Original Article

Korean J Transplant 2023;37:49-56
https://doi.org/10.4285/kjt.22.0056

KJT
KOREAN JOURNAL OF TRANSPLANTATION

pISSN 2671-8790
eISSN 2671-8804

Different antibody responses between liver and kidney transplant recipients elicited by third doses of COVID-19 mRNA vaccines

So Yun Lim[1,*], Young-In Yoon[2,*], Ji Yeun Kim[1,*], Eunyoung Tak[3,*], Hyunwook Kwon[4], Sung Shin[4], Young Hoon Kim[4], Gi-Won Song[2], Sung-Han Kim[1], Sung-Gyu Lee[2]

[1]Department of Infectious Diseases, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea
[2]Division of Hepatobiliary Surgery and Liver Transplantation, Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea
[3]Department of Convergence Medicine, Asan Medical Institute of Convergence Science and Technology (AMIST), Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea
[4]Division of Kidney and Pancreas Transplantation, Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

Background: Solid organ transplant recipients exhibit decreased antibody responses, mainly due to their weakened immune systems. However, data are limited on antibody responses after the primary series of coronavirus disease 2019 (COVID-19) vaccines among recipients of various solid organ transplant types. Thus, we compared the antibody responses after three COVID-19 vaccine doses between liver transplant (LT) and kidney transplant (KT) recipients.
Methods: We prospectively enrolled solid organ transplant recipients who received three COVID-19 vaccine doses from June 2021 to February 2022 and measured S1-specific immunoglobulin G antibodies using an enzyme-linked immunosorbent assay.
Results: Seventy-six LT and 17 KT recipients were included in the final analysis. KT recipients showed consistently lower antibody responses even after the third vaccine dose (86.2% vs. 52.9%, P=0.008) and lower antibody titers (median, 423.0 IU/mL [interquartile range, 99.6–2,057 IU/mL] vs. 19.7 IU/mL [interquartile range, 6.9–339.4 IU/mL]; P=0.006) than were observed in LT recipients. Mycophenolic acid was a significant risk factor for a seropositive antibody response after the third vaccine dose in the multivariable analysis (odds ratio, 0.06; 95% confidence interval, 0.00–0.39; P=0.02).
Conclusions: We found a weaker antibody response despite the completion of the primary series of COVID-19 vaccines in KT recipients than in LT recipients. Mycophenolic acid use in KT recipients might be the main contributor to this observation.

Keywords: SARS-CoV-2; COVID-19 vaccines; COVID-19 vaccine booster shot; Organ transplantation; Liver transplantation; Kidney transplantation

Received November 30, 2022
Revised January 5, 2023
Accepted January 7, 2023

Corresponding author: Sung-Han Kim
Department of Infectious Diseases, Asan Medical Center, University of Ulsan College of Medicine, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Korea
E-mail: kimsunghanmd@hotmail.com

Co-corresponding author: Young Hoon Kim
Division of Kidney and Pancreas Transplantation, Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Korea
E-mail: gskyh@amc.seoul.kr

Co-corresponding author: Gi-Won Song
Division of Hepatobiliary Surgery and Liver Transplantation, Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Korea
E-mail: drsong71@amc.seoul.kr

*These authors contributed equally to this work.

HIGHLIGHTS

- Kidney transplant recipients showed inadequate antibody responses after the coronavirus disease 2019 (COVID-19) primary series.
- Mycophenolate use was a risk factor for a seronegative antibody response to COVID-19 vaccination.
- Solid organ transplant recipients showed a heterogeneous distribution of antibody titers after COVID-19 vaccination.

