



ORIGINAL ARTICLE

Comparison of antibody response to SARS-CoV-2 after two doses of inactivated virus and BNT162b2 mRNA vaccines in kidney transplant

Mariana Seija ^{1,2,*}, Florencia Rammauro^{3,4,*}, José Santiago¹, Natalia Orihuela⁵, Catherine Zurberti⁵, Danilo Machado⁶, Cecilia Recalde⁶, Javier Noboa^{1,4}, Victoria Frantchez⁷, Rossana Astesiano¹, Federico Yandián¹, Ana Guerisoli¹, Álvaro Morra⁵, Daniela Cassinelli⁸, Cecilia Coelho⁸, Belén de Aramburu⁸, Paulina González-Severgnini⁸, Romina Moreno⁸, Aldana Pippolo⁸, Gabriela López⁹, Mónica Lemos⁹, Lorena Somariva⁹, Eliana López⁹, Soledad Fumero⁹, Carla Orihuela⁹, Rosalía Rodríguez⁶, Gonzalo Acuña⁶, Victoria Rabaza⁶, Nancy Perg⁶, Rossana Cordero⁶, Cristina Reinfeld⁶, Paula Olivera⁶, Paola Montero⁶, Cecilia Nogueira⁶, Catheryn Nalerio⁵, Sergio Orihuela⁵, Lilián Curi⁵, Ema Burgstaller⁶, Oscar Noboa¹, Otto Pritsch^{3,4}, Marcelo Nin^{1,5} and Sergio Bianchi ^{2,10}

¹Centro de Nefrología, Hospital de Clínicas, Facultad de Medicina, Universidad de la República, Montevideo, Uruguay, ²Departamento de Fisiopatología, Hospital de Clínicas, Facultad de Medicina, Universidad de la República, Montevideo, Uruguay, ³Laboratorio de Inmunovirología, Institut Pasteur de Montevideo, Montevideo, Uruguay, ⁴Departamento de Inmunobiología, Facultad de Medicina, Universidad de la República, Montevideo, Uruguay, ⁵Centro de Trasplante INU, Hospital Italiano, Montevideo, Uruguay, ⁶Centro de Trasplante, Hospital Evangélico, Montevideo, Uruguay, ⁷Cátedra de Enfermedades Infecciosas, Hospital de Clínicas, Facultad de Medicina, Universidad de la República, Montevideo, Uruguay, ⁸Students of Scientific Methods 2, Medical Doctor Degree, Facultad de Medicina, Universidad de la República, Montevideo, Uruguay, ⁹Departamento de Enfermería, Hospital de Clínicas, Facultad de Medicina, Universidad de la República, Montevideo, Uruguay and ¹⁰Laboratorio de Genómica Funcional, Institut Pasteur de Montevideo, Montevideo, Uruguay

*These authors contributed equally to this work.

Correspondence to: Sergio Bianchi; E-mail: sbianchi@fmed.edu.uy

Received: 6.9.2021; Editorial decision: 15.12.2021

© The Author(s) 2021. Published by Oxford University Press on behalf of the ERA. This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

