Association Between SARS-CoV-2 Messenger RNA Vaccines and Lower Infection Rates in Kidney Transplant Recipients
A Registry-Based Report

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Background: The real-world protection provided by SARS-CoV-2 messenger RNA (mRNA) vaccines to kidney transplant recipients (KTRs) remains uncertain.

Objective: To study the association between mRNA vaccination and SARS-CoV-2 infection rate in KTRs.

Design: Retrospective observational cohort study.

Setting: The Czech Republic (17 February to 16 May 2021).

Patients: 2101 KTRs followed in the Department of Nephrology at the Institute for Clinical and Experimental Medicine.

Measurements: Positive result for SARS-CoV-2 on polymerase chain reaction test and vaccination status of KTRs.

Results: The incidence rate in the vaccinated group was 0.474 per 1000 person-days (33 cases in 69 672 days at risk). The incidence rate in the unvaccinated group was 1.370 per 1000 person-days (79 cases in 57 658 days at risk). The

unadjusted incidence rate ratio (IRR; incidence rate of vaccinated/incidence rate of unvaccinated) for KTRs was 0.346 (95% CI, 0.227 to 0.514). The multivariable adjusted IRR for KTRs was 0.544 (CI, 0.324 to 0.876).

Limitation: Retrospective observational design, uneven follow-up of patient groups, and different exposition to SARS-CoV-2 stemming from strong temporal trends and differences in clinical and probably behavioral characteristics.

Conclusion: Vaccination of KTRs is associated with lower risk for SARS-CoV-2 infection.

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K idney transplant recipients (KTRs) are considered particularly vulnerable to SARS-CoV-2 infection, as higher rates of inpatient mortality, far exceeding those seen in the general population, have been reported (1–4). The SARS-CoV-2 messenger RNA (mRNA) vaccines have shown high clinical efficacy in preventing COVID-19 in the immunocompetent population (5, 6). However, impaired humoral and cellular responses to mRNA vaccines have recently been reported in KTRs (7–9). The assumption of an impaired vaccine response in KTRs is further supported by the well-known fact of a decreased immune response to influenza or pneumococcal vaccines in the transplant population (10–12). However, data about the effectiveness of SARS-CoV-2 vaccines are conflicting (13–15), and to what extent the 2 doses of an mRNA vaccine protect KTRs from COVID-19 is unclear. Furthermore, a third booster dose of an mRNA SARS-CoV-2 vaccine has been recently tested and applied in many countries (16–18).

Because randomized controlled trials in immunocompromised populations may not be ethically feasible, registry data may provide information on the association between SARS-CoV-2 vaccines and clinical protection of KTRs. Thus, to evaluate the association between SARS-CoV-2 mRNA vaccines and infection rates in KTRs, we did a retrospective registry-based cohort study of 2101 KTRs followed at our center.

METHODS
Design Overview
This study is a single-center, retrospective, observational, registry-based cohort study enrolling 2101 KTRs between

17 February and 16 May 2021. The aim of the study was to evaluate the association between 2-dose mRNA vaccination and incidence of SARS-CoV-2 infection among KTRs.

Outcomes and Follow-up
The primary outcome of the study was the incidence of SARS-CoV-2 infection, defined as a positive result for SARS-CoV-2 on a polymerase chain reaction (PCR) test, among fully vaccinated KTRs compared with unvaccinated KTRs. In addition, we analyzed COVID-19–related deaths and breakthrough infections.

The follow-up period started on 17 February and ended on 16 May 2021. The follow-up was ended on reaching the end point (PCR positivity), censoring (death or return to long-term dialysis), or on reaching the end of the study period. Study participants were divided into 2 subgroups depending on vaccination status (that is, vaccinated or unvaccinated) at the end of the follow-up.

The person-time for every participant was first counted toward the total person-days of the unvaccinated group, regardless of the latter vaccination. Those who survived without having a positive PCR test result until reaching full vaccination status (2 weeks after the second dose) were moved to the vaccinated subgroup, and their person-time started counting toward the total person-days of the vaccinated group. Therefore, vaccinated participants initiated their follow-up designated as unvaccinated, and their designation was later changed to vaccinated. This means that they contributed their follow-up time to both groups at