INTRODUCTION

After the roll-out of coronavirus disease 2019 (COVID-19) vaccines, concerns emerged regarding their limited protective effect in solid organ transplant recipients, mainly due to those patients' weakened immune response. Indeed, two-dose COVID-19 vaccination showed weak antibody responses in solid organ transplant recipients [1]. These immunological data were consistent with epidemiological data that showed lower clinical effectiveness of COVID-19 vaccines in preventing infection, hospitalization, or death from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in solid organ transplant recipients [2] than in the general population [3,4]. However, recent data on the immune response after the third dose of COVID-19 vaccines in solid organ transplant recipients showed increased antibody conversion. Thus, the Centers for Disease Control and Prevention recommended three-dose COVID-19 mRNA vaccination as a primary series and a booster vaccination to stay up-to-date with the COVID-19 vaccine in moderately or severely immunocompromised individuals [5]. Interestingly, kidney transplant (KT) recipients showed prominently weaker antibody responses [6-10] compared to the unexpectedly high seroconversion rate in liver transplant (LT) recipients [1,8,11] after two-dose vaccination. However, there are limited data directly comparing antibody responses after the third dose of COVID-19 vaccines between LT and KT recipients. Thus, we conducted a prospective cohort study investigating antibody responses induced by the second and third COVID-19 vaccine doses as the primary series in solid organ transplant recipients.

METHODS

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Review Board of the Asan Medical Center (IRB No. 2021-0746 and 2021-0170), with written informed consent obtained from each patient.

Study Design, Specimen Collection, and Participant Enrollment

This study was conducted at Asan Medical Center, a tertiary referral hospital in Seoul, Korea, which performs over 500 LT and 300 KT procedures per year. We prospectively enrolled healthy healthcare workers (HCWs) without previous SARS-CoV-2 infection who received three doses of the BNT162b2 vaccine from March to November 2021 as a control group. We also enrolled LT and KT recipients who completed the primary series of the COVID-19 vaccines from June 2021 to February 2022. Patients with previous SARS-CoV-2 infections were excluded from the final analysis. This study was based partly on the cohort from our previous study [12]. In their regular outpatient visits at our center, study participants were asked whether they had previously experienced COVID-19 symptoms or infection. Blood samples were collected 2–3 weeks after the two- and three-dose vaccine series. Participants with SARS-CoV-2 infection during the study period were excluded from the final analysis.

Immunologic Evaluation

The laboratory measurements for the SARS-CoV-2 S1-specific immunoglobulin G (IgG) antibody were performed using an in-house developed enzyme-linked immunosorbent assay, as described in our previous study [12]. IgG antibody titers are presented in IU/mL in accordance with the World Health Organization international standards, qualified with reference pooled sera from the International Vaccine Institute (Seoul, Korea).

Definitions

The glomerular filtration rate (GFR) was divided into above and below 45 mL/min/1.73 m^2 according to the Kidney Disease Improving Global Outcomes grade. High-dose steroids were defined as the use of >20 mg of methylprednisolone for >10 days. The mammalian target of rapamycin (mTOR) inhibitor used as a maintenance immunosuppressive drug in this study's participants was either everolimus or sirolimus. Heterologous three-dose

https://doi.org/10.4285/kjt.22.0056

mRNA vaccination referred to the use of an mRNA vaccine (BNT161b2 or mRNA-1273) for the third dose after two doses of ChAdOx1 nCoV-19, and homologous three-dose mRNA vaccination denoted the use of three mRNA vaccines as the primary series.

Statistical Analysis

Categorical variables were analyzed using the chi-square test or the Fisher exact test. Continuous variables were analyzed with the Student t-test or the Mann-Whitney U-test according to the results of normality testing. A multiple logistic regression model was fitted to estimate the independent risk factors. Variables with P<0.10 in the univariable analysis were included in the multivariable analysis. P<0.05 were considered statistically significant. R ver. 4.2.1 (The R Foundation) was used for the statistical analysis, and GraphPad Prism ver. 8.0 (GraphPad Software) was used to plot the results.

RESULTS

Study Participants

In total, 34 HCWs were enrolled in this study. Of the 89 LT recipients and 22 KT recipients enrolled in this study, participants infected with SARS-CoV-2 before the third vaccine dose and those who did not receive the third vaccine dose after study enrollment were excluded. Overall, 76 LT recipients and 17 KT recipients were included in the final analysis. Among the LT recipients, 13 (17%) received the third dose with an mRNA vaccine after two doses of ChAdOx1 nCoV-19. A flow diagram of study participants is shown in Fig. 1.

