0.712 for class II antibodies; Figure 1I–J), nor calculated virtual PRA (P = 0.265; Figure 1K). Furthermore, we computed a principal component analysis of MFI in highly sensitized candidates for multivariable analysis. There was a significant overlap between the measurements before and after vaccination and no significant differential clustering. Permutational multivariate ANOVA showed that there were no significant differences between the two timepoints (Figure 1L).

In conclusion, our study demonstrates that the 2-dose vaccination with mRNA severe acute respiratory syndrome coronavirus 2 vaccines in kidney transplant candidates was not associated with the increased risk of allosensitization.

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FIGURE 1. The dynamics of PRA and anti-HLA antibodies in regard to vaccination. In spaghetti plots, the dots denote absolute PRA/MFI/cPRA level, and lines connect dots from the same patient. In boxplots, bold horizontal lines denote median, and upper and lower box boundaries are the 25th and 75th quantile, respectively. PRA categories were defined as low (PRA <21%), medium (PRA 21%–50%), and high (PRA > 51%) according to the mean PRA of the candidate during the study period. One-sided paired Wilcoxon test was used to compare the difference between the PRA/MFI/cPRA before and after vaccination. (A)–(D) show PRA levels before and after vaccination in (A) the whole study group, (B) high PRA group, (C) medium PRA group, and (D) low PRA group. E, The dynamics of mean PRA for each group of vaccinated candidates. The error bars represent the bootstrapped 95% confidence interval. Vaccination is denoted by the vertical line. F–J, The anti-HLA MFI levels/cPRA before and after vaccination in the subset of highly sensitized candidates (maximum PRA above 50%): F, change of averaged MFI from all anti-HLA antibodies; G, change of averaged MFI from class I antibodies; H, change of averaged MFI from class II antibodies; I, change of MFI of up to 2 immunodominant class I antibodies; J, change of MFI of up to 2 immunodominant class II antibodies. K, Change of cPRA, and cPRA were computed using the Eurotransplant Reference Laboratory calculator. L, The principal component analysis (PCA) of anti-HLA antibodies measured before and after vaccination. There is no visible differential clustering of the two time points. The ellipses in the PCA plot represent 1 SD. PERMANOVA showed no significant difference ($p > 0.999$; analysis of dispersion $p = 0.996$). Ab, antibody; cPRA, calculated virtual panel-reactive antibody; MFI, mean fluorescence intensity; PERMANOVA, permutational multivariate ANOVA; PRA, panel-reactive antibody.
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