ABSTRACT

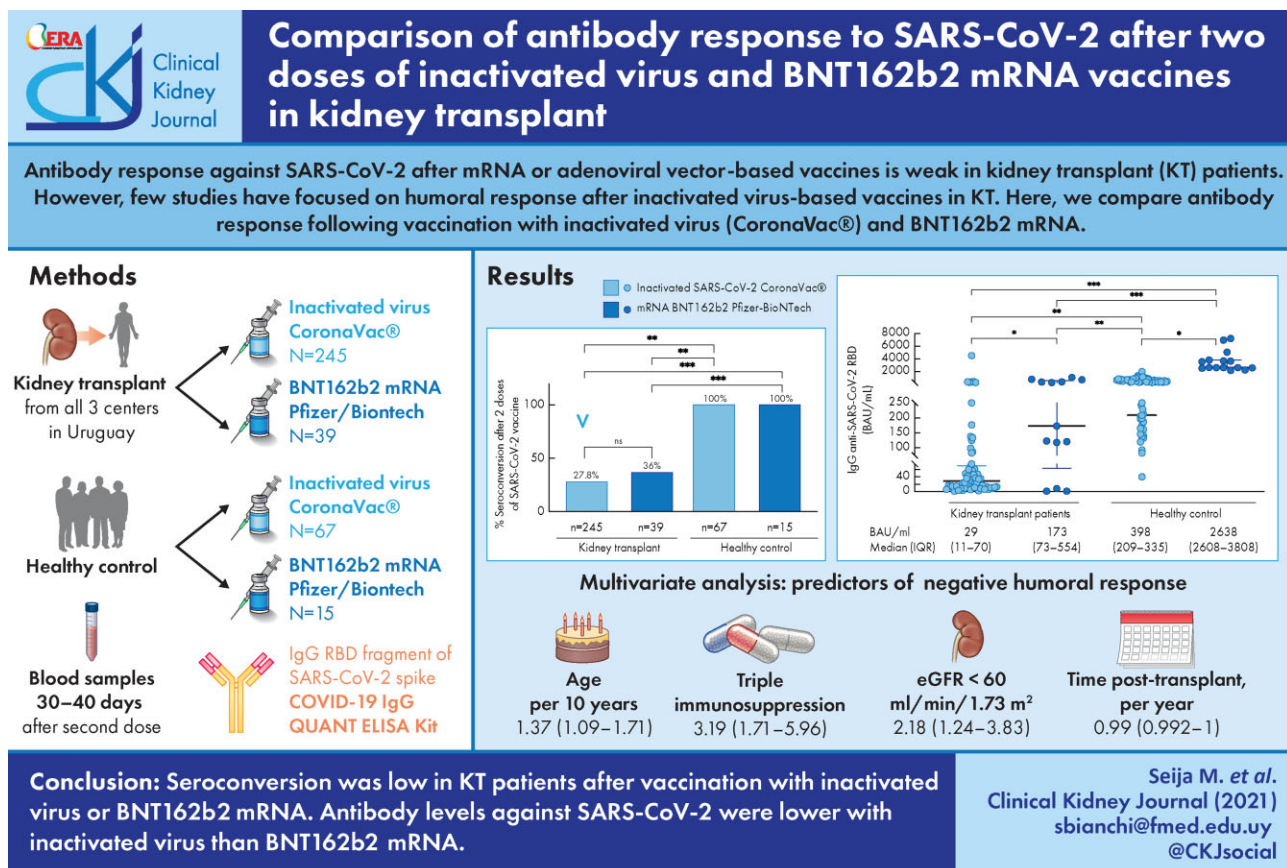
Background. Antibody response against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) after mRNA or adenoviral vector-based vaccines is weak in kidney transplant (KT) patients. However, few studies have focused on humoral response after inactivated virus-based vaccines in KT. Here, we compare antibody response following vaccination with inactivated virus (CoronaVac®) and BNT162b2 mRNA.

Methods. A national multicentre cross-sectional study was conducted. The study group was composed of patients from all KT centres in Uruguay, vaccinated between 1 and 31 May 2021 (CoronaVac®, $n = 245$ and BNT162b2, $n = 39$). The control group was constituted of 82 healthy individuals. Participants had no prior confirmed coronavirus disease 2019 (COVID-19) test. Blood samples were collected between 30 and 40 days after the second dose. Serum-specific immunoglobulin G (IgG) antibodies against the receptor-binding domain (RBD) of SARS-CoV-2 Spike protein were determined using the COVID-19 IgG QUANT ELISA Kit.

Results. Only 29% of KT recipients showed seroconversion (36.5% BNT162b2, 27.8% inactivated virus, $P = 0.248$) in comparison with 100% in healthy control with either vaccine. Antibody levels against RBD were higher with BNT162b2 mRNA than with inactivated virus [median (interquartile range) 173 (73–554) and 29 (11–70) binding antibody units (BAU)/mL, $P < 0.034$] in KT and 10 times lower than healthy control [inactivated virus: 308 (209–335) and BNT162b2: 2638 (2608–3808) BAU/mL, $P < 0.034$]. In multivariate analysis, variables associated with negative humoral response were age, triple immunosuppression, estimated glomerular filtration rate and time post-KT.

Conclusion. Seroconversion was low in KT patients after vaccination with both platforms. Antibody levels against SARS-CoV-2 were lower with inactivated virus than BNT162b2 mRNA. These findings support the need for strategies to improve immunogenicity in KT recipients after two doses of either vaccine.

GRAPHICAL ABSTRACT



INTRODUCTION

Kidney transplant (KT) patients are at high risk of severe severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection [1–5]. Hence, vaccination in this population is recommended. Recent evidence suggests that antibody response among solid organ transplant (SOT) patients is weak after two doses of mRNA-based vaccine or adenoviral vector platform [6–23]. However, only one study has addressed humoral response after inactivated virus-based vaccine in KT patients [24].

