



Immunologic response to SARS-CoV-2 mRNA vaccination in pediatric kidney transplant recipients

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Abstract

Background COVID-19 disease in kidney transplant (KT) recipients is associated with increased morbidity, mortality, and hospitalization rates. Unfortunately, KT recipients also have a reduced response to SARS-CoV-2 immunization. The primary aim of this study was to assess immunologic response to SARS-CoV-2 mRNA vaccines in pediatric kidney transplant recipients 12–18 years of age. Secondary aims were to assess response rates following a third immunization and determine factors that influence immunization response.

Methods Pediatric KT recipients in a single tertiary center received SARS-CoV-2 mRNA vaccination as per local protocol. SARS-CoV-2 immunoglobulin (IgG) was measured following second and/or third vaccination. Demographics including patient factors (age, gender, and underlying disease), transplant factors (time and type of transplant), and immunosuppression (induction, maintenance, and immunomodulatory therapies such as IVIG) were collected from the medical records.

Results Of 20 participants, 10 (50%) responded following a two-dose vaccine schedule, which increased to 15 (75%) after three doses. Maintenance immunosuppression affected immunologic response, with azathioprine demonstrating a higher rate of response to vaccine compared to mycophenolate (100% vs. 38%, $p = 0.04$). Increasing prednisolone dose had a negative impact on immunologic response (0.01 mg/kg/day increase: OR 1.60 95% CI 1.01 to 2.57). Tacrolimus dose and trough levels, age, time post-transplant, underlying disease, and other immunosuppression did not impact immunologic response.

Conclusions Pediatric KT recipients had similar response rates following SARS-CoV-2 immunization as adult KT recipients. Immunologic response improved following a third immunization. Choice of antimetabolite and prednisolone dosing influenced the rate of response.

Keywords Pediatric · Kidney · Transplantation · COVID · Vaccination · Immune response

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Introduction

The current COVID-19 pandemic has had a significant impact on clinical practice in adult and pediatric medicine. Importantly, it has facilitated rapid approval and implementation of new immunizations, including mRNA vaccines.

COVID-19 disease is caused by SARS-CoV-2. Clinical presentation is predominated by upper respiratory tract symptoms and children generally exhibit a milder disease when compared with adults [1]. In 2020, it was noted that a small proportion of children were affected by a multisystem inflammatory syndrome, similar to Kawasaki disease [2]. There is increasing evidence that some children may demonstrate persistent symptoms following the acute phase of their COVID-19 illness, referred to as long COVID. These symptoms include fatigue, dyspnea, reduced exercise tolerance, and palpitations and have been reported by up to 50% of children more than 2 months after their initial diagnosis [3, 4].

Adult kidney transplant (KT) recipients have a greater risk of severe disease associated with SARS-CoV-2 with significantly higher mortality and hospitalization rates when compared to healthy individuals [5, 6]. Factors associated with increased fatality include abnormal/worsening kidney function, advanced age, tachypnea, and use of prednisolone prior to presentation [5, 7, 8]. Data in pediatric KT recipients is limited. Small cohort studies suggest COVID-19 disease is mild in pediatric KT recipients with predominantly upper respiratory symptoms and reversible acute kidney injury [9, 10]. Given COVID-19's variable presentation and potential for significant morbidity and mortality, it is important to ensure immunocompromised individuals are appropriately vaccinated against SARS-CoV-2.

SARS-CoV-2 vaccines have been shown to be safe and efficacious in lowering the rates of SARS-CoV-2 infection, intensive care unit (ICU) admissions, and death in previously healthy adults [11, 12]. This data has been replicated in adult KT recipients. A single center study in Spain demonstrated that of the 117 detected infections in immunized KT recipients, 88% (103) occurred prior to immunization [13].

Studies in adult KT recipients suggest weaker humoral and cellular immune responses to these vaccines resulting in poor immunologic response rates and suboptimal protection to SARS-COV-2 when compared to the healthy population [14–17]. There is little data in pediatric KT recipients; however, several small cohort studies of adolescents and young adults have demonstrated similar absence of antibodies post-SARS-COV-2 immunizations [18, 19]. Factors associated with poor response rates following

a two-dose vaccination schedule include advanced age, immunization within 12 months of transplantation, non-mRNA vaccines, use of mycophenolate mofetil (MMF), or use of more than two immunosuppressant agents [17, 20].