Figure 1. Flow chart of study participants.
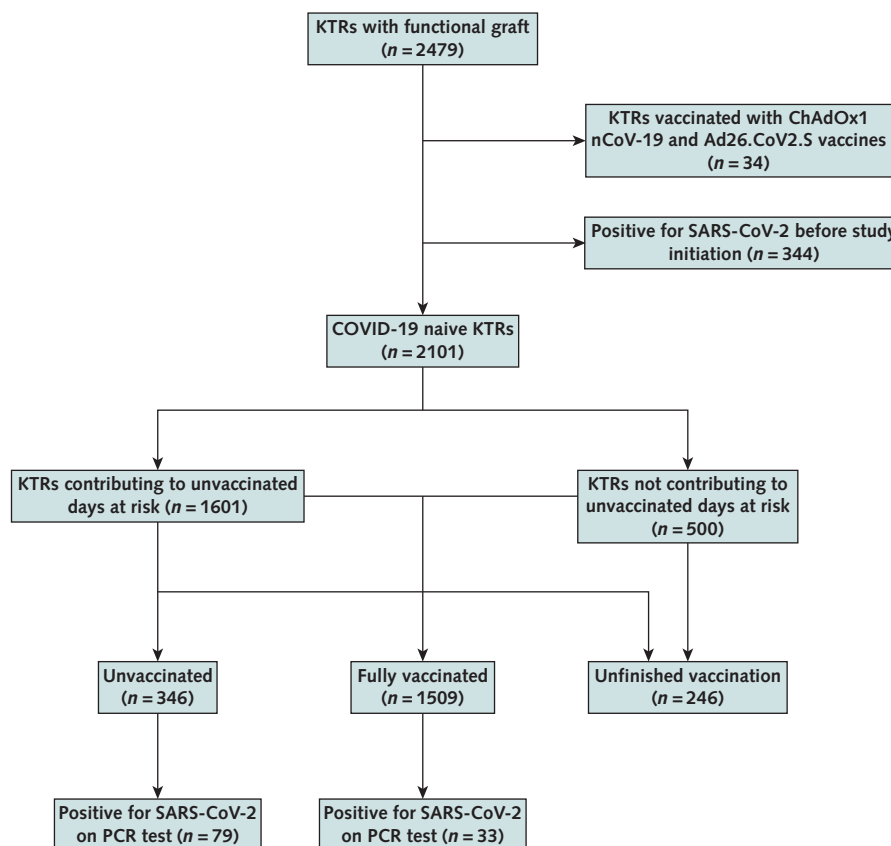
Overall, 2479 KTRs with functional grafts were considered for inclusion to the study. To establish a SARS-CoV-2–naive cohort, patients with previous positive results for SARS-CoV-2 infection were excluded, as were patients vaccinated with non–messenger RNA vaccines. In total, 2101 KTRs were considered as the SARS-CoV-2–naive cohort. Of these, 1601 KTRs contributed at least part of their follow-up time to the unvaccinated days at risk, whereas 500 did not contribute. These were the KTRs vaccinated between 13 January and 17 February, 6 of whom did not finish vaccination and thus did not contribute to any days at risk, and 494 of whom entered the study denoted as unfinished vaccination but afterward reached full vaccination status and, therefore, contributed only toward vaccinated days at risk. A total of 246 KTRs did not finish full vaccination because they had a positive result for SARS-CoV-2 infection after the first dose (n = 28), they did not receive the second dose for other reasons (n = 5), or they received the first dose before the end of the study period but reached full vaccination status after its end (n = 213). Kidney transplant recipients who did not finish full vaccination contributed to the unvaccinated days at risk and were censored at the day of first vaccine dose. A total of 1509 reached full vaccination and contributed toward vaccination days at risk; of these, 33 became positive for SARS-CoV-2 during the study period. A total of 346 were unvaccinated by the end of the study period, and 79 of them became positive for SARS-CoV-2 during the study period. KTR = kidney transplant recipient; PCR = polymerase chain reaction.

some point but never to both at the same time. The person-time between the administration of the first vaccine dose and reaching full vaccination status was eliminated and was therefore not counted toward total person-days of either category (vaccinated or unvaccinated).

To establish a SARS-CoV-2–naive cohort, KTRs infected before the vaccination campaign were excluded. Waitlisted patients who received a transplant during the study period and those vaccinated by vector vaccines were also excluded. For more details, see **Figure 1**.

Vaccination of the eligible groups from the general population started on 1 January 2021, with critical infrastructure workers, health care workers, and elderly citizens first, in accordance with the government's strategic protocol (19). Vaccination of KTRs was initiated on 13 January 2021. Participants were considered fully vaccinated 2 weeks

after receiving the second dose of an mRNA vaccine, as was recommended (20). Thus, the beginning of the study period was chosen to be 17 February, which is the day when the first KTR (vaccinated on 13 January) reached full vaccination status. The end of the study period was chosen to be on 16 May for several reasons. First, most of the cohort was already vaccinated at that time and, thus, there were no events in the unvaccinated group from that time on (the last infection in an unvaccinated KTR was observed on 10 May). Second, the spring pandemic was dissipating at that point, with overall low rates of infection in the vaccinated KTRs. Finally, because we used a calendar time adjustment with 1-month intervals, making 16 May three months away from the beginning of the study.