Inactivated virus vaccines are a well-known technology and have several advantages for large-scale utilization, including their stability at non-extreme refrigeration temperatures and their long lifespan [25]. These characteristics make them a useful tool in the global fight against coronavirus disease 2019 (COVID-19), although more data are needed on its efficacy in KT recipients. Furthermore, recently it has been approved by the European Medicine Agency for emergency use in Europe and to date, more than 750 000 000 have been administered in more than 40 countries [26, 27].

In Uruguay, the Ministry of Public Health approved inactivated SARS-CoV-2 (CoronaVac®, Sinovac Biotech Ltd) and BNT162b2 mRNA (Pfizer/BioNTech) vaccines for emergency use [28, 29]. Healthcare workers were vaccinated with BNT162b2 mRNA. SOT patients were prioritized and vaccinated according to age group (people between 18 and 70 years received inactivated virus-based and those over 70 years were vaccinated with BNT162b2 mRNA). CoronaVac® was administered to almost 70% of the Uruguayan population, including SOT patients, with a reduction of infection and intensive care admissions according to the Health Ministry Authority.

The aim of this work was to compare humoral response after inactivated virus and BNT162b2 mRNA vaccines in KT patients and evaluate adverse events associated with vaccination.

MATERIALS AND METHODS

We conducted a national multicentre cross-sectional study to evaluate humoral response after SARS-CoV-2 vaccination in KT patients. The study group was composed of KT recipients from all KT centres in Uruguay (INU-Hospital Italiano, Hospital Evangélico and Hospital de Clínicas). Inclusion criteria were age >18 years old, kidney or kidney-pancreas transplant, no prior confirmed COVID-19 and had a second dose of either vaccine, BNT162b2 mRNA or inactivated virus (CoronaVac®), between 1 and 31 May. The control group was constituted by 82 healthy individuals [40.2% men; median age 41 years, interquartile range (IQR) 33–49], without immunosuppression medication, no prior confirmed COVID-19 and have the second dose of either vaccine BNT162b2 mRNA (15 individuals, 40% men; median age 42 years, IQR 37–47) or inactivated virus (CoronaVac®) (67 individuals, 40.3% men; median age 41 years, IQR 30–49).

All subjects received two doses (30 µg each) of BNT162b2 mRNA or two doses (600 SU each) of inactivated virus, both 28 days apart, according to the recommendations of the Uruguayan National Health Authority. None of the participants had prior confirmed COVID-19. Clinical data were recorded. A questionnaire of adverse events was performed, including all symptoms 7 days after each dose, which included local side effects such as pain, redness, swelling and regional lymphadenopathy, and systemic side effects such as fever, chills, headache, fatigue, myalgia, arthralgia, nausea, vomiting and diarrhoea. Estimated glomerular filtration rate (eGFR) was calcu-

lated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula.

Blood samples were collected between 30 and 40 days after the second dose injection. Freshly collected blood in clot activator and gel tube was centrifuged (2500 r.p.m., 15 min). Sera were separated and stored at –20°C until analysis.

The level of serum-specific Immunoglobulin G (IgG) antibodies against the receptor-binding domain (RBD) of SARS-CoV-2 Spike protein was determined using the COVID-19 IgG QUANT ELISA Kit (developed by Universidad de la República, Institut Pasteur de Montevideo and ATGen Company), according to manufacturer's instruction. The assay has a sensitivity of 97.7% and specificity 96.2%. Quantitative test results were expressed in binding antibody units (BAU)/mL referring to the First WHO International Standard for anti-SARS-CoV-2 immunoglobulin (NIBSC code: 20/136) used for assay calibration. Seroconversion was defined as presence of specific IgG antibodies against the RBD.

The study was approved by the ethical institutional review board (MSP 3535533-956220).

Continuous variables were tested for normal distribution (Kolmogorov-Smirnov). Normally distributed variables were expressed as mean ± standard deviation (SD), non-normally distributed as median and interquartile range, and qualitative variables as number and percentage. Categorical variables were compared using Chi-squared statistic. Continuous variables were compared using t-test (normally distributed) or Kruskal-Wallis/Mann-Whitney (non-normally distributed).

Group analysis included two groups according to SARS-CoV-2 IgG antibodies status: positive or negative.

Binary logistic regression models for negative serology test risk were fitted including the significant variables in univariate analysis. $P < 0.05$ was considered statistically significant. IBM® SPSS® version 22 (Chicago, IL, USA) statistical software was used for statistical analyses and Graph Pad 8 for charts constructs.

RESULTS

Among 1400 KT patients in Uruguay, 284 KT recipients were included in this study. In addition, 82 healthy individuals were included as a control group. Both groups underwent serological testing for SARS-CoV-2-specific antibodies after two doses of inactivated virus or BNT162b2 mRNA vaccine. Baseline patients' characteristics are detailed in Table 1. Seroconversion was lower in KT patients than healthy control (29% versus 100%). Seroconversion in KT with BNT162b2 mRNA (36.5%) was higher than inactivated virus (27.8%), but without statistical significance ($P = 0.248$, Figure 1A).