Given the poor response rates following a two-dose immunization schedule, many countries, including Australia, have implemented a three-dose regimen for immunocompromised individuals, including children [21–23].

Our primary aim was to assess the response rates to SARS-CoV-2 mRNA vaccination in pediatric KT recipients following a two-dose vaccination schedule. Our secondary aims included assessing factors that impact response rates following a two-dose regimen and immunologic response rates following a third immunization.

Ethics approval

This study was approved by local human ethics research committee and research governance (2019/ETH05919).

Materials and methods

KT recipients aged 12–18 years, who received the second dose of BNT162b2 mRNA vaccine (Pfizer), between August 2021 and January 2022, were eligible for the study. Exclusion criteria included previous COVID-19 illness, transition to adult services, and lack of consent or inability to be tested during lockdown. Immunizations were administered as per standard local protocol and following a national guideline, with a second dose 3 weeks after the first, and a third dose 8 weeks after the second dose [21].

Participant's age, gender, primary diagnosis, donor type, time from transplant, induction and maintenance immunosuppression, additional immune-modulating therapy (including rituximab, immunoglobulin (IVIG), anti-thymocyte globulin (ATG), and tocilizumab), and prior COVID-19 infection were recorded (self-reported or from electronic medical records).

The presence of SARS-CoV-2 immunoglobulin G (IgG) in serum was measured at 4–8 weeks post the second and third dose of mRNA immunization as a part of routine care. SARS-CoV-2 IgG was measured using the Vidas® (BioMérieux, Sydney, Australia) enzyme-linked fluorescence assay which determines an index of the relativity fluorescence value (RFV) of patient RFV to background RFV. A negative result was defined as an index less than one and a positive result as an index greater than or equal to one. This assay was directed against the SARS-Cov-2 spike protein and therefore did not differentiate between natural infection and vaccination, but participants were excluded from the study if they had had proven (by rapid antigen test or PCR) COVID-19 infection.

Continuous variables were reported as a mean and standard deviation (SD) and mean differences between vaccine response groups assessed using *t*-test. Categorical variables were reported as proportions, with a Fisher exact test used to assess differences between groups. To investigate the association with immunologic response (defined as positive SARS-CoV-2 IgG result) following second dose, we used logistic regression. Statistical analysis was conducted using STATA.

Results

Of 46 eligible participants, 25 were excluded due to inability to present to our tertiary center for testing, presentation for testing outside the specified time, inability to provide consent and one was excluded due to previous COVID-19 illness. Twenty participants were included in the study and completed SARS-CoV-2 IgG testing after their second, third, or both doses of vaccines. SARS-CoV-2 IgG results were obtained a median of 38.5 days (IQR 32.5–57.5) after the second dose and 44 days (IQR 40–52) after the third dose. Vaccines were well-tolerated with no adverse reactions reported during follow-up visits.

The median age of participants at administration of the second vaccine was 15 years (IQR 12–16). The median time of post-kidney transplantation at second vaccination was 11 years (range 2 months to 14 years) with two participants receiving immunizations within 6 months of transplant. Induction immunosuppression for all participants was standard with basiliximab, methylprednisolone, tacrolimus, and MMF. All participants were managed with a three-agent maintenance immunosuppression protocol. This included prednisolone, an antimetabolite (MMF or azathioprine), and tacrolimus. Prednisolone doses ranged from 0.06 to 0.2 mg/kg/day, depending on clinician preference, patient tolerance, and ease of administration. Fourteen (70%) participants were managed with MMF and the remainder with azathioprine (30%). Participants on azathioprine had been changed from MMF due to poor tolerance, including persistent diarrhea and/or lymphopenia. All participants were managed with tacrolimus, dose ranged from 0.02 to 0.22 mg/kg/day and was guided by trough tacrolimus levels, aiming for 5–7 for those greater than 12 months post-transplant and 6–8 for those less than 12 months post-transplant. No participants developed COVID-19 disease during the study. The cohort demographics are shown in Table 1.