All patients have signed an informed consent for administration of SARS-CoV-2 vaccination, independent of our

Table 1. Demographic Characteristics of the COVID-19–Naive KTRs

Characteristic	Vaccinated (n = 1509)	Unvaccinated (n = 346)	Standardized Mean Differences (95% CI)*
Mean age (SD), y	61.28 (11.78)	54.20 (14.26)	0.58 (0.46 to 0.7)
Male, n (%)	986 (65.34)	215 (62.14)	3.2 (−2.62 to 9.03)
Mean BMI (SD), kg/m²	26.74 (4.38)	25.79 (4.53)	0.21 (0.1 to 0.33)
Retransplant, n (%)	168 (11.13)	47 (13.58)	−2.45 (−6.57 to 1.67)
Mean most recent estimated glomerular filtration rate (Chronic Kidney Disease Epidemiology Collaboration) (SD), mL/min/1.73 m²	49.2 (21)	48.6 (20.4)	1.8 (−4.8 to 9)
Mean time from transplant (SD), y	8.45 (6.87)	8.53 (6.91)	−0.01 (−0.13 to 0.1)
Mean follow-up time (SD), d	46.17 (26.67)	72.81 (29.78)	−0.98 (−1.1 to −0.86)
Vaccination status against influenza in 2019, n (%)†	323 (47.71)	33 (24.63)	23.08 (14.43 to 31.74)
University/college degree, n (%)	192 (12.72)	31 (8.96)	3.76 (0.14 to 7.39)
Urban place of residence, n (%)	360 (23.86)	75 (21.68)	2.18 (−5.3 to 4.3)
Tacrolimus in maintenance immunosuppression, n (%)	1249 (82.77)	287 (82.95)	−0.18 (−4.75 to 4.4)
Cyclosporine A in maintenance immunosuppression, n (%)	152 (10.07)	31 (8.96)	1.11 (−2.44 to 4.66)
Prednisone in maintenance immunosuppression, n (%)	1336 (88.54)	301 (86.99)	1.55 (−2.53 to 5.61)
Mycophenolate in maintenance immunosuppression, n (%)	1228 (81.38)	275 (79.48)	1.9 (−2.97 to 6.76)
Mechanistic target of rapamycin inhibitor in maintenance immunosuppression, n (%)	115 (7.62)	20 (5.78)	1.84 (−1.14 to 4.82)
Belatacept in maintenance immunosuppression, n (%)	9 (0.6)	2 (0.58)	0.02 (−0.89 to 0.93)
SARS-CoV-2 vaccine, n (%)			
BNT162b2	1274 (84.43)	–	-
mRNA-1273	235 (15.57)	–	-

BMI = body mass index; KTR = kidney transplant recipient.
* Standardized mean differences are reported specifically as Cohen d with pooled SD for continuous variables and proportion differences for binary variables. There were 33 cases of SARS-CoV-2 infection detected among vaccinated KTRs and 79 cases among unvaccinated KTRs during the study period.
† Data missing for 832 (55.1%) and 212 (61.3%) patients in the vaccinated and unvaccinated groups, respectively.

study. Institutional review board approval is not required for anonymous retrospective observational studies under the current legislature in the Czech Republic.

Setting and Participants

All KTRs with functioning kidney allografts followed at our transplant center were considered for inclusion in the study. The Institute for Clinical and Experimental Medicine (IKEM) is a high-volume transplant center (21) that primarily covers geographic regions of the country's capital Prague and the regions of Central, Southern, and Northern Bohemia, accounting for about 50% of the population of the Czech Republic. To illustrate, in 2019, IKEM performed 58% of the total number of kidney transplants in the country (299 kidney transplants out of 510).

The Czech Republic is a small country with 10.7 million inhabitants with a very homogeneous structure of population and habitation. There are no significant racial minorities –99.8% of Czech citizens are White. The population density is roughly the same around the country, with an average of 139 citizens per square kilometer.

National Registry for Infectious Diseases and Other Sources of Data

The National Registry for Infectious Diseases gathers all data about each PCR and antigen test done, each vaccine dose applied in the country, and all mandatory quarantines ordered by the Public Health authorities (22). These data are mandatorily reported in the registry from every laboratory and all health care providers in the country. Because of the comprehensive nature of a central registry with mandatory data reporting, the National Registry for Infectious Diseases registry allows for detailed

large-cohort analyses and was thus selected as the source of data for primary analysis (PCR tests and vaccination status). Vaccines were administered only by health care providers, and expenses were covered by the national health care system.

