Risk of Breakthrough SARS-CoV-2 Infections in Adult Transplant Recipients

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It is well established at this point that solid organ transplant recipients (SOTRs) have substantially diminished antibody responses to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccines.[1,2] The correlation of this suboptimal antibody response to disease susceptibility is clinically important but poorly understood. In this multicenter study, we estimated the breakthrough infection rates after SARS-CoV-2 mRNA vaccination in SOTRs and compared them with rates reported in the general population.

This study was approved by our institutional review board. We identified transplant centers that were able to provide information about the number of SOTRs who had been fully vaccinated, developed breakthrough infections after vaccination, developed breakthrough infections and were hospitalized, and developed breakthrough infections and died, through personal inquiries among colleagues and corresponding author contacts from PubMed and Scopus searches. Data were collected as summary counts; no patient-level data were provided or studied. Breakthrough infections were defined per Centers for Disease Control and Prevention criteria (≥14 d after completing all recommended vaccine doses).

Among a total of 18 215 fully vaccinated SOTRs at 17 transplant centers, there were 151 breakthrough infections (0.83%), 87 with associated hospitalization (0.48%) and 14 with associated death (0.077%). Mortality among SOTRs with breakthrough infection was 14 of 151 (9.3%). Center-level breakthrough infection rates varied from 0.23% to 2.52% (Table 1).

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TABLE 1.

Center-level summary of SARS-CoV-2 breakthrough infections

No. of vaccinated (N = 18215)	No. of infected (N = 151)	No. of hospitalized (N = 87)	No. of dead (N = 14)	Breakthrough infection rate (%)
870	2	1	0	0.23
1640	7	5	1	0.43
2350	13	7	3	0.55
459	3	1	0	0.65
3457	24	14	1	0.69
1432	10	6	1	0.70
133	1	1	1	0.75
891	7	1	1	0.79
629	5	3	0	0.79
1072	10	3	0	0.93
904	9	2	0	1.00
350	4	3	1	1.14
2292	27	23	1	1.18
847	11	8	4	1.30
360	6	0	0	1.67
212	4	3	0	1.89
317	8	6	0	2.52

No., number; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Of 101 million fully vaccinated adults in the United States through April 30, 2021, Centers for Disease Control and Prevention reported 10262 breakthrough infections (0.0102%), 995 with associated hospitalization (0.00099%) and 160 with associated death (0.00016%).[3] Compared with the general population, SOTRs in our study had an 82-fold higher risk of breakthrough infection and 485-fold higher risks of breakthrough infection with associated hospitalization and death.

There are a number of limitations to this study. First, enumerating the population of fully vaccinated SOTRs is challenging, and, in most cases, these numbers should be viewed as estimates. That said, even if there were an estimation error as extreme as twice as many vaccinated SOTRs, the risk of breakthrough infections would still be 41-fold higher than the general population. Second, despite potential ascertainment bias in SOTRs, many centers expressed to us the possibility of not fully capturing all SARS-CoV-2 infections in their SOTR population: patients could have been seen at other hospitals, seen by nontransplant providers at the same hospital, or tested positive in the community without informing their transplant centers. As such, the number of breakthrough infections is likely an underestimate.

Our main finding is that, compared with the general population, SOTRs have lower protection from SARS-CoV-2 infection after vaccination. This emphasizes the clinical relevance of a growing literature describing decreased immunogenicity in this population and highlights the critical need to better understand and improve vaccine response.[4,5] For now, it is clear that SOTRs should continue to practice all recommended safety precautions such as masks and distancing, household contacts should be vaccinated if at all possible, priority should be given to vaccination pretransplantation, and other interventions for potential protection should be explored.

However, another important question is whether SOTRs benefit from vaccination: rather than comparing vaccinated SOTRs with the vaccinated general population, it is also important to compare vaccinated SOTRs with unvaccinated SOTRs. Any comparisons are inherently limited by temporal and treatment bias, but it does seem that standard vaccination provides protection: the majority of SOTRs produce some antibodies, the breakthrough infection rate in our study is lower than reported de novo infection rates as high as 5% in unvaccinated SOTRs,[6] and the mortality rate from breakthrough infections in our study is lower than the commonly reported mortality of 20.5% from de novo infections in unvaccinated SOTRs.[7] Finally, there is growing evidence that boosters will ultimately improve vaccine effectiveness even further. As such, vaccination is critically important and should be prioritized in all SOTRs.

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