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BRIEF COMMUNICATION

WILEY

Clinical effectiveness of COVID-19 vaccination in solid organ transplant recipients

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Abstract

Goal: We aimed to assess the incidence rate of coronavirus disease 2019 (COVID-19) in vaccinated versus unvaccinated solid organ transplant recipients (SOTR) at our center.

Methods: We abstracted the following clinical data from our transplant registry from 1/1/2021 to 6/2/2021: demographics, details of COVID-19 vaccination, incidence of COVID-19, and related mortality. We calculated incidence of symptomatic COVID-19 per 1000/person days at risk and incidence rate ratio (IRR).

Results: Among 2151 SOTRs, 912 were fully vaccinated, and 1239 were controls (1151 unvaccinated, 88 partially vaccinated). Almost 70% of vaccinated subjects received the mRNA-1273 vaccine. There were 65 cases of COVID-19 that occurred during the study period – four occurred among fully vaccinated individuals and 61 among controls (including two in partially vaccinated individuals). Incidence rate for COVID-19 was 0.065 (95% CI 0.024–0.17) per 1000 person days in vaccinated versus 0.34 (95% CI 0.26–0.44) per 1000/person days in the control group; IRR was 0.19 (95% CI 0.049 −0.503, $p < 0.005$). There were no COVID-19 related deaths in the four breakthrough infections and two of 61 (3.3%) among controls.

Conclusion: We demonstrate real world clinical effectiveness of COVID-19 vaccination in SOTRs with an almost 80% reduction in the incidence of symptomatic COVID-19 versus unvaccinated SOTRs during the same time.

KEYWORDS
COVID-19, SARS-CoV-2, Solid organ transplant, vaccine

1 | BACKGROUND

In the light of data demonstrating reduced antibody responses to SARS-CoV-2 in solid organ transplant recipients (SOTRs) and variable effect on T-cell responses, there is a need to study clinical effectiveness and breakthrough infections in vaccinated SOTRs.[1,2] Recent papers note breakthrough infection in SOTRs of <1% though comparison to a control arm of unvaccinated SOTRs has not been published.[3] We aimed to assess the incidence rate of coronavirus disease 2019 (COVID-19) in vaccinated versus unvaccinated SOTRs at our center.

2 | METHODS

After obtaining IRB approval with a waiver of informed consent from the University of California San Diego (UCSD) Human Research Protections Program (IRB#210948XX), we queried our transplant registry for records between 1/1/2021 and 6/2/2021. Abstracted data included age, sex, type, and date of transplant, documentation of COVID-19 vaccination with type and date, symptomatic COVID-19, and death. Fully vaccinated patients had received either two doses of an mRNA vaccine (mRNA-1273, Moderna or BNT162b2,

TABLE 1 Details of four breakthrough cases of COVID-19 in fully vaccinated transplant recipients

	Case 1	Case 2	Case 3	Case 4
Transplanted organ	Kidney	Heart	Heart	Liver
Brief clinical history	67 yr old diabetic male s/p DDRT in 2015, complicated by chronic rejection	22 yr old female with NICM s/p heart transplant in 2013. Recent episode of rejection 6 mths prior treated with methylprednisolone, rituximab, thymoglobulin, plasmapheresis, and IVIG	61 yr old male with ischemic cardiomyopathy s/p heart transplant in 2020.	27 yr old male with a liver transplant in 2017 for fulminant hepatic failure.
Immunosuppression	Cyclosporine and prednisone	Sirolimus, tacrolimus, and prednisone	Tacrolimus, mycophenolate mofetil, and prednisone	Cyclosporine and mycophenolate mofetil
Type of vaccine	BNT162b2	mRNA-1273	BNT162b2	mRNA-1273
Days from vaccination to COVID-19 diagnosis	72 days	15 days	30 days	70 days
Clinical course of COVID-19	Moderate: Admitted with diarrhea, no respiratory symptoms. Treated with remdesivir. Household contact+	Moderate: Admitted with nausea, vomiting, cough and shortness of breath. Not hypoxic during admission. Treated with remdesivir.	Mild: Outpatient with rhinorrhea and headache. Treated with casirivimab/imdevimab.	Mild: Outpatient with fatigue, body aches, diarrhea, nasal congestion, and mild cough. Treated with casirivimab/imdevimab.

Abbreviations: DDRT, deceased donor renal transplant; IVIG, intravenous immune globulin; mth, months; NICM, nonischemic cardiomyopathy; s/p, status post; yr, year.

Pfizer-BioNTech) or a single dose of the Johnson and Johnson non-replicating viral vector vaccine (Ad26.COV2.S, Janssen); all patients had at least 2 weeks of follow-up from the date of last vaccination. The control arm consisted of SOTRs during the same time who were either unvaccinated or partially vaccinated. Diagnosis of COVID-19 required a positive SARS-CoV-2 polymerase chain reaction test. We excluded patients who had a diagnosis of symptomatic COVID-19 prior to 1/1/2021. We calculated incidence of symptomatic COVID-19 per 1000/person days at risk and incidence rate ratio (IRR). We also assessed for difference in cumulative probability of symptomatic COVID-19 in the two groups via Kaplan–Meir curves and associated log-rank test. Sensitivity analysis was done by excluding patients with partial vaccination. We used Stata version 17 (Statacorp, TX, USA) for statistical analysis.