The clinical characteristics of the KTRs (age at the time of positive PCR test result, sex, body mass index (BMI), retransplantation status, most recent estimated glomerular filtration rate, years from transplant, vaccination status against influenza in 2019, university or college degree, urban or rural place of residence, and maintenance immunosuppression) (Table 1) were obtained from the hospital information system of IKEM. The clinical course of COVID-19 and the outcomes were recorded by a transplantation coordinator and a physician (M.M.) for each KTR with SARS-CoV-2 infection.

COVID-19 Setting and Baseline Risk for Infection

The Czech Republic was severely affected by the COVID-19 pandemic, and with 155 464 cases per million at the end of June 2021, it became the fourth most heavily affected country in the world at the time. In contrast, the cumulative incidence in the United States was 101 289 per million (Figure 2) and 44 531 in neighboring Germany at the same point in time.

The study period covers the entirety of the third and most severe wave of the pandemic (Figure 2). The highest number of confirmed infections was reported on 7 January 2021, with 17 773 positive PCR tests in a single day (0.17% of the whole Czech population). In the first week of January 2021, almost 1% of the population tested positive (90 684 new cases between 3 January and 9 January 2021) (23).

Therefore, when the study was initiated, the risk for infection was high, and a large proportion of events was

Figure 2. Seven-day moving average of new cases per 100 000 persons in the Czech Republic and the United States.
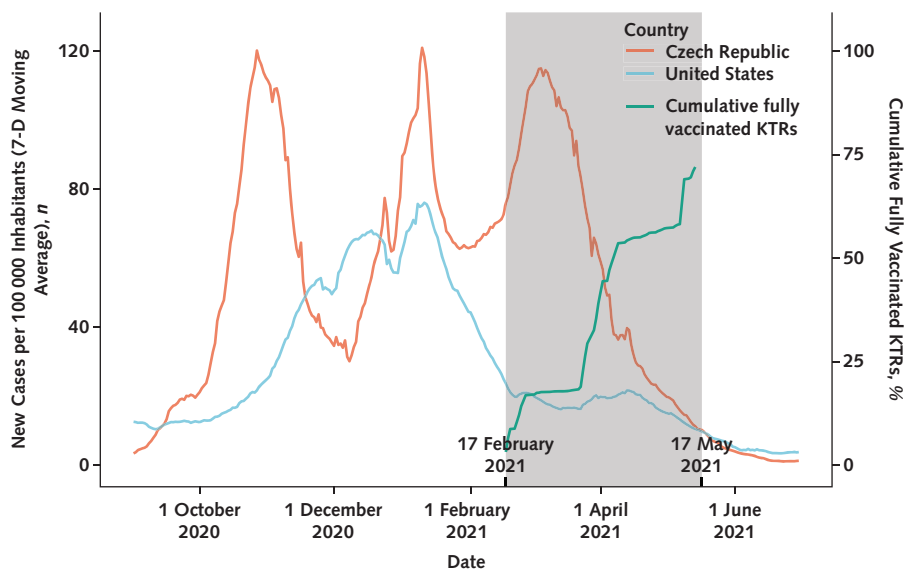
The shaded area denotes the study period. The red and blue lines denote new cases per 100 000 persons in the Czech Republic and the United States, respectively. The green line represents the cumulative proportion of fully vaccinated KTRs during the study period. KTR = kidney transplant recipient.

seen early on, and at the time, the proportion of vaccinated participants was low. Over time, the proportion of vaccinated participants was increasing, whereas the baseline risk for infection was decreasing. Thus, the final rate of SARS-CoV-2 infections in the unvaccinated cohort at the end of the study was unusually high. The study captures a public health crisis of a catastrophic scale and therefore provides unique data to evaluate SARS-CoV-2 mRNA vaccines in a real-world setting and with an extremely high risk for infection.

Testing for COVID-19 was covered by national health insurance; therefore, participants could be tested without hindrance. However, we acknowledge the KTR group may have had a slightly higher diagnostic rate. Our transplant center used an attentive system of KTR follow-up and support during the COVID-19 pandemic. Each KTR at our center has the means to directly contact their physician or transplant coordinator at any time. To boost early case detection, KTRs were repeatedly advised and educated to have a PCR test done if presenting any signs of COVID-19 illness. During the third wave of the pandemic, the government introduced mandatory regular testing for COVID-19 for employees, thereby increasing the detection rate in asymptomatic participants.

Statistical Analysis

Continuous variables are expressed as mean (SD). Categorical variables are expressed as number (percentage) of participants within each group. The intergroup differences are reported as standardized mean differences (that is, Cohen *d* with pooled SD) for continuous variables and proportion differences for binary variables (both measures are reported along with their 95% CIs).

Incidence Rate Ratios and Poisson Regression Models

The unadjusted incidence rate ratio (IRR) is a ratio of the incidence rate in the vaccinated group and the unvaccinated group. The incidence rate is a ratio of the number of events and the days at risk for either the vaccinated or unvaccinated group.