Of the 20 included participants, 18 had SARS-CoV-2 IgG levels recorded post their second dose of vaccine and a total of 10 (50%) had detectable IgG. Of the 8 participants who did not respond, 5 had SARS-CoV-2 IgG assessed post their third vaccine and 3 demonstrated positive results (see Fig. 1). Two participants did not have SARS-CoV-IgG

Table 1 Demographics of the entire cohort

Patient demographics	Participants <i>N</i> =20
	Number (%) or mean (SD) or median (IQR)
Sex	
Female	7 (35)
Age at second dose	15 (12–16)
Year post-transplant	11 (5–14)
Transplant	
Living donor	14 (70)
Cause of kidney failure	
CAKUT	7 (35)
Glomerular disease	7 (35)
Cystic kidney disease	4 (19)
Other	2 (10)
Antimetabolite	
MMF	14 (70)
Azathioprine	6 (30)
Immunosuppressant dose (mg/kg/day)	
Tacrolimus	0.1 (0.1)
MMF	21 (3.8)
Azathioprine	1.7 (0.4)
Prednisolone	0.1 (0.04)
Drug level	
Tacrolimus level (mean tacrolimus level over preceding 3 months)	6.3 (1.9)
Additional immune-modulating therapy	
Rituximab	2 (10)
ATG	1 (5)
Tocilizumab	4 (20)
IVIG	6 (30)

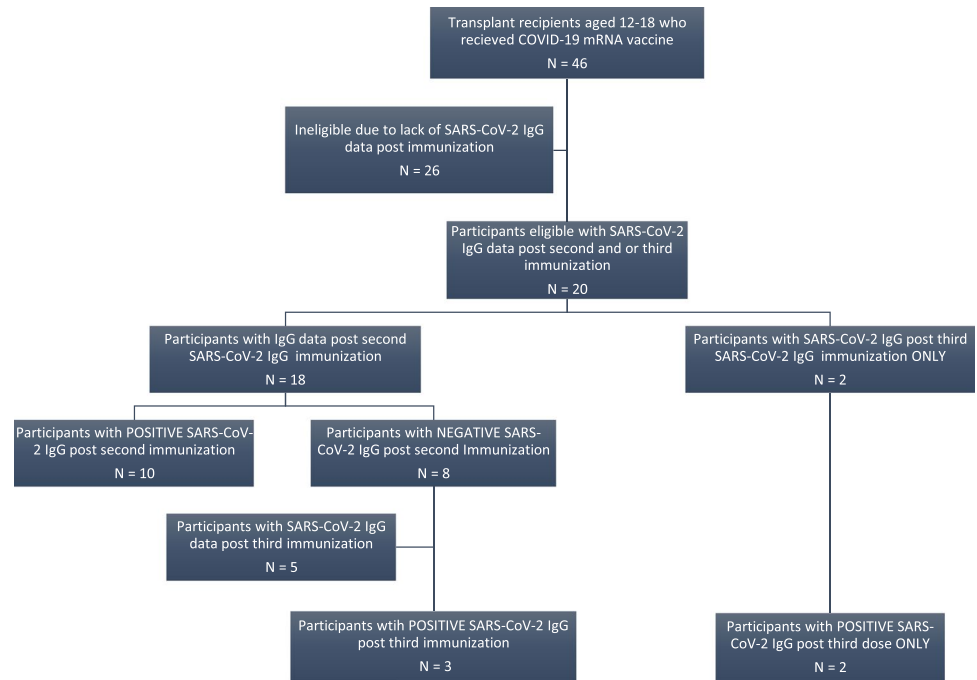
CAKUT, congenital anomalies of the kidney and urinary tract; *MMF*, mycophenolate mofetil; *ATG*, anti-thymocyte globulin; *IVIG*, intravenous immunoglobulin

measured post their second vaccine but did demonstrate a positive IgG following their third dose (see Fig. 1). In total, 15 (75%) participants demonstrated immunologic response following completion of a 3-dose regimen.

The data of the 18 participants who had SARS-CoV-IgG measured post their second dose of vaccine was further analyzed. Sex, age, time post-transplant, type of transplant, underlying kidney disease, and use of other immune-modulating therapy (rituximab, IVIG, tocilizumab, and ATG) did not differ between those with positive and those with negative IgG following two-dose regimen (see Table 2).

