# Title

Assessment of Antibody-Titer Changes after Second and Third Severe Acute Respiratory Syndrome Coronavirus 2 mRNA Vaccination in Japanese Post-Kidney-Transplant Patients.

## **Key Points**

•More than half of the post-kidney transplant recipients could not acquire antibodies only by two vaccinations against SARS-CoV-2, but about 70% of them could acquire antibodies after three vaccinations.

 $\cdot$  Once antibody was acquired, post-kidney transplant recipients tended to retain antibody titers six months after the second dose of vaccine.

•This fact may be a basis for recommending third vaccination in post-kidney transplant recipients.

#### Summary

A research group, Kumiko Fujieda, Akihito Tanaka, Shoji Saito, Kazuhiro Furuhashi, Shoichi Maruyama, Ryosuke Kikuchi, Nami Takai, Takashi Fujita, Masashi Kato, have investigated antibody-titer changes after second and third severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) mRNA vaccination in Japanese post-kidney-transplant patients. Antibody acquisition rates increased after the third vaccination, indicating the importance of additional third vaccination in post-kidney-transplant recipients.

It has been reported that antibody titers are low after SARS-CoV-2 mRNA vaccination in patients receiving immunosuppressive treatment, especially after kidney transplantation. In a previous report, the research group measured antibody titers in Japanese post-kidney transplant recipients 3 weeks to 3 months after 2 doses of SARS-CoV-2 mRNA vaccinations. As a result, the antibody acquisition rate of Japanese post-kidney-transplant recipients was lower than that of healthy subjects and post-kidney-transplant recipients in other countries. Therefore, it was necessary to clarify the differences in antibody acquisition rates in Japan, the trends in antibody titers, and the need for additional vaccinations.

The research group conducted an observational study of post-kidney-transplant patients attending Nagoya University Hospital, measuring antibody levels against anti-SARS-CoV-2 three times: three weeks to three months after two doses of SARS-CoV-2 mRNA vaccine, five to six months

after two doses, and three weeks to three months after three doses. The results showed that the antibody acquisition rate was 45% at 3 weeks to 3 months after the second immunization, and 50% at 5 to 6 months after the second immunization. The percentage of antibodies acquisition after the third vaccination was 71%, a significant increase. In addition, lower body mass index (BMI)<sup>\*1</sup> and lower estimated glomerular filtration rate (eGFR)<sup>\*2</sup> were associated with lower antibody acquisition rates.

These results suggest that the risk of infection SARS-CoV-2 may be reduced in post-kidney-transplant recipients after the third vaccination. In addition, those who show low BMI or have decreased eGFR are likely to have a lower rate of antibody acquisition and should pay particular attention to infection control.

#### **Research Background**

Patients who are receiving immunosuppressive treatment, especially kidney transplant recipients, are taking immunosuppressants to prevent rejection of the kidney grafts. It has been reported from overseas that the acquisition rate of antibodies after SARS-CoV-2 mRNA vaccination is lower in patients taking immunosuppressants. However, the situation surrounding transplantation, such as the ratio of living donor kidney transplantation, the ratio of kidney transplants, ABO-incompatible and or doses of types immunosuppressants, is different between Japan and other countries. Specifically, the percentage of living donor kidney transplants is high in Japan due to the lack of donors, and ABO-incompatible kidney transplantation are aggressively performed. In order to overcome blood type incompatibility, the intensity of perioperative immunosuppression may be stronger. In addition, there may be ethnic differences. Therefore, there is a possibility that there are differences in the rate of antibody acquisition between Japan and other countries, and this needed to be clarified.

### **Research Results**

### Patient Background and Antibody Acquisition Rate

We studied 73 transplant recipients (45 men and 28 women) who received two doses of SARS-CoV-2 mRNA vaccine. The median age at the time of vaccination was 61 years (interquartile range [IQR], 50-69 years), and the median age at transplant was 53 years (IQR, 41-61 years). Median time from transplant to vaccination was 74 months (IQR, 30-131 months); median BMI was 22.5 (IQR, 21.0-25.7). Of them, 23 patients (31.5%) were antibody positive. No patient failed to receive the second vaccination due to anaphylaxis or other adverse reactions.

The current study examined 62 transplant recipients (40 men and 22 women) who received three doses of the SARS-CoV-2 mRNA vaccine. The median age at the time of the third vaccination was 54 years (interguartile range [IQR], 49-67 years) and the median age at transplant was 50 years (IQR, 38-58 years). The median time from transplant to vaccination was 84 months (IQR, 34-154 months); median BMI was 22.9 (IQR, 21.4-26.2); median eGFR was 42.8 mL/min/1.73 m2 (IQR, 34.1-51.4 mL/min/1.73m2). Forty-five percent showed positive for antibodies 3 weeks to 3 months after 2 doses of vaccine, and 50% showed positive for antibodies 5-6 months after 2 doses of vaccine. A patient negative from positive antibody. Four patients became became antibody-positive from negative 5 to 6 months after the second vaccination. The percentage of those who showed positive for antibodies 3 weeks to 3 months after the third dose of vaccine increased significantly to 71%.

### Comparison of Antibody Acquisition Rates by Vaccine Type

We compared those who received only Pfizer's vaccine, those who received only Moderna's vaccine, and those who received both Pfizer's and Moderna's vaccines. As a result, no differences in antibody acquisition rates were observed between the types or combinations of vaccines.

### Examination of Factors Associated with Antibody Acquisition

Next, we used statistical methods to examine factors associated with antibody acquisition rates. The results suggested that BMI and eGFR were significantly correlated with the antibody acquisition rate, even after statistically adjusting for various factors.

### Research Summary and Future Perspective

The results showed that the acquisition rate of antibodies increased after three doses of the SARS-CoV-2 vaccine in Japanese post-kidney transplant recipients. We will need to investigate how antibody titers change with additional fourth vaccinations and over time.

### Publication

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