Participants' Characteristics

Table 1 shows the clinical characteristics and immunological responses of the study participants according to the transplanted organ. The time interval after transplant was similar between LT and KT recipients (2.5 vs. 2.6 years, P=0.530). More KT recipients (23.5%) than LT recipients (3.9%) had histories of graft rejection within 1 year (P=0.020), and the KT recipients also included higher proportions of participants who received rituximab (41.2% vs. 5.3%, P<0.001) and high-dose steroids (64.7% vs. 28.9%, P=0.010) than the LT recipients. The frequency of T cell immunosuppressive drug use, including basiliximab or anti-thymocyte globulin (ATG) use, was similar between LT (22.4%) and KT recipients (47.1%, P=0.080). Five LT (6.6%) and four (23.5%) KT recipients had impaired kidney function and a GFR <45 mL/min/1.73 m^2 (P=0.090). The most common immunosuppressants for maintenance after LT and KT were tacrolimus (92.1% and 100%, respectively; P=0.520), followed by mycophenolic acid (53.9% and 88.2%, respectively; P=0.020). Low-dose steroids were more frequently maintained after KT (76.5%) than after LT (5.3%, P<0.001), and serum tacrolimus concentrations around the third vaccine dose were higher in KT recipients (median, 4.3 ng/mL; interquartile range [IQR], 2.1–6.5 ng/mL) than in LT recipients (median, 6.5 ng/mL; IQR, 5.3–7.6 ng/mL; P=0.006). The median interval between the second and third vaccine doses was 67 days (IQR, 63–76 days) in LT recipients and 99 days (IQR, 78–105 days in KT recipients) (Table 1). The baseline characteristics of the HCWs in this study are presented in Supplementary Table 1. The HCWs were all healthy volunteers.

Antibody Responses

Fig. 2 presents the antibody responses of the study participants after the second and third doses of COVID-19

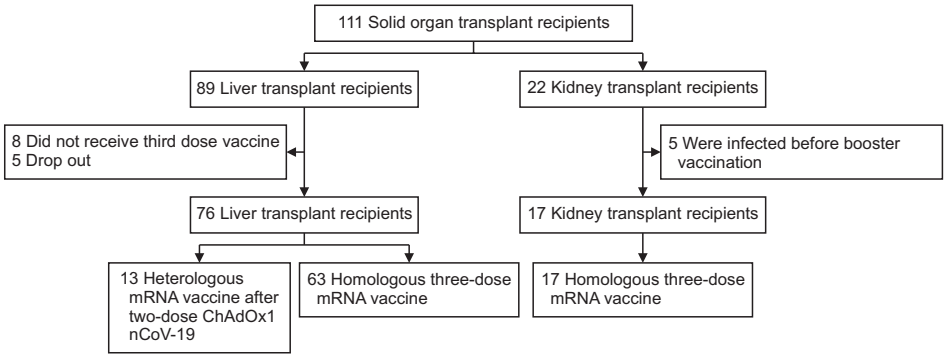


Fig. 1. Schematic diagram of the study participants.

Table 1. Clinical characteristics and immunological responses of the liver and kidney transplant recipients in this study