Serum levels of anti-RBD IgGs were significantly higher in KT patients who received BNT162b2 mRNA compared with inactivated virus vaccine, with a median of 173 (73–554) and 29 (11–70) BAU/mL respectively ($P < 0.034$, Figure 1B). Compared with the healthy control group, KT had lower levels of antibody with either vaccine.

Seropositive patients for anti-RBD were significantly younger, had higher eGFR and lymphocyte count, and longer time since transplantation. With regard to immunosuppression treatment, these patients were less frequently on triple therapy (antimetabolite, calcineurin inhibitor and prednisone) and more often on everolimus treatment (Table 1).

In multivariate analysis, variables associated with negative humoral response were age [per 10 years, odds ratio 1.372 [95% confidence interval (CI) 1.097–1.715], $P = 0.006$], triple immunosuppression [3.197 (1.714–5.96), $P = 0.000$] and eGFR

Table 1. Clinical characteristics of patients according to IgG anti-RBD SARS-CoV-2 status after inactivated SARS-CoV-2 or BNT162b2 mRNA vaccine

Variable	IgG anti-RBD SARS-CoV-2		Total	P-value
	Negative	Positive		
N, (%)	204 (71)	80 (29)	284 (100)	
Type of vaccine, n (%)				
Inactivated SARS-CoV-2	179 (87.7)	66 (82.5)	245 (86.3)	0.335
mRNA BNT162b2	25 (12.5)	14 (17.5)	39 (17.3)	
Age years, median (IQR)	56 (45–73)	52 (39–72)	55 (43–72)	0.039
Sex, men n (%)	119 (59.5)	46 (58)	165 (59)	0.759
Comorbidities, n (%)				
Stroke	7 (4.5)	1 (1.8)	8 (3.8)	0.369
Ischaemic heart disease	17 (11)	4 (7.3)	21 (10)	0.433
Peripheral arteriopathy	4 (2.6)	0 (0)	4 (1.9)	0.229
Diabetes mellitus, n (%)	61 (30.2)	16 (20.3)	77 (27.4)	0.093
BMI	26.3 (23.1–35)	25.3 (22.3–35.2)	26 (22–35)	0.187
Type of transplant, n (%)				
Kidney	194 (95)	78 (98)	272 (95)	0.365
Kidney–pancreas	10 (5)	2 (2)	12 (4.2)	
Time of transplant months, median (IQR)	57 (29–221)	76 (37–263)	61 (32–230)	0.061
Patients in the first year of transplant, n (%)	19 (9.4)	7 (8.9)	26 (9.3)	0.887
Triple immunosuppression, n (%)	167 (82.7)	48 (68.8)	215 (76.5)	0.000
Antimetabolite, n (%)				0.000
None	19 (9.5)	21 (25.6)	40 (14.3)	
Mycophenolate	178 (88.6)	48 (60.8)	226 (80.7)	
Azathioprine	4 (2)	10 (12.7)	14 (5)	
Calcineurin inhibitors, n (%)				0.023
None	5 (2.5)	8 (10.1)	13 (4.6)	
Tacrolimus	166 (82.2)	60 (75.9)	226 (80.4)	
Cyclosporine	31 (15.3)	11 (13.9)	42 (16.9)	
Prednisone, n (%)	192 (95)	71 (89.9)	263 (93.6)	0.111
Everolimus, n (%)	18 (9)	22 (27.8)	40 (14.3)	0.000
Rituximab, n (%)	3 (1.5)	0 (0)	3 (1.1)	0.274
Thymoglobulin, n (%)	29 (14.6)	9 (11.4)	38 (13.7)	0.477
Rejection in last 3 months, n (%)	6 (3)	2 (2)	8 (2.9)	0.838
Lymphocyte count, cells/ μ L, median (IQR)	1900 (1400–3696)	2213 (1740–4200)	2000 (1454–3820)	0.09
Serum creatinine μ mol/L, median (IQR)	124 (101–1414)	112 (91–241)	120 (97–352)	0.020
eGFR mL/min/1.73 m ² , mean \pm SD	50.3 \pm 23	58.4 \pm 22	52 \pm 22	0.011

BMI, body mass index; triple immunosuppression, antimetabolite + calcineurin inhibitor + prednisone.