All participants received tacrolimus and prednisolone as part of their maintenance immunosuppression. Tacrolimus levels were higher in participants who did not respond following their second vaccine, but neither the drug level nor tacrolimus dose (mg/kg/day) in each group reached

Fig. 1 Patient flow diagram



statistical significance. Similarly, mycophenolate use and dose (mg/kg/day) did not differ between the two groups.

When compared with MMF, azathioprine demonstrated a statistically significant positive correlation with immunologic response ($p = 0.04$). Of the six participants who received azathioprine as part of their maintenance immunosuppression, only five were tested after their second vaccination, all of whom had a positive IgG result following a two-dose regimen (see Fig. 1 and Table 2).

The mean dose of prednisolone was significantly lower in the group who did respond to vaccination compared to the KT recipients who did not (0.1 vs. 0.13 mg/kg/day, $p = 0.01$). Univariate logistic regression found increases in prednisolone dose increased the chance of non-response to two doses of vaccination (0.01 mg/kg/day increase: OR 1.60 95% CI 1.01 to 2.57).

Additional immune-modulating therapies were utilized in several participants because of rejection episodes. Two participants received rituximab (both more than 12 months prior to immunization), one that had a positive SARS-CoV-2 IgG result post their second vaccine. One participant received ATG (again more than 12 months prior to immunization) and did not demonstrate an immune response following a two-dose vaccine schedule. Tocilizumab was administered monthly to four participants between 1 and 11 months prior to immunization. Fifty percent of these individuals demonstrated a positive SARS-CoV-2 IgG result post their second vaccine. The two participants with a negative IgG received their most recent tocilizumab dose 1 and 11 months prior to their immunization. Finally, six participants received IVIG between 1 and 18 months prior to immunization (see

Table 2). Three (50%) demonstrated a positive IgG result post their second immunization and received IVIG between 1 and 16 months prior. Similarly, those who demonstrated a negative IgG result received IVIG between 2 and 18 months prior.

Discussion

This retrospective study of pediatric KT recipients demonstrated a 50% immunologic response rate following a two-dose schedule with a SARS-CoV-2 mRNA vaccination. This improved to 75% following a third immunization. The use of mycophenolate rather than azathioprine and increments in prednisolone dose were both associated with poor immunologic response; however, given the small sample size, it is possible that other factors may have impacted vaccine response.

An inadequate and variable response to standard two-dose immunization schedules to SARS-COV-2 in KT recipients has been well-documented in the adult population [16, 17, 24, 25]. In one cohort, immunosuppressed KT recipients did not develop immunity to COVID-19 following a standard immunization course. Only 1 out of 40 had detectable levels of IgG and this was due to post-COVID-19 disease rather than immunization [26]. Other reports cite response rates between 36 and 60% [27–32].

Immune responses to COVID-19 vaccinations have not been as widely assessed in pediatric KT recipients. A single center cohort study of adolescent patients (aged 18–20) who received BNT162b2 demonstrated a 52% positive spike

Table 2 Comparison of pediatric KT recipients who seroconverted post second dose of immunization, statistically significant results in bold ($N=18$, excluding individual with history of COVID-19 infection)

Analysis of variables and their potential impact on immune response to two-dose immunization regimen			
Variable	IgG positive, N (%) or mean (SD)	IgG negative, N (%) or mean (SD)	p value
Total	10	8	
Sex			
Female	4 (40)	3 (38)	0.9
Transplant			
Living donor	6 (60)	6 (75)	0.50
Age at second dose	15 (1.3)	15 (1.8)	0.85
Year post-transplant	8 (3.9)	7 (4.8)	0.5
Cause of kidney failure			0.7
CAKUT			
Glomerular disease			
Cystic disease			
Other			
Tacrolimus:			
Dose (mg/kg)	0.11 (0.1)	0.13 (0.2)	0.05
Tacrolimus level	6 (1.1)	7.1 (2.7)	0.19
Antimetabolite			0.04
MMF number	5 (50)	8 (100)	
Azathioprine number	5 (50)	0	
MMF dose (mg/kg/day)	21 (2.1)	21 (4.9)	0.93
Azathioprine dose (mg/kg/day)	1.6 (0.5)	0 (0)	
Prednisolone			
Dose (mg/kg/day)	0.1 (0.02)	0.13 (0.04)	0.01
Rituximab			
Number	1(50)	1(50)	0.9
IVIG			
Number	3 (50)	3 (50)	0.7
ATG			
Number	0 (0)	1 (100)	
Tocilizumab			
Number	2 (50)	2 (50)	0.8

