

Humoral and T cell Responses to SARS-CoV-2 Vaccine Booster and Anti-SARS-CoV-2 Monoclonal Antibodies in Patients With End-Stage Kidney Disease



and the high number of comorbidities, a condition that is particularly concerning for kidney transplant recipients (KTx).^{1,2} Patients may obtain immunity against SARS-CoV2 through different ways, including active (vaccine or infection) or passive immunization anti-SARS-CoV2 antibodies; however, no study has formally compared the efficacy of the various approaches in patients with end-stage kidney disease who are in renal replacement therapy (hemodialysis and kidney transplantation).

To the Editor: Patients with end-stage kidney disease remain at a high risk for COVID-19 morbidity and mortality because of their poor responses to vaccination

In a prospective-cohort study, we measured serial changes in anti-SARS-CoV-2 IgG and T cells in 42 KTx who had received 3 mRNA vaccine doses and subsequently experienced a breakthrough infection (confirmed by PCR), fourth vaccine dose, or anti-SARS-

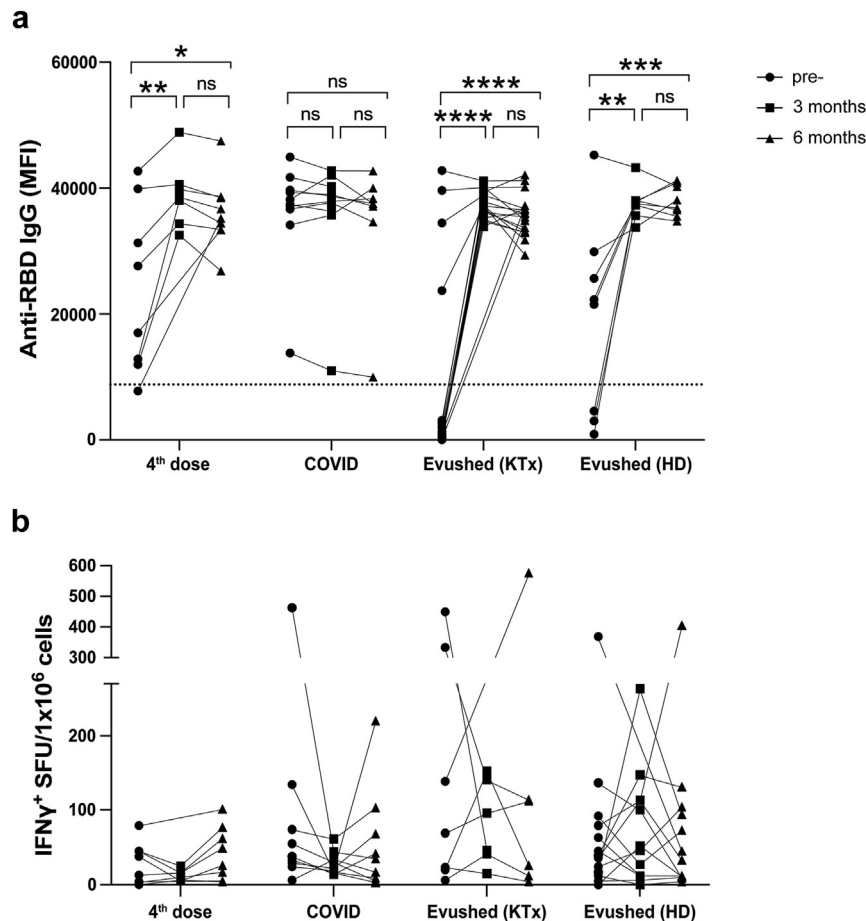


Figure 1. (a) Humoral and Cell-mediated immunity before and after booster vaccination, breakthrough infection, or anti-SARS-CoV-2 monoclonal antibodies in kidney transplant recipients and in dialysis patients. Anti-RBD IgG concentrations were measured from serum samples using a Luminex based assay.⁵¹ The dashed horizontal line indicates the cutoff used to determine a positive antibody level on the basis of mean plus $3 \times$ SD of pre-COVID sera samples. (b) Cellular reactivity was assessed using frozen peripheral blood mononuclear cells by interferon gamma-ELISpot assay after stimulation with SARS-CoV-2 RBD. IFN γ -producing cell clones were quantified by SFUs per 1×10^6 cells after background subtraction. Connecting lines between the time points indicate matched serum of peripheral blood mononuclear cells samples. The “pre-” time-point for patients with breakthrough infection is at 1 to 3 months after infection. One asterisk denotes $P < 0.05$, 2 asterisks denote $P < 0.01$, 3 asterisks denote $P < 0.001$, and 4 asterisks denote $P < 0.0001$. HD, hemodialysis; IFN γ , interferon gamma; KTx, kidney transplant; MFI, mean fluorescence intensity; RBD, recombinant binding domain; SFU, spot-forming units.

CoV-2 monoclonal antibodies (Evusheld), and in 10 patients on hemodialysis who were receiving Evusheld (Supplementary Methods and Table S1). We found that anti-recombinant binding domain (RBD) IgG concentration significantly increased at 3 months after the fourth vaccine dose and remained elevated up to 6 months after vaccination, reaching levels that were similar to those observed in KTx with breakthrough COVID-19 infection (Figure 1a). Both KTx and patients on hemodialysis receiving Evusheld had a dramatic and persistent increase in anti-RBD IgG concentrations, even though a large fraction of these patients had baseline antibody levels below the threshold of positivity (Figure 1a). At study entry, 78%, 70%, 62%, and 77% of patients had more than 25 circulating cells producing interferon gamma in response to RBD antigen per million of cells in the breakthrough infection, fourth vaccine dose, Evusheld KTx, and Evusheld hemodialysis groups, respectively. In contrast to the increase in anti-RBD IgG, we did not detect any significant changes in the numbers of SARS-CoV-2 responsive T cells (Figure 1b).

These data reveal that repeated mRNA vaccine boosters can elicit the formation and maintenance of high concentrations of anti-SARS-CoV2 antibodies in KTx, similar to those obtained in patients with breakthrough infection. Passive immunization with anti-SARS-CoV-2 neutralizing monoclonal antibodies allow patients to reach and maintain high levels of circulating antibodies for at least 6 months, even in KTx and patients undergoing dialysis with very low initial antibody levels.

None of the patients developed symptomatic breakthrough infection during the study follow-up. However, lack of information on the neutralizing response of the circulating anti-RBD IgG demands caution in the interpretation of these data because the high IgG concentration of anti-SARS-CoV2 may not be enough to provide effective immunity, especially in the setting of evolving viral variants.³

Most patients had circulating interferon gamma+T cells against SARS-CoV2 because of prior immunization, but repeated booster vaccination did not further increase their number. The lack of correlation between humoral and cellular responses in KTx has been described prior.⁴ Regardless of the mechanisms responsible for this phenomenon, published data by others indicate that spike-specific T cell is insufficient to prevent breakthrough infections in KTx.⁴

In summary, with the limitations of a single-center study with a small sample size, our findings suggest that repeated active or passive immunization are required to maintain immunity against SARS-CoV2 in patients with end-stage kidney disease. Bivalent

vaccines and novel anti-SARS-CoV2 antibodies may improve responses against new SARS-CoV2 lineages in KTx.⁵

DISCLOSURE

JSM is on the scientific advisory board of Qihan Biotech and his spouse is employed by Iconovir Bio. PC is a consultant for Chinook Therapeutics, Calliditas Therapeutics, and Repertoire Immune Medicines. All other authors have declared no conflicting interests.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Supplementary Methods.

Table S1. Clinical characteristics.

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