Table 2. Binary logistic regression model of predictors of negative humoral response 30 days after two doses of inactivated SARS-CoV-2 or BNT162b2 mRNA vaccine

Predictor	Odd ratio	95% CI	P-value
Immunosuppression			
Other	Ref		
Triple immunosuppression	3.197	1.714–5.962	0.000
Age, per 10 years old	1.372	1.097–1.715	0.006
eGFR			
≥ 60 mL/min/1.73 m ²	Ref		
< 60 mL/min/1.73 m ²	2.184	1.243–3.838	0.007
Time after KT, per year	0.996	0.992–1.000	0.034

Triple immunosuppression, antimetabolite + calcineurin inhibitor + prednisone.

< 60 mL/min/1.73 m² [2.18 (1.24–23.83), $P = 0.007$], whereas time post-KT was negatively associated with negative humoral response [0.996 (0.992–1)] (Table 2).

The most frequent adverse event with each vaccine dose was pain at the site of injection, with significant difference between platforms (24% CoronaVac[®] and 48% mRNA, $P < 0.05$). Other less

frequent events were headache, arthralgia, myalgia and pruritus, without difference in frequency comparing the first with the second dose. There were no severe side-effects reported in this cohort (Figure 2).

DISCUSSION

Prior studies have shown low seroconversion after two doses of mRNA and viral vector-based vaccines [6–23]. To our knowledge, this is the first study that analyses the humoral response after two doses of inactivated SARS-CoV-2 vaccine in KT patients. Only 29% of KT recipients had antibody response against SARS-CoV-2 vaccine, in contrast to 100% of healthy controls. There was no difference in seroconversion between the two vaccine platforms analysed. Nonetheless, mean antibody titres were higher with mRNA-based vaccine than with inactivated SARS-CoV-2 platform.

These findings agree with previous studies that report a seroconversion between 10% and 40% with mRNA-based vaccine [6–8, 17–23]. In concordance with other studies, mean antibody titres in KT patients were up to 10 times lower than healthy controls [17]. There is only one study that