CAKUT, congenital anomalies of the kidney and urinary tract; MMF, mycophenolate mofetil; ATG, anti-thymocyte globulin; IVIG, intravenous immunoglobulin

antibody following a two-dose schedule with no adverse events [18]. A similar study of adolescents who received the same vaccine (aged 18 ± 3 years) demonstrated a slightly higher immune response of 63% (vs. 100% in healthy matched controls) with mild to moderate adverse reactions (primarily local reaction) but no episodes of myocarditis or cardiac side effects [19]. Quantitative antibody levels were obtained and noted to be almost 30 times higher in healthy children when compared to transplant recipients [19]. Our study demonstrated a similar rate (58%) of immunologic response following the second dose of vaccination in a younger cohort of children.

Given the poor rates of immunologic response, a three-dose regimen for immunocompromised individuals has been implemented, and was reported to be associated

with a marked improvement in immunologic response in KT recipients [33–36]. In a French cohort of 78 adult KT recipients, SARS-COV-2 antibodies were detected in 40% of patients following the second dose compared to 68% following the third dose [34]. These studies are consistent with our results, with immunologic response rates improving from 50 to 75% following a third dose of vaccination. Unfortunately, we were unable to quantify the level of IgG antibody due to lack of a suitable assay.

Lack of immunologic response after two-dose vaccination in KT recipients has been associated with advanced age (> 60 years), transplantation within 12 months, use of MMF, B cell depletion (e.g. rituximab), and use of non-mRNA vaccines [17–19, 29–32, 37].

In our cohort, six participants were managed on azathioprine (rather than MMF) and five of these had a SARS-CoV-2 IgG level available following their second vaccination. One hundred percent of these five participants demonstrated a positive SARS-CoV-2 IgG, which was significantly greater than those who received MMF (38%) (p value = 0.04). We acknowledge that while this is statistically significant, it is a small sample and we are lacking data from one individual on azathioprine (who only had an IgG level available following the third dose). Recent cohort studies have demonstrated similar phenomena, where MMF was associated with poor immunologic response and decreased response rates by up to 81% [18, 27]. Mean MMF dose was not statistically different between the groups of responders and non-responders in our cohort. This is not consistent with previous reports, where there appears to be a dose-dependent effect of MMF, with KT recipients with a higher dose per kilogram or greater MMF level demonstrating a poor immune response [27, 37]. This effect is not isolated to SARS-CoV-2 immunizations. MMF has been implicated in inadequate response to oral cholera, influenza, and the 13-valent pneumococcal vaccines [38–40].

Increments in prednisolone dose were associated with a reduced immunologic response. This is similar to previous studies which found the use of prednisolone in maintenance immunosuppression has been associated with a poor response in KT recipients [30, 41]. A dose-related effect, however, has not previously been documented.

Interestingly, time post-transplantation did not affect the response rates in this cohort as has been demonstrated in previous studies with vaccination within 12 months of transplantation negatively impacting immunologic response [20]. The use of rituximab, tocilizumab, IVIG, and/or ATG also did not influence immune response in this cohort; however, the sample sizes for these factors were small. Only two participants received rituximab in the past and both more than 12 months prior to immunization. Rituximab has been shown to reduce immunization effectiveness, particularly SARS-CoV-2 immunization; however, this was assessed when utilized within 12 months [14, 19, 32].

The primary limitation of this study was sample size, particularly relating to other immunomodulatory therapies such as rituximab, IVIG, ATG, and tocilizumab. This limits the ability to detect significant associations between patient characteristics, immunosuppressive regimens, and immunologic response. Further limitations include the lack of quantitative SARS-CoV-2 IgG data, which were not available at the time of the study. Quantitative data

would have provided an opportunity to comment on the effect of immunosuppression (when compared to the general population).