Multivariable Poisson regression was used to derive the adjusted IRR. The models were adjusted for sex, BMI at the last check-up before study initiation, college or university degree, days from transplant, immunosuppression, and rural or urban place of residence. Because there are strong temporal trends in terms of the risk for infection (**Figure 2**) during the study follow-up, further adjustment was done. The model was adjusted to baseline risk by using a categorical covariate representing 1 of the 3 months of the study period in which the patient's follow-up started. No variable for which we adjusted the models had missing values.

The multivariable Poisson regression model was not adjusted to age because of multicollinearity between calendar time, vaccination status, and age. We computed the variance inflation factor for the covariates in the adjusted model, and we obtained 2.02 for vaccination, 1.68 for age, and 1.45 for calendar interval 2. We decided on variance inflation factor cutoff 2 for vaccination. We cannot remove vaccination and calendar interval covariates from the model (otherwise we would have no treatment effect or adjustment to background risk); therefore, we removed the age covariate to avoid multicollinearity. In the modified model, the variance inflation factor decreased to 1.49 for vaccination and 1.39 for interval 2. For a detailed description of the regression model, see the Appendix (available at Annals.org).

Figure 3. Incidence of COVID-19 during the study period for the unvaccinated and vaccinated KTRs, along with the general population.
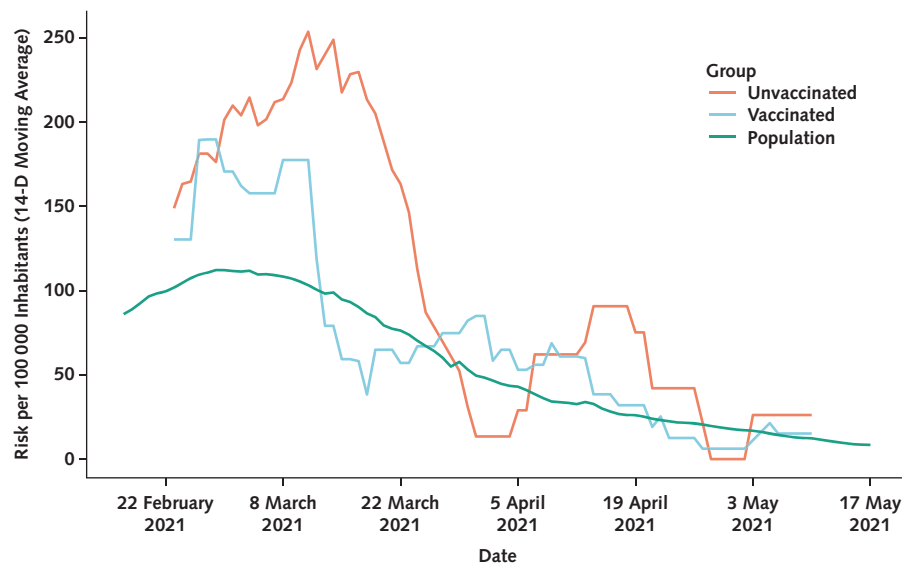
The incidence for each group is computed as the number of new cases divided by the number of persons at risk for that group. The values are smoothed using 14-d moving average. KTR = kidney transplant recipient.

Apart from the adjusted IRR, we also report marginally standardized incidence rates (24). To compute the marginally standardized incidence rate for the unvaccinated group, we predicted the response of each observation using the fitted model while assuming that each observation belongs to the unvaccinated group. Analogously, the marginally standardized incidence rate for the vaccinated group was computed by predicting the response of each observation using the fitted model while assuming that each observation belongs to the vaccinated group. Having predicted responses for each observation, we sum up these responses and divide them by the total follow-up time of all of the observations. The CIs for the marginally standardized incidence rates were computed using the bootstrap method (R package *boot* [R Foundation for Statistical Computing], type percentile, 2000 replicates). The statistical analysis was done in R, version 4.1.1 (R Foundation for Statistical Computing).

Role of the Funding Source

The funding source had no role in the design and conduct of the study; collection, management, analysis or interpretation of the data; preparation, review, or approval of the manuscript; or the decision to submit the manuscript for publication.

RESULTS
Participants

A total of 2479 KTRs were considered for inclusion. After the exclusion of KTRs previously infected with SARS-CoV-2 and those vaccinated with vector-based vaccines (ChAdOx1 nCoV-19 and Ad26.CoV2.S), 2101 KTRs were included in the analysis. Of those, 1509 reached

full vaccination status, 346 were not fully vaccinated until the end of the study period, and 246 did not have complete vaccination (**Figure 1** and **Table 1**). No patient was lost to follow-up, 11 patients during the follow-up period were censored (9 patients died from causes unrelated to COVID-19, and 2 patients had graft failure). The fully vaccinated and unvaccinated groups did not vary in basic characteristics, apart from age, length of follow-up in the study, and, interestingly, in the rate of vaccination against influenza in 2019.