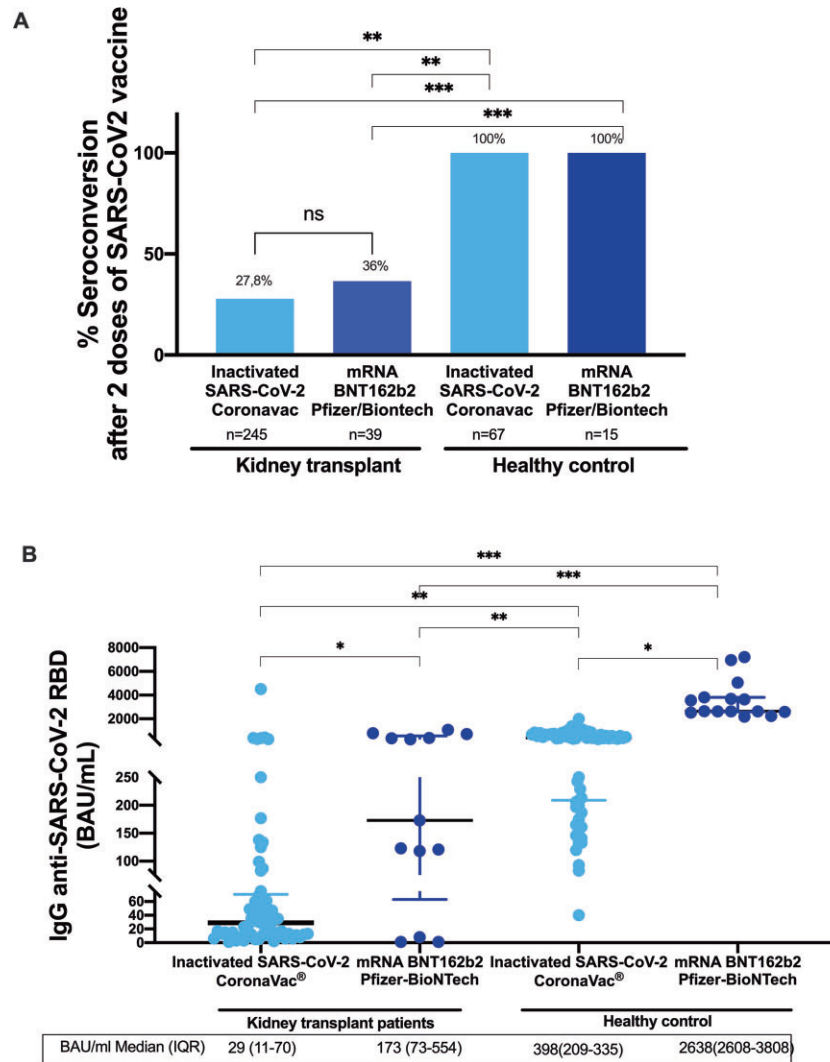


FIGURE 1: Serological response after two doses of inactivated SARS-CoV-2 or BNT162b2 mRNA vaccine in kidney transplant patients and healthy control. (A) Percentage of seroconversion. (B) IgG anti-RBD SARS-CoV-2 titres (BAU/mL) in patients with seroconversion. * $P < 0.05$ mRNA versus inactivated SARS-CoV-2, ** $P < 0.05$ versus inactivated SARS-CoV-2 in healthy control, *** $P < 0.05$ versus BNT162b2 mRNA in healthy control. ns, not significant.

compares antibody titres between two different vaccine platforms in KT patients, showing enhanced humoral responses with BNT162b2 mRNA-based compared with ChAdOx1-based vaccine. The clinical significance of this finding should be further evaluated [8].

The most important risk factors for no serological response to vaccines are associated with net immunosuppression such as age, triple immunosuppression, tacrolimus and mycophenolate, low lymphocyte count and eGFR.

Our results provide additional evidence of a weak immune response with two different vaccine platforms. To reinforce immunity, higher and/or supplemental booster doses are the more common solutions. Recently, it has been reported that a third and a fourth dose of BNT162b2 mRNA to SOT recipients improved immunogenicity [30–32]. There is growing evidence that combination of different platforms enhanced immunity [33].

A potential bias for this study was the criteria to receive each platform vaccine in Uruguay. BNT162b2 mRNA-vaccinated

group had small size and included healthcare workers from all ages and patients older than 70 years. However, since most patients were vaccinated with inactivated virus vaccine, this work contributes to understanding the humoral response after inactivated SARS-CoV-2 vaccine in KT population. Another drawback of this work could be the absence of anti-RBD IgGs determination before vaccination in these patients.

In conclusion, we report a weak humoral response after two doses of inactivated SARS-CoV-2 or BNT162b2 mRNA vaccine in KT recipients (29% of seroconversion). IgG antibody titres in KT were 10 times lower than healthy controls, even though they were higher with mRNA vaccine. Further study is needed to determine the impact of COVID-19 in these patients. Different strategies could improve immunogenicity, such as additional doses or a combination of platforms [30–32, 34, 35]. Based on these findings, we strongly recommend that all transplant recipients should continue with the non-pharmacological protection measures, including masks, hand hygiene and social distancing.

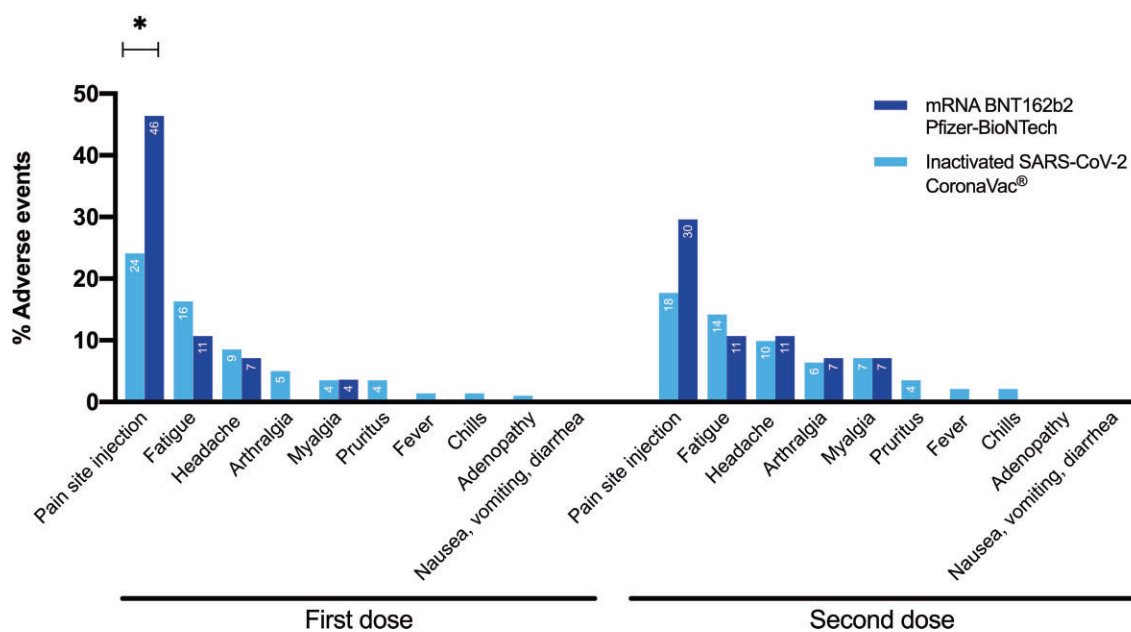


FIGURE 2: Side effects with first and second dose of inactivated SARS-CoV-2 or BNT162b2 mRNA vaccine. * $P < 0.05$ mRNA versus inactivated SARS-CoV-2.