Conclusion

In summary, this study provides additional information on immune responses to COVID vaccination in pediatric KT recipients aged 12–18. Immunologic response rates were similar to other pediatric and adult KT cohorts (50% and 75% following second and third vaccine dose, respectively). Factors associated with poor immunologic response included prednisolone dose and MMF use, whereas age, sex, underlying kidney disease, and time from transplant did not impact the outcome.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s00467-022-05679-y>.

Declarations The authors declare no competing interests.

References

1. Cui X, Zhao Z, Zhang T, Guo W et al (2021) A systematic review and meta-analysis of children with coronavirus disease 2019 (COVID-19). *J Med Virol* 93:1057–1069. <https://doi.org/10.1002/jmv.26398>
2. Cheung EW, Zachariah P, Gorelik M, Boneparth A et al (2020) Multisystem inflammatory syndrome related to COVID-19 in previously healthy children and adolescents in New York City. *JAMA* 324:294–296. <https://doi.org/10.1001/jama.2020.10374>
3. Asadi-Pooya AA, Nemati H, Shahisavandi M, Akbari A et al (2021) Long COVID in children and adolescents. *World J Pediatr* 17:495–499. <https://doi.org/10.1007/s12519-021-00457-6>
4. Buonsenso D, Munblit D, De Rose C, Sinatti D et al (2021) Preliminary evidence on long COVID in children. *Acta Paediatr* 110:2208–2211. <https://doi.org/10.1111/apa.15870>
5. Hilbrands LB, Duijvenvoorden R, Vart P, Franssen CFM et al (2020) COVID-19-related mortality in kidney transplant and dialysis patients: results of the ERACODA collaboration. *Nephrol Dial Transplant* 35:1973–1983. <https://doi.org/10.1093/ndt/gfaa261>
6. Vaid N, Ardissino M, Reed TAN, Goodall J et al (2021) Clinical characteristics and outcomes of immunosuppressed patients hospitalized with COVID-19: experience from London. *J Intern Med* 289:385–394. <https://doi.org/10.1111/joim.13172>
7. Williamson EJ, Walker AJ, Bhaskaran K, Bacon S et al (2020) Factors associated with COVID-19-related death using OpenSAFELY. *Nature* 584:430–436. <https://doi.org/10.1038/s41586-020-2521-4>
8. Akalin E, Azzi Y, Bartash R, Seethamraju H et al (2020) COVID-19 and kidney transplantation. *N Engl J Med* 382:2475–2477. <https://doi.org/10.1056/NEJMc2011117>