Variable	Homologous or heterologous three-dose mRNA vaccine in LT recipients (n=76)	Homologous three-dose mRNA vaccine in KT recipients (n=17)	P-value
Age (yr)	55.8 (49.3–59.9)	50.1 (42.8–53.8)	0.010
Male sex	50 (65.8)	9 (52.9)	0.470
GFR (mL/min/1.73 m^2)			0.090
≥30 & <45	5 (6.6)	4 (23.5)	
≥45	71 (93.4)	13 (76.5)	
Year from transplant	2.5 (1.0–8.2)	2.6 (0.7–6.2)	0.530
Rejection history within 1 yr	3 (3.9)	4 (23.5)	0.020
ABO-incompatible transplant	17 (22.4)	4 (23.5)	>0.990
Rituximab use within 1 yr	4 (5.3)	7 (41.2)	<0.001
High-dose steroid use within 1 yr[a)]	22 (28.9)	11 (64.7)	0.010
Basiliximab or anti-thymocyte globulin use within 1 yr	17 (22.4)	8 (47.1)	0.080
Basiliximab	17 (22.4)	6 (35.3)	0.090
Anti-thymocyte globulin	0	2 (11.8)	0.032
Immunosuppressant			
Tacrolimus	70 (92.1)	17 (100.0)	0.520
Cyclosporine	2 (2.6)	0	>0.990
Steroid	4 (5.3)	13 (76.5)	<0.001
Mycophenolic acid	41 (53.9)	15 (88.2)	0.020
mTOR inhibitor	11 (14.5)	4 (23.5)	0.580
Tacrolimus serum concentration (ng/mL)	4.3 (2.1–6.5)	6.5 (5.3–7.6)	0.006
Vaccination regimen			0.150
Heterologous mRNA booster vaccination after two-dose ChAdOx1 nCoV-19	13 (17.1)	0	
Homologous booster vaccination with mRNA vaccine	63 (82.9)	17 (100)	
Booster vaccine			>0.990
mRNA-1273	17 (22.4)	4 (23.5)	
BNT162b2	59 (77.6)	13 (76.5)	
Interval between second and third dose (day)	67 (63.0–76.0)	99 (78.0–105.0)	<0.001
Interval between third dose and blood sampling (day)	18 (14.0–29.0)	33 (30.0–47.0)	0.001
Antibody titer after booster dose (IU/mL)	423 (99.6–2,057)	19 (6.9–339.4)	0.006

Values are presented as median (interquartile range) or number (%).

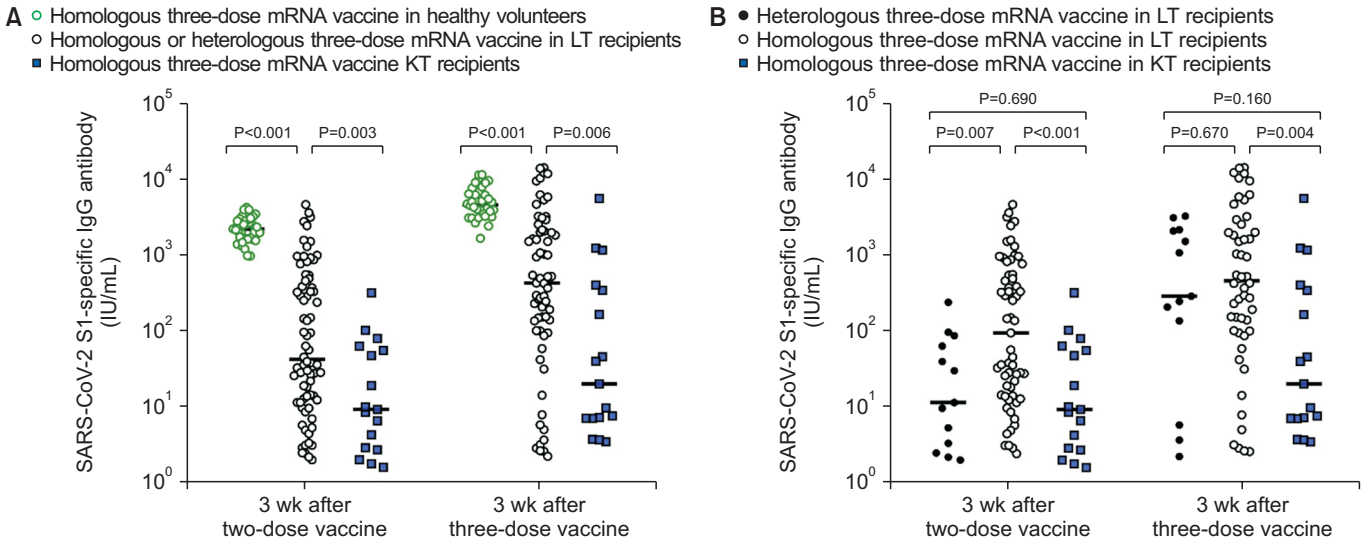
LT, liver transplant; KT, kidney transplant; GFR, glomerular filtration rate; mTOR, mammalian target of rapamycin.