FUNDING

This work was supported by: Fondo para la Convergencia Estructural del Mercosur (FOCEM, COF 03/11); Agencia Nacional de Investigación e Innovación (ANII), Uruguay; and Fondo de Investigación en Nefrología (FOINE), Hospital de Clínicas, Uruguay.

This protocol was approved by Hospital de Clínicas, Facultad de Medicina, Universidad de la República Ethics Committee.

CONFLICT OF INTEREST STATEMENT

The authors of this manuscript have no conflict of interest to disclose.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on reasonable request from the corresponding author S.B., or M.S. The data are not publicly available due to restrictions for containing information that could compromise the privacy of research participants.

REFERENCES

- Cravedi P, Mothi SS, Azzi Y et al. COVID-19 and kidney transplantation: results from the TANGO International Transplant Consortium. *Am J Transplant* 2020; 20: 3140–3148
- Hilbrands LB, Duivenvoorden R, Vart P et al. COVID-19-related mortality in kidney transplant and dialysis patients: results of the ERACODA collaboration. *Nephrol Dial Transplant* 2020; 35: 1973–1983
- Crespo M, Mazuecos A, Rodrigo E et al. Respiratory and gastrointestinal COVID-19 phenotypes in kidney transplant recipients. *Transplantation* 2020; 104: 2225–2233
- Elias M, Pievani D, Randoux C et al. COVID-19 infection in kidney transplant recipients: disease incidence and clinical outcomes. *J Am Soc Nephrol* 2020; 31: 2413–2423
- Jager KJ, Kramer A, Chesnaye NC et al. Results from the ERA-EDTA Registry indicate a high mortality due to COVID-19 in dialysis patients and kidney transplant recipients across Europe. *Kidney Int* 2020; 98: 1540–1548
- Boyarsky BJ, Werbel WA, Avery RK et al. Antibody response to 2-dose SARS-CoV-2 mRNA vaccine series in solid organ transplant recipients. *JAMA* 2021; 325: 2204–2206
- Danthu C, Hantz S, Dahlem A et al. Humoral response after SARS-CoV-2 mRNA vaccine in a cohort of hemodialysis patients and kidney transplant recipients. *J Am Soc Nephrol* 2021; 32: 2153
- Predecki M, Thomson T, Candice L et al. Willicombe M in collaboration with the OSC. Comparison of humoral and cellular responses in kidney transplant recipients receiving BNT162b2 and ChAdOx1 SARS-CoV-2 vaccines. *medRxiv* <https://doi.org/10.1101/2021.07.09.21260192>; preprint: not peer reviewed
- Miele M, Busà R, Russelli G et al. Impaired anti-SARS-CoV-2 humoral and cellular immune response induced by Pfizer-BioNTech BNT162b2 mRNA vaccine in solid organ transplanted patients. *Am J Transplant* 2021; 21: 2919–2921
- Marinaki S, Adamopoulos S, Degiannis D et al. Immunogenicity of SARS-CoV-2 BNT162b2 vaccine in solid organ transplant recipients. *Am J Transplant* 2021; 21: 2913–2915
- Grupper A, Rabinowich L, Schwartz D et al. Reduced humoral response to mRNA SARS-CoV-2 BNT162b2 vaccine in kidney transplant recipients without prior exposure to the virus. *Am J Transplant* 2021; 21: 2719–2726
- Hall VG, Ferreira VH, Ierullo M et al. Humoral and cellular immune response and safety of two-dose SARS-CoV-2 mRNA-1273 vaccine in solid organ transplant recipients. *Am J Transplant* 2021; 21: 3980
- Herrera S, Colmenero J, Pascal M et al. Cellular and humoral immune response after mRNA-1273 SARS-CoV-2 vaccine in