9. Marlais M, Wlodkowski T, Vivarelli M, Pape L et al (2020) The severity of COVID-19 in children on immunosuppressive medication. *Lancet Child Adolesc Health* 4:e17–e18. [https://doi.org/10.1016/s2352-4642\(20\)30145-0](https://doi.org/10.1016/s2352-4642(20)30145-0)
10. Melgosa M, Madrid A, Álvarez O, Lumbreras J et al (2020) SARS-CoV-2 infection in Spanish children with chronic kidney pathologies. *Pediatr Nephrol* 35:1521–1524. <https://doi.org/10.1007/s00467-020-04597-1>
11. Polack FP, Thomas SJ, Kitchin N, Absalon J et al (2020) Safety and Efficacy of the BNT162b2 mRNA COVID-19 Vaccine. *N Engl J Med* 383:2603–2615. <https://doi.org/10.1056/NEJMoa2034577>
12. Thomas SJ, Moreira ED Jr, Kitchin N, Absalon J et al (2021) Safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine through 6 months. *N Engl J Med* 385:1761–1773. <https://doi.org/10.1056/NEJMoa2110345>
13. Bestard O, Jouve T, Castells L, Lopez M et al (2021) Reconciling short-term clinical and immunological outcomes of SARS-CoV-2 vaccination in solid organ transplant recipients. *Am J Transplant* 22:673–675. <https://doi.org/10.1111/ajt.16855>
14. Prendecki M, Thomson T, Clarke CL, Martin P et al (2021) Immunological responses to SARS-CoV-2 vaccines in kidney transplant recipients. *Lancet* 398:1482–1484. [https://doi.org/10.1016/s0140-6736\(21\)02096-1](https://doi.org/10.1016/s0140-6736(21)02096-1)
15. Bertrand D, Hamzaoui M, Lemée V, Lamulle J et al (2021) Antibody and T-cell response to a third dose of SARS-CoV-2 mRNA BNT162b2 vaccine in kidney transplant recipients. *Kidney Int* 100:1337–1340. <https://doi.org/10.1016/j.kint.2021.09.014>
16. Benning L, Morath C, Bartenschlager M, Nussbag C et al (2022) Neutralization of SARS-CoV-2 variants of concern in kidney transplant recipients after standard COVID-19 vaccination. *Clin J Am Soc Nephrol* 17:98–106. <https://doi.org/10.2215/cjn.11820921>
17. Russo G, Lai Q, Poli L, Perrone MP et al (2022) SARS-COV-2 vaccination with BNT162B2 in renal transplant patients: risk factors for impaired response and immunological implications. *Clin Transplant* 36:e14495. <https://doi.org/10.1111/ctr.14495>
18. Crane C, Phebus E, Ingulli E (2021) Immunologic response of mRNA SARS-CoV-2 vaccination in adolescent kidney transplant recipients. *Pediatr Nephrol* 37:449–453. <https://doi.org/10.1007/s00467-021-05256-9>
19. Haskin O, Ashkenazi-Hoffnung L, Ziv N, Borovitz Y et al (2021) Serological response to the BNT162b2 COVID-19 mRNA vaccine in adolescent and young adult kidney transplant recipients. *Transplantation* 105:e226–e233. <https://doi.org/10.1097/tp.0000000000003922>
20. Correia AL, Leal R, Pimenta AC, Fernandes M et al (2022) The type of SARS-CoV-2 vaccine influences serological response in kidney transplant recipients. *Clin Transplant* 36:e14585. <https://doi.org/10.1111/ctr.14585>
21. Australian Government. Department of Health and Aged Care (2022) ATAGI recommendations on the use of a third primary dose of COVID-19 vaccine in individuals who are severely immunocompromised. <https://www.health.gov.au/sites/default/files/documents/2022/04/atagi-recommendations-on-the-use-of-a-third-primary-dose-of-covid-19-vaccine-in-individuals-who-are-severely-immunocompromised.pdf>
22. UK Kidney Association (2021) Updated COVID-19 guidance for children with kidney disease on dialysis, and immunosuppression (including kidney transplants). <https://ukkidney.org/sites/renal.org/files/BAPN/BAPN%20Covid%20advice%20for%20Children%20and%20Young%20People%20Dec%202021%20final.pdf>
23. American Society of Transplantation (2022) Joint Statement about COVID-19 Vaccination in Organ Transplant Candidates and Recipients. <https://www.myast.org/joint-statement-about-covid-19-vaccination-organ-transplant-candidates-and-recipients>
24. Sanders JF, Bemelman FJ, Messchendorp AL, Baan CC et al (2021) The RECOVAC Immune-response Study: the immunogenicity, tolerability, and safety of COVID-19 vaccination in patients with chronic kidney disease, on dialysis, or living with a kidney transplant. *Transplantation* 106:821–834. <https://doi.org/10.1097/tp.0000000000003983>
25. Danthu C, Hantz S, Dahlem A, Duval M et al (2021) Humoral response after SARS-CoV-2 mRNA vaccination in a cohort of hemodialysis patients and kidney transplant recipients. *J Am Soc Nephrol* 32:2153–2158. <https://doi.org/10.1681/asn.2021040490>
26. Rincon-Arevalo H, Choi M, Stefanski AL, Halleck F et al (2021) Impaired humoral immunity to SARS-CoV-2 BNT162b2 vaccine in kidney transplant recipients and dialysis patients. *Sci Immunol* 6:1031. <https://doi.org/10.1126/sciimmunol.abj103110.1126/sciimmunol.abj1031>
27. Rozen-Zvi B, Yahav D, Agur T, Zingerman B et al (2021) Antibody response to SARS-CoV-2 mRNA vaccine among kidney transplant recipients: a prospective cohort study. *Clin Microbiol Infect* 27:1173.e1–1173.e4. <https://doi.org/10.1016/j.cmi.2021.04.028>
28. Marinaki S, Adamopoulos S, Degiannis D, Roussos S et al (2021) Immunogenicity of SARS-CoV-2 BNT162b2 vaccine in solid organ transplant recipients. *Am J Transplant* 21:2913–2915. <https://doi.org/10.1111/ajt.16607>
29. Fernández-Ruiz M, Almendro-Vázquez P, Carretero O, Ruiz-Merlo T et al (2021) Discordance between SARS-CoV-2-specific cell-mediated and antibody responses elicited by mRNA-1273 vaccine in kidney and liver transplant recipients. *Transplant Direct* 7:e794. <https://doi.org/10.1097/txd.0000000000001246>
30. Dębska-Ślizień A, Ślizień Z, Muchlado M, Kubanek A et al (2021) Predictors of humoral response to mRNA COVID19 vaccines in kidney transplant recipients: a longitudinal study-the COViNEPH Project. *Vaccines (Basel)* 9:1165. <https://doi.org/10.3390/vaccines9101165>
31. Prendecki M, Clarke C, Edwards H, McIntyre S et al (2021) Humoral and T-cell responses to SARS-CoV-2 vaccination in patients receiving immunosuppression. *Ann Rheum Dis* 80:1322–1329. <https://doi.org/10.1136/annrheumdis-2021-220626>
32. Magicova M, Zahradka I, Fialova M, Neskudla T et al (2022) Determinants of immune response to anti-SARS-CoV-2 mRNA vaccines in kidney transplant recipients: a prospective cohort study. *Transplantation* 106:842–852. <https://doi.org/10.1097/tp.0000000000004044>
33. Hall VG, Ferreira VH, Ku T, Ierullo M et al (2021) Randomized trial of a third dose of mRNA-1273 vaccine in transplant recipients. *N Engl J Med* 385:1244–1246. <https://doi.org/10.1056/NEJMc2111462>
34. Kamar N, Abravanel F, Marion O, Couat C et al (2021) Three doses of an mRNA COVID-19 vaccine in solid-organ transplant recipients. *N Engl J Med* 385:661–662. <https://doi.org/10.1056/NEJMc2108861>
35. Massa F, Cremoni M, Gérard A, Grabsi H et al (2021) Safety and cross-variant immunogenicity of a three-dose COVID-19 mRNA vaccine regimen in kidney transplant recipients. *EBioMedicine* 73:103679. <https://doi.org/10.1016/j.ebiom.2021.103679>
36. Charmetant X, Espi M, Barba T, Ovize A et al (2022) Predictive factors of a viral neutralizing humoral response after a third dose