The cumulative proportion of fully vaccinated KTRs during the study period is shown in **Figure 2**.

Incidence Rates and IRR in the KTR Cohort

Infection with SARS-CoV-2 was reported in 33 vaccinated and 79 unvaccinated KTRs. The incidence rate in the vaccinated group was 0.474 per 1000 person-days (33 cases in 69 672 days at risk), and the incidence rate in the unvaccinated group was 1.370 per 1000 person-days (79 cases in 57 658 days at risk). Thus, the unadjusted IRR was 0.346 (95% CI, 0.227 to 0.514). Incidence of COVID-19 during the study period for the unvaccinated and vaccinated KTRs, along with the general population, are shown in **Figure 3**.

Furthermore, the adjusted IRR was calculated (using a multivariable Poisson regression model) for KTR sex, BMI, days from transplant, maintenance immunosuppressive regimen, university or college degree, place of residence (rural or urban), and calendar time. The adjusted IRR was 0.544 (CI, 0.324 to 0.876). The marginally standardized incidence rate for the vaccinated group was 0.06 (CI, 0.037 to 0.085), whereas the rate for the unvaccinated

Table 2. Outcomes in Fully Vaccinated and Unvaccinated KTRs

Outcome	Vaccinated (n = 1509), n (%)	Unvaccinated (n = 346), n (%)
Infections during the study period	33 (2.2)	79 (22.3)
Intensive care unit admission	4 (0.3)	12 (3.5)
Mechanical ventilation	1 (0.07)	4 (1.2)
Death	8 (0.5)	11 (3.2)

KTR = kidney transplant recipient.

group was 0.11 (CI, 0.083 to 0.143). The detailed model is shown in **Appendix Table 1** (available at Annals.org).

Clinical Characteristics of the Infections in the KTR Cohorts

To explore possible effectiveness of vaccination against COVID-19 severity, we have analyzed clinical data from vaccinated and unvaccinated patients infected with SARS-CoV-2. The clinical outcomes are summarized in **Table 2**.

Eighteen KTRs died of COVID-19–related causes during the study period—10 unvaccinated and 8 vaccinated. Vaccinated KTRs who were infected (median age, 71 vs. 50 years) and who died (median age, 72.5 vs. 61 years) were older than unvaccinated KTRs. Granular description of these cases is given in **Appendix Table 2** (available at Annals.org).

DISCUSSION

Despite the rapid publication activity of COVID-19–related studies and reports, evidence lags behind the urgency for decision makers. Both the humoral and cellular immune responses had been reported to be substantially impaired in KTRs (7–9), and the current expert boards' recommendations about additional booster doses in solid organ transplant recipients are based mainly on these observations (17, 18). It is, however, the clinical vaccine effectiveness that matters to patients, society, and decision makers.

Our study points toward an association between 2 doses of SARS-CoV-2 mRNA vaccines and a lower risk for COVID-19 illness in KTRs. Data of the general population obtained from the National Registry for Infectious Diseases registry, however, show that infection risk was one order of magnitude higher for KTRs than the general population (unadjusted IRR, 0.036 from January to June 2021; data not shown).

To date, only a handful of studies reporting the real-world effectiveness of SARS-CoV-2 vaccines in solid organ recipients with conflicting results were published. In a study by Aslam and colleagues (15), clinical effectiveness with almost 80% reduction in the incidence of symptomatic COVID-19 among vaccinated solid organ recipients was seen in a U.S. cohort between 1 January and 2 June 2021. Kidney transplant recipients represented 44.5% of the cohort, and almost 70% were vaccinated with mRNA vaccines. On the other hand, a recent study by Callaghan and colleagues (14) showed no effectiveness against SARS-CoV-2 infection in a British cohort from 1 June to 31 August 2021, although SARS-CoV-2 vaccination was associated with reduced COVID-19–related death. The conflicting outcomes

could be at least partly attributed to the differences between the studies—for example, during Callaghan and colleagues' study, the Delta variant was the dominant virus variant as opposed to the Alpha variant being the dominant variant during Aslam and colleagues' study and our study. Because SARS-CoV-2 vaccination is less effective against the Delta variant than it is against the Alpha variant in the general population (25), one may speculate that perhaps 2-dose vaccination in solid organ recipients reached its limits with this virus variant. Another study by Qin and colleagues (13) showed that the risk for breakthrough infections is higher in solid organ recipients than in the general population, but a missing comparison to unvaccinated persons limits the interpretation of vaccine effectiveness. These findings are in line with the findings from our study.