[a)]>20 mg of methylprednisolone for >10 days.

vaccines. HCWs showed a 100% seropositive antibody response both after the primary series and the booster vaccination, and the median antibody titer after the booster dose was 4,586 IU/mL (IQR, 3,300–7,028 IU/mL). HCWs showed higher seropositivity and antibody titers than solid organ transplant recipients (both P<0.05) (Fig. 2A). A significant difference was found in the seropositive antibody response between LT and KT recipients after the second (78.7% vs. 41.2%, P=0.005) and third (86.2% vs. 52.9%, P=0.008) vaccine doses. Furthermore, the median SARS-CoV-2 S1-specific IgG antibody titers were significantly higher in LT recipients than in KT recipients after the second vaccines (41.7 IU/mL [IQR, 12.1–451.7 IU/mL] vs. 9.0 IU/mL [IQR, 2.8–54.3 IU/mL]; P=0.003) and third (423.0 IU/mL [IQR, 99.6–2,057 IU/mL] vs. 19.7 IU/mL [IQR, 6.9–339.4 IU/mL]; P=0.006).

Among LT recipients, heterologous third mRNA vaccine doses induced comparable seropositivity (76.9% vs. 88.5%, P=0.280) and antibody titers (284.0 IU/mL [IQR, 133.8–2,057.0 IU/mL] vs. 455.3 IU/mL [IQR, 99.0–2,256.0

https://doi.org/10.4285/kjt.22.0056



Seropositivity (%)	100	78.7	41.2	100	86.2	52.9
n/N	34/34	59/75	7/17	34/34	56/65	9/17

Seropositivity (%)	53.8	83.9	41.2	76.9	88.5	52.9
n/N	7/13	52/62	7/17	10/13	46/52	9/17

Fig. 2. Antibody response 3 weeks after the second and third doses of coronavirus disease 2019 (COVID-19) vaccines. Thick horizontal lines indicate the median values. Seropositivity is presented as the percentage (%), calculated by the number of participants of seropositive antibody response (n) divided by the total participants (N). (A) Healthy volunteers and solid organ transplant recipients. (B) Liver transplant (LT) recipients with heterologous or homologous three-dose mRNA vaccination series and kidney transplant (KT) recipients with homologous three-dose mRNA vaccination series. SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; IgG, immunoglobulin G.

IU/mL]; P=0.670) to those of the homologous third mRNA vaccine doses (Fig. 2B).

Risk Factors Associated with Seropositivity and Higher Antibody Titer

Table 2 presents the risk factors for a seropositive antibody response after the third vaccine dose. A >3-year interval from transplantation (odds ratio [OR], 6.43; 95% confidence interval [CI], 1.64–42.9; P=0.020), rituximab (OR, 0.24; 95% CI, 0.06–0.97; P=0.040) and basiliximab or ATG use (OR, 0.19; 95% CI, 0.06–0.59; P=0.004) within 1 year were associated with a seropositive antibody response after the third vaccine dose in univariable analysis. Moreover, steroid use (OR, 0.26; 95% CI, 0.08–0.86; P=0.030) and mycophenolic acid use (OR, 0.06; 95% CI, 0.00–0.35; P=0.010) as maintenance immunosuppressive drugs showed associations with antibody seroconversion in the univariable analysis. However, mycophenolic acid (OR, 0.06; 95% CI, 0.00–0.39; P=0.020) was the only significant risk factor for a seronegative antibody response (Table 2). Furthermore, mycophenolic acid use (OR, 0.35; 95% CI, 0.14–0.91; P=0.030) and a >3-year posttransplantation interval (OR, 7.15; 95% CI, 2.28–22.40; P=0.001) were significant risk factors for low antibody titers after the third vaccine dose in the multivariable analysis (Supplementary Table 2).