- liver and heart transplant recipients. *Am J Transplant* 2021; 21: 3971
14. Ducloux D, Colladant M, Chabannes M et al. Factors associated with humoral response after BNT162b2 mRNA COVID-19 vaccination in kidney transplant patients. *Clin Kidney J* 2021; 14: 2270–2272
 15. Bertrand D, Hanoy M, Edet S et al. Antibody response to SARS-CoV-2 mRNA BNT162b2 vaccine in kidney transplant recipients and in-centre and satellite centre haemodialysis patients. *Clin Kidney J* 2021; 14: 2127–2128
 16. Wijtvliet V, Ledeganck K, Peeters B et al. SARS-CoV-2 breakthrough infections in vaccinated kidney transplant recipients: an issue of concern. *Clin Kidney J* 2021; 14: 2261–2262
 17. Broseta JJ, Rodríguez-Espinosa D, Rodríguez N et al. Humoral and cellular responses to mRNA-1273 and BNT162b2 SARS-CoV-2 vaccines administered to hemodialysis patients. *Am J Kidney Dis* 2021; 78: 571–581
 18. Grupper A, Rabinowich L, Schwartz D et al. Reduced humoral response to mRNA SARS-CoV-2 BNT162b2 vaccine in kidney transplant recipients without prior exposure to the virus. *Am J Transplant* 2021; 21: 2719–2726
 19. Benotmane I, Gautier-Vargas G, Cognard N et al. Weak anti-SARS-CoV-2 antibody response after the first injection of an mRNA COVID-19 vaccine in kidney transplant recipients. *Kidney Int* 2021; 99: 1487–1489
 20. Sattler A, Schrezenmeier E, Weber UA et al. Impaired humoral and cellular immunity after SARS-CoV2 BNT162b2 (Tozinameran) prime-boost vaccination in kidney transplant recipients. *J Clin Invest* 2021; 131: e150175
 21. Rincon-Arevalo H, Choi M, Stefanski AL et al. Impaired humoral immunity to SARS-CoV-2 BNT162b2 vaccine in kidney transplant recipients and dialysis patients. *Sci Immunol* 2021; 6: 1–15
 22. Benotmane I, Gautier-Vargas G, Cognard N et al. Low immunization rates among kidney transplant recipients who received 2 doses of the mRNA-1273 SARS-CoV-2 vaccine. *Kidney Int* 2021; 99: 1498–1500
 23. Korth J, Jahn M, Dorsch O et al. Impaired humoral response in renal transplant recipients to SARS-CoV-2 vaccination with BNT162b2 (Pfizer-BioNTech). *Viruses* 2021; 13: 4–9
 24. Medina-Pestana J, Cristelli MP, Viana LA et al. Clinical impact, reactogenicity, and immunogenicity after the first CoronaVac dose in kidney transplant recipients. *Transplantation* 2021; doi: 10.1097/TP.0000000000003901 (published ahead of print)
 25. Teijaro JR, Farber DL. COVID-19 vaccines: modes of immune activation and future challenges. *Nat Rev Immunol* 2021; 21: 195–197
 26. Jara A, Undurraga EA, González C et al. Effectiveness of an inactivated SARS-CoV-2 vaccine in Chile. *N Engl J Med* 2021; 385: 875–884
 27. Wilder-Smith A, Mulholland K. Effectiveness of an inactivated SARS-CoV-2 vaccine. *N Engl J Med* 2021; 385: 946–948
 28. Zhang Y, Zeng G, Pan H et al. Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine in healthy adults aged 18–59 years: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial. *Lancet Infect Dis* 2021; 21: 181–192
 29. Polack FP, Thomas SJ, Kitchin N et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med* 2020; 383: 2603–2615
 30. Benotmane I, Gautier G, Perrin P et al. 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* 2021; 326: 1063
 31. Chavarot N, Morel A, Leruez-Ville M et al. Weak antibody response to 3 doses of mRNA vaccine in kidney transplant recipients treated with belatacept. *Am J Transplant* 2021; 21: 4043
 32. Alejo JL, Mitchell J, Chiang TP-Y et al. Antibody response to a fourth dose of a SARS-CoV-2 vaccine in solid organ transplant recipients. *Transplantation* 2021; 105: e280–e281; doi: 10.1097/TP.0000000000003934
 33. Barros-Martins J, Hammerschmidt SI, Cossmann A et al. Immune responses against SARS-CoV-2 variants after heterologous and homologous ChAdOx1 nCoV-19/BNT162b2 vaccination. *Nat Med* 2021; 27: 1525–1529
 34. Mossad SB. SARS-CoV-2 vaccine effectiveness trumps immunogenicity in solid organ transplant recipients. *Am J Transplant* 2021; 21: 4105
 35. Grupper A, Katchman H. Reduced humoral response to mRNA SARS-CoV-2 BNT162b2 vaccine in kidney transplant recipients without prior exposure to the virus: not alarming, but should be taken gravely. *Am J Transplant* 2021; 21: 2909