The estimates of real-world vaccine effectiveness in the general population had also been reported. For instance, Angel and colleagues (26) reported unadjusted IRR (0.03 [CI, 0.01 to 0.06]) in health care workers. However, this report, like many others, uses methods that may at times misrepresent vaccine effectiveness. The problem stems from the days-at-risk calculation method when the vaccinated group is followed up only from the moment of reaching full vaccination status, whereas the unvaccinated group's follow-up starts from an arbitrarily decided point in time. This produces a 2-fold problem. First, the follow-up time of the vaccinated participants is then inherently shorter, and second, because of the strong temporal trends in COVID-19 outbreaks, the risk for infection may vary during the study period. Therefore, even though the days at risk for 2 patient groups could be the same, the risk for being infected during that time could be substantially different, which was the case in our study. These issues have been addressed by several statistical approaches, such as calendar time adjustments in a multivariable Poisson regression model.

It should be emphasized that this report was possible only because of several factors. First, the extremely high viral load in the population and resulting incidence of new cases during the second and third waves in the first half of 2021, combined with a relatively fast SARS-CoV-2 vaccine rollout in the KTR population, resulting in a unique combination of many events in both vaccinated and unvaccinated control participants during a relatively narrow time frame of the study. Second, the National Registry for Infectious Diseases provided a reliable, nationwide source of data on the KTR population followed at IKEM.

The strengths of this study are the use of reliable data from the central nationwide registry (22), the large cohort in a high-volume transplant center, and the high rates of COVID-19 cases due to the severe wave of COVID-19 in the spring of 2021.

The limitations of this study are the retrospective observational design and uneven follow-up. The observational design is especially limiting because of the strong temporal trends in terms of the changing risk for baseline infection, and no statistical adjustment can fully substitute a well-designed randomized controlled trial in this scenario. However, because KTRs are at such high risk for a serious course of the disease, it may not be ethically feasible to deny them any kind of protection. Observational

data may therefore be the only alternative to estimate the vaccination effectiveness. The uneven follow-up is largely corrected by the statistical method and follow-up time definition. Furthermore, different behavioral patterns that could be assumed in persons who decided either for or against vaccination may also be a source of bias.

It is important to note that the available data on disease severity in breakthrough infections and deaths must be interpreted cautiously. The inherent differences between the groups, especially in terms of age, hinder direct comparison, and the low number of observed events precludes multivariable modeling and further adjustments.

It is also necessary to stress that these data are pertinent only for the study period, which was done during a time when the Alpha variant was predominant. The change of the baseline setting, mainly due to the emerging variants of concern, can lead to further attenuation of the real-world effectiveness (27).

In conclusion, the association between 2 doses of mRNA SARS-CoV-2 vaccines and lowered risk for infection shown in our study provides much needed real-world evidence. However, despite the effectiveness in KTRs, there were still breakthrough infections, and indirect comparisons suggest lower effectiveness compared with the general population. Thus, we believe that the current recommendations for additional booster doses based on laboratory immune-monitoring studies are also supported by our clinical report. Kidney transplant recipients should continue to be prioritized for booster doses in vaccination programs.

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APPENDIX: STATISTICAL APPENDIX—DETAILED DESCRIPTION OF THE POISSON MULTIVARIABLE REGRESSION MODEL

The Poisson regression was fitted using the following covariates:

vaccination status (binary, 1 = vaccinated),
sex (binary, 1 = man),
university/college degree (binary, 1 = yes),
urban place of residence (binary, 1 = yes),
BMI (continuous),
time from kidney transplantation (continuous, in years),
immunosuppression Tacrolimus, Cyclosporine A, Prednisone, Mycophenolate, mTOR inhibitor, Belatacept (all binary variables, 1 = yes),
and month (categorical, see below for details).

The offset is a logarithm of the follow-up days and the response variable is binary with 1 representing that the event occurred. The data are provided at individual level.

The model was adjusted to baseline risk by using a categorical covariate month representing the time interval, in which the patient's follow-up started. The time intervals are: 17 February to 16 March 2021 (reference interval), 17 March to 16 April 2021, and 17 April to 16 May 2021. Please note that vaccinated patients that contribute both to vaccinated and unvaccinated days at risk are represented twice in the data with different value of month covariate.

The fitting was done in R language using glm function and family = "poisson."