DISCUSSION

In this prospective cohort study investigating antibody responses in solid organ transplant recipients, we found that KT recipients showed consistently weaker antibody responses after two- and three-dose COVID-19 vaccination series that LT recipients. The antibody responses after the heterologous and homologous third doses of primary series vaccines in LT recipients were comparable. The use of mycophenolic acid as a maintenance immunosuppressive drug was an independent risk factor for negative antibody responses after the third vaccine dose. These findings are significant in terms of the booster vaccination policy and the prioritization of pre-exposure prophylaxis such as tixagevimab or cilgavimab in transplant recipients.

There are three important findings. First, the weak an-

Table 2. Risk factors associated with seropositivity 3 weeks after COVID-19 mRNA vaccination in solid organ transplant recipients

Variable	Univariable analysis		Multivariable analysis[a)]	
	OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Age ≥60 yr	0.81 (0.24–3.25)	0.75	-	-
Male sex	1.20 (0.39–3.53)	0.75	-	-
GFR (mL/min/1.73 m^2)				
≥30 & <45	0.48 (0.11–2.46)	0.33	-	-
45≤	Reference	Reference	-	-
Years from transplant				
≤3	Reference	Reference	Reference	Reference
>3	6.43 (1.64–42.9)	0.02	4.18 (0.66–36.73)	0.15
ABO-incompatible transplant	0.81 (0.24–3.25)	0.75	-	-
Rituximab use within 1 yr	0.24 (0.06–0.97)	0.04	1.19 (0.16–10.57)	0.87
High-dose steroid use within 1 yr	0.36 (0.12–1.06)	0.07	1.37 (0.28–7.39)	0.70
Basiliximab or anti-thymocyte globulin use within 1 yr	0.19 (0.06–0.59)	0.004	0.56 (0.10–2.92)	0.49
Maintenance immunosuppressant				
Tacrolimus serum concentration ≥8 ng/mL	1.02 (0.22–7.24)	0.98	-	-
Steroid	0.26 (0.08–0.86)	0.03	0.37 (0.07–1.98)	0.24
Mycophenolic acid	0.06 (0.00–0.35)	0.01	0.06 (0.00–0.39)	0.02
mTOR inhibitor	1.88 (0.45-12.84)	0.44	-	-
Vaccination regimen				
Heterologous booster	Reference	Reference	-	-
Homologous booster	1.18 (0.24–4.49)	0.82	-	-
Booster vaccine				
mRNA-1273	Reference	Reference	-	-
BNT162b2	2.80 (0.87–8.80)	0.08	3.45 (0.72–17.69)	0.12
Interval between second and third doses >3 mo	1.29 (0.06-10.88)	0.83	-	-

COVID-19, coronavirus disease 2019; OR, odds ratio; CI, confidence interval; GFR, glomerular filtration rate; mTOR, mammalian target of rapamycin.
[a)]Tjur's R^2=0.30.

tibody response even after the third dose of the COVID-19 vaccine in KT recipients than in LT recipients might be partially explained by the different clinical characteristics of LT and KT recipients in our cohort. KT recipients were more likely to maintain steroid and mycophenolic acid use after transplantation. Mycophenolic acid use was also a significant risk factor influencing seropositivity after the third vaccine dose in the multivariable analysis. Mycophenolic acid use has been traditionally considered a risk factor for a decreased antibody response because it counteracts B cell proliferation and differentiation [13], and immunological data on antibody response elicited by the COVID-19 vaccine have supported this hypothesis [14,15], including our results in this study. However, the use of rituximab, another strong B cell immunosuppressant, within 1 year was not significantly associated with antibody seropositivity after the third vaccine dose in the multivariable analysis. Although assessing the short-term effects of rituximab on antibody response is difficult, all the participants in our study received the third vaccine dose at least 6 months after rituximab use. Second, we investigated the risk factors influencing seropositive antibody responses after the third vaccine dose in transplant recipients. In our study, impaired kidney function with a GFR between 30 and 45 mL/min/1.73 m^2 was not a significant predictor of seropositive antibody response in our study. Considering that patients with a GFR >30 mL/min/1.73 m^2 or those on dialysis showed a generally comparable antibody response to participants with normal kidney function in a previous study [16], impaired kidney function does not appear to significantly affect the antibody response than that of immunosuppressants.