- of COVID-19 mRNA vaccine. *Am J Transplant* 22:1442–1450. <https://doi.org/10.1111/ajt.16990>
37. Kantauskaite M, Müller L, Kolb T, Fischer S et al (2021) Intensity of mycophenolate mofetil treatment is associated with an impaired immune response to SARS-CoV-2 vaccination in kidney transplant recipients. *Am J Transplant* 22:634–639. <https://doi.org/10.1111/ajt.16851>
 38. Jonker EFF, Uijlings MAC, Visser LG, Soonawala D (2019) Comparison of the immunogenicity of Dukoral® oral cholera vaccine between renal transplant recipients on either a calcineurin inhibitor or mycophenolate - a controlled trial. *Vaccine* 37:3133–3139. <https://doi.org/10.1016/j.vaccine.2019.04.010>
 39. Salles MJ, Sens YA, Boas LS, Machado CM (2010) Influenza virus vaccination in kidney transplant recipients: serum antibody response to different immunosuppressive drugs. *Clin Transplant* 24:E17–E23. <https://doi.org/10.1111/j.1399-0012.2009.01095.x>
 40. Oesterreich S, Lindemann M, Goldblatt D, Horn PA et al (2020) Humoral response to a 13-valent pneumococcal conjugate vaccine in kidney transplant recipients. *Vaccine* 38:3339–3350. <https://doi.org/10.1016/j.vaccine.2020.02.088>
 41. Benotmane I, Gautier G, Perrin P, Olagne J et al (2021) Antibody response after a third dose of the mRNA-1273 SARS-CoV-2 vaccine in kidney transplant recipients with minimal serologic response to 2 doses. *JAMA* 326:1063–1065. <https://doi.org/10.1001/jama.2021.12339>

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