Appendix Table 1. Adjusted IRR With Poisson Regression Modeling*

Covariate	Adjusted IRR (95% CI)
Vaccinated	0.544 (0.324–0.876)
Male	0.831 (0.569–1.225)
University/college degrees	1.216 (0.625–2.162)
Urban place of residence	0.887 (0.538–1.402)
BMI	0.996 (0.95–1.039)
Years from kidney transplant	0.98 (0.945–1.014)
Tacrolimus in maintenance immunosuppression	1.889 (0.593–8.604)
Cyclosporine A in maintenance immunosuppression	2.444 (0.682–11.77)
Prednisone in maintenance immunosuppression	1.541 (0.747–3.610)
Mycophenolate in maintenance immunosuppression	1.1 (0.644–1.997)
Mechanistic target of rapamycin inhibitor in maintenance immunosuppression	0.75 (0.204–2.127)
Belatacept in maintenance immunosuppression	3.473 (0.162–30.82)
Calendar time adjustment	
17 February–16 March	Reference
17 March–16 April	0.409 (0.189–0.834)
17 April–17 May	0.385 (0.021–1.845)

BMI = body mass index; IRR = incidence rate ratio; KTR = kidney transplant recipient.
* There were 33 cases of SARS-CoV-2 infection detected among vaccinated KTRs and 79 cases among unvaccinated KTRs during the study period.

Appendix Table 2. COVID-19–Related Deaths in KTRs

Case Number	Vaccination Status	Sex	Age, y	Time From Transplant, mo	BMI, kg/m²	Diabetes Mellitus	Retransplant	Human Leukocyte Antigen Mismatch, n	Maximum Pretransplant Panel-Reactive Antibodies, n	eGFR, mL/min/1.73 m²	Maintenance Immunosuppression	Induction	Rejection Treatment in the Past Year	Cause of Death
1	Vaccinated	Male	70	202	26.2	No	No	4	4	93.6	CyA + MMF + CS	None	No	COVID-19–related pneumonia + generalized cancer
2	Vaccinated	Female	78	182	20.2	No	No	3	0	22.2	CyA + MMF	None	No	COVID-19–related pneumonia
3	Vaccinated	Male	82	143	25.8	No	No	3	0	56.4	CyA + CS	None	No	COVID-19–related pneumonia + terminal dementia
4	Vaccinated	Female	71	96	30.3	Yes	No	2	2	10.8	TAC + CS	T-cell depletive	No	COVID-19–related pneumonia
5	Vaccinated	Male	71	87	27.3	Yes	No	3	16	20.4	CyA + MMF + CS	T-cell depletive	No	COVID-19–related pneumonia
6	Vaccinated	Male	74	43	26	Yes	No	2	48	27.6	TAC + MMF + CS	T-cell depletive	No	COVID-19–related pneumonia + bilateral heart failure
7	Vaccinated	Male	70	49	32.5	No	No	3	2	46.2	TAC + MMF + CS	Basiliximab	No	COVID-19–related pneumonia
8	Vaccinated	Female	74	23	30.1	Yes	No	5	56	51.6	TAC + MMF + CS	Basiliximab	No	COVID-19–related pneumonia
9	Unvaccinated	Male	54	4	17.6	No	No	4	6	33	CyA + MMF + CS	Basiliximab	No	COVID-19–related pneumonia
10	Unvaccinated	Female	54	128	41	Yes	No	3	78	31.8	TAC + MMF + CS	T-cell depletive	No	COVID-19–related pneumonia
11	Unvaccinated	Male	62	123	21.7	Yes	No	5	0	10.8	TAC + MMF + CS	Basiliximab	No	COVID-19–related pneumonia
12	Unvaccinated	Male	72	89	35.8	Yes	No	2	4	22.2	CyA + MMF + CS	Basiliximab	No	COVID-19 illness + terminal dementia
13	Unvaccinated	Male	69	98	33.2	Yes	No	1	0	27.6	TAC + CS	T-cell depletive	No	COVID-19–related pneumonia
14	Unvaccinated	Male	69	74	29.7	No	No	2	0	31.8	TAC + MMF + CS	T-cell depletive	No	COVID-19–related pneumonia
15	Unvaccinated	Male	60	39	45.4	No	No	5	6	18.6	TAC + MMF + CS	T-cell depletive	No	COVID-19–related pneumonia + bilateral heart failure
16	Unvaccinated	Male	48	39	30.9	Yes	No	1	4	39	TAC + CS	T-cell depletive	No	COVID-19–related pneumonia
17	Unvaccinated	Male	46	45	35.1	No	No	3	0	66	TAC + MMF + CS	Basiliximab	No	COVID-19–related pneumonia
18	Unvaccinated	Male	70	37	23.7	No	No	3	0	37.2	TAC + MMF + CS	T-cell depletive	No	COVID-19–related pneumonia

BMI = body mass index; CyA = cyclosporine A; CS = corticosteroids; eGFR = estimated glomerular filtration rate with Chronic Kidney Disease Epidemiology Collaboration equation; KTR = kidney transplant recipient; MMF = mycophenolate mofetil or mycophenolic acid; TAC = tacrolimus.