Furthermore, the T cell-immunosuppressive drugs used for desensitization in ABO-incompatible transplants

https://doi.org/10.4285/kjt.22.0056

or T cell-mediated rejection therapy at our center did not significantly affect seropositive antibody response in transplant recipients. Basiliximab is a T cell-nondepleting agent, unlike ATG, a T cell-depleting agent, and it was presumed that the number of patients who received ATG was too small to evaluate the effect of T cell immunosuppressants on antibody responses [17]. Finally, as shown in Fig. 2, the S1-specific IgG antibody titers of the solid organ transplant recipients after receiving the COVID-19 vaccine showed a much more heterogeneous distribution than that of the HCWs. The different immune statuses due to various doses and duration of immunosuppressive agents might partially explain this phenomenon. These heterologous immune responses in transplant recipients may necessitate a more individualized approach by developing a surrogate marker of immune responses against COVID-19 to recommend additional vaccine doses in transplant recipients in the future.

There are several limitations to our study. First, the relatively small sample size of KT recipients may limit further interpretation of our results. Moreover, the number of participants who received strong immunosuppressive therapy within 1 year was too small to adequately evaluate the effect on the antibody response. Second, the lack of cell-mediated immune responses and neutralizing antibody assays against SARS-CoV-2 or its variants may limit the completeness of our understanding of immune responses after COVID-19 vaccination in transplant recipients. Despite these limitations, we found a weaker antibody response even after the third dose of the COVID-19 vaccine in KT recipients compared to that in LT recipients, and more use of mycophenolic acid in KT recipients appears to be the main risk factor for decreased antibody responses.

ACKNOWLEDGMENTS

Conflict of Interest
No potential conflict of interest relevant to this article was reported.

Funding/Support
This study was supported by a grant from the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), which is funded by the National Institute of Infectious Diseases, National Institute of Health, Republic of Korea (grant No. HD22C2045).

ORCID
So Yun Lim https://orcid.org/0000-0002-5647-3718
Young-In Yoon https://orcid.org/0000-0002-5306-912x
Ji Yeun Kim https://orcid.org/0000-0001-6955-6427
Eunyoung Tak https://orcid.org/0000-0002-2595-3639
Hyunwook Kwon https://orcid.org/0000-0001-5018-5304
Sung Shin https://orcid.org/0000-0001-7318-4208
Young Hoon Kim https://orcid.org/0000-0003-3840-8426
Gi-Won Song https://orcid.org/0000-0002-1581-7051
Sung-Han Kim https://orcid.org/0000-0002-6596-8253
Sung-Gyu Lee https://orcid.org/0000-0001-9161-3491

Author Contributions
Conceptualization: HK, SS, YHK, GWS, SHK, SGL. Data curation: SYL, YIY, HK, SS, YHK, GWS. Formal analysis: SYL, JYK, ET. Funding acquisition: SHK. Methodology: JYK, ET. Project administration: SYL, YIY. Visualization: SYL, JYK, ET. Writing–original draft: SYL, YIY, SHK. Writing–review & editing: all authors. All authors read and approved the final manuscript.

Supplementary Materials
Supplementary materials can be found via https://doi.org/10.4285/kjt.22.0056.