3 | RESULTS

Among 2151 SOTRs, 912 were fully vaccinated, and 1239 were controls (1151 unvaccinated, 88 partially vaccinated) as noted in Table S1. The study cohort consisted of 1389 men (64.6%), mean age 57 years (standard deviation, SD 13.9), and median time since last transplanted organ of 57.5 months (interquartile range, IQR 24.6–120). Based on primary transplanted organ, the study cohort consisted of 376 (17.4%) heart, 205 (9.5%) lung, 603 (28%) liver, and 967 (44.5%) kidney transplant recipients. Almost 70% of vaccinated subjects received the mRNA-1273 vaccine. Vaccinated patients were older than the control group and had a shorter time from transplant. Mean days at risk was longer in the control group versus the vaccinated group (144 [SD 31.6] vs. 691.1 [SD 28.1] days, $p < 0.0001$).

There were 65 cases of COVID-19 that occurred during the study period – four occurred among fully vaccinated individuals and 61 among controls (including two of 88 partially vaccinated individuals that occurred 5 days and 26 days after the first BNT162b2 and first mRNA-1273 vaccine dose respectively). Details of cases with breakthrough infection among fully vaccinated subjects are in Table 1. There were no COVID-19 related deaths in the four breakthrough infections and two of 61 (3.3%) among controls.

Incidence rate for COVID-19 was 0.065 (95% CI 0.024–0.17) per 1000/person days in vaccinated versus 0.34 (95% CI 0.26–0.44) per 1000/person days in the control group; IRR was 0.19 (95% CI 0.049–0.503, $p < 0.005$). Kaplan–Meier curves (Figure 1) demonstrate a significant difference between the groups as well ($p < 0.0001$). Similar results were obtained with exclusion of partially vaccinated subjects (data not shown).

4 | DISCUSSION

We demonstrate real world clinical effectiveness of COVID-19 vaccination in SOTRs with an almost 80% reduction in the incidence of symptomatic COVID-19 versus unvaccinated SOTRs during the same time. This reduction in COVID-19 incidence is better than expected based on literature demonstrating that only about half of SOTRs

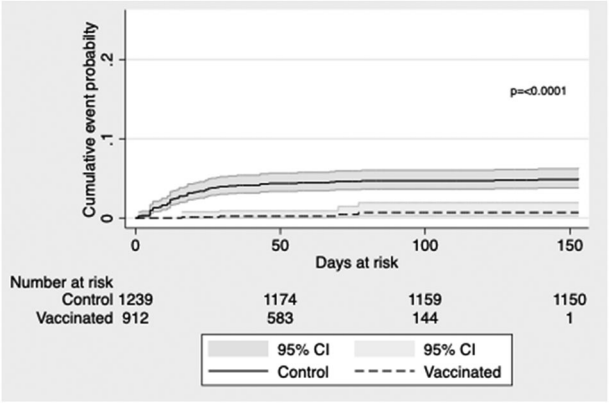

FIGURE 1 Kaplan–Meir curves demonstrating difference in cumulative probability of developing COVID-19 in the control and vaccinated groups, along with 95% confidence intervals and *p*-value of the associated log-rank test

develop detectable anti-spike antibodies following vaccination.[1] Thus, despite recent data demonstrating increased rate of detectable antibodies following a third dose of the BNT162b2 vaccine in SOTRs, based on our data it is unclear if a third dose is clinically warranted.[4] Evaluation of neutralizing antibody and T-cell responses following COVID-19 vaccination may identify predictors of subsequent risk for SARS-CoV-2 infection.[5] Prioritizing at risk subsets of transplant recipients based on immunological profiles and clinical characteristics for a third vaccine dose could be considered. Lastly, almost half of the study population was unvaccinated, and thus there is a great need to improve outreach activities in the transplant community to promote COVID-19 vaccination.

There are several limitations of this study including the retrospective data collection and single center cohort. Additionally, there is a potential for under-reporting of vaccination status. In general, our patients were either vaccinated at UCSD or at local medical facilities (we share our medical record system with some of these). For others, patients either called us with a vaccination update or we specifically asked and updated this information during clinic visits. There is still a chance of under-reporting this variable but we think that that number is probably low. If there is under-reporting and in fact some vaccinated patients are in the control arm, this would make the IRR more in favor of vaccination and further widen the difference between the two groups. There is also a potential that we missed some cases of symptomatic COVID-19 but in general we are a regional referral center, and our transplant patients admitted at other centers are generally transferred to us. As noted earlier, some of the local medical centers share medical records with UCSD. Additionally, patients generally call the transplant team with changes in clinical status so that we can assess them further, and thus we are aware of outcomes. We also lacked baseline SARS-CoV-2 serology in our patients as checking serology is not recommended by the FDA at this time and was not routinely performed.

In summary, we demonstrate significant clinical effectiveness of COVID-19 vaccination in SOTRs.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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