REFERENCES

1. Boyarsky BJ, Werbel WA, Avery RK, Tobian AA, Massie AB, Segev DL, et al. Antibody response to 2-dose SARS-CoV-2 mRNA vaccine series in solid organ transplant recipients. JAMA 2021;325:2204-6.
2. Naylor KL, Kim SJ, Smith G, McArthur E, Kwong JC, Dixon SN, et al. Effectiveness of first, second, and third COVID-19 vaccine doses in solid organ transplant recipients: a population-based cohort study from Canada. Am J Transplant 2022;22:2228-36.
3. Barda N, Dagan N, Cohen C, Hernán MA, Lipsitch M, Kohane IS, et al. Effectiveness of a third dose of the BNT162b2 mRNA COVID-19 vaccine for preventing severe outcomes in Israel: an observational study. Lancet 2021;398:2093-100.
4. Tartof SY, Slezak JM, Fischer H, Hong V, Ackerson BK, Ranasinghe ON, et al. Effectiveness of mRNA

BNT162b2 COVID-19 vaccine up to 6 months in a large integrated health system in the USA: a retrospective cohort study. Lancet 2021;398:1407-16.
5. Centers for Disease Control and Prevention (CDC). COVID-19 vaccines for people who are moderately or severely immunocompromised [Internet]. CDC; 2022 [cited 2022 Aug 17]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/immuno.html
6. Caillard S, Thaunat O. COVID-19 vaccination in kidney transplant recipients. Nat Rev Nephrol 2021;17:785-7.
7. Benotmane I, Gautier-Vargas G, Cognard N, Olagne J, Heibel F, Braun-Parvez L, et al. Low immunization rates among kidney transplant recipients who received 2 doses of the mRNA-1273 SARS-CoV-2 vaccine. Kidney Int 2021;99:1498-500.
8. Rozen-Zvi B, Yahav D, Agur T, Zingerman B, Ben-Zvi H, Atamna A, et al. Antibody response to SARS-CoV-2 mRNA vaccine among kidney transplant recipients: a prospective cohort study. Clin Microbiol Infect 2021;27:1173.e1-4.
9. Cucchiari D, Egri N, Bodro M, Herrera S, Del Risco-Zevallos J, Casals-Urquiza J, et al. Cellular and humoral response after MRNA-1273 SARS-CoV-2 vaccine in kidney transplant recipients. Am J Transplant 2021;21:2727-39.
10. Grupper A, Rabinowich L, Schwartz D, Schwartz IF, Ben-Yehoyada M, Shashar M, 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;21:2719-26.
11. Nazaruk P, Monticolo M, Jędrzejczak AM, Krata N, Moszczuk B, Sańko-Resmer J, et al. Unexpectedly high efficacy of SARS-CoV-2 BNT162b2 vaccine in liver versus kidney transplant recipients-is it related to immunosuppression only? Vaccines (Basel) 2021;9:1454.
12. Lim SY, Yoon YI, Kim JY, Tak E, Song GW, Kim SH, et al. Antibody response induced by two doses of ChAdOx1 nCoV-19, mRNA-1273, or BNT162b2 in liver transplant recipients. Immune Netw 2022;22:e24.
13. Karnell JL, Karnell FG 3rd, Stephens GL, Rajan B, Morehouse C, Li Y, et al. Mycophenolic acid differentially impacts B cell function depending on the stage of differentiation. J Immunol 2011;187:3603-12.
14. Rabinowich L, Grupper A, Baruch R, Ben-Yehoyada M, Halperin T, Turner D, et al. Low immunogenicity to SARS-CoV-2 vaccination among liver transplant recipients. J Hepatol 2021;75:435-8.
15. Meunier L, Sanavio M, Dumortier J, Meszaros M, Faure S, Ursic Bedoya J, et al. Mycophenolate mofetil decreases humoral responses to three doses of SARS-CoV-2 vaccine in liver transplant recipients. Liver Int 2022;42:1872-8.
16. Sanders JF, Bemelman FJ, Messchendorp AL, Baan CC, van Baarle D, van Binnendijk R, et al. 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 2022;106:821-34.
17. Macedo C, Hadi K, Walters J, Elinoff B, Marrari M, Zeevi A, et al. Impact of induction therapy on circulating T follicular helper cells and subsequent donor-specific antibody formation after kidney transplant. Kidney Int Rep 2018;4:455-69.

https://doi.org/10.4285/kjt.22.0056