The effectiveness and safety of mRNA (BNT162b2) and inactivated (CoronaVac) COVID-19 vaccines among individuals with chronic kidney diseases

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The ongoing coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has posed a serious threat to individuals with underlying chronic kidney disease (CKD). People with CKD are immunocompromised and therefore result in poorer outcomes including increased risk of hospitalization and mortality after COVID-19.[1] Despite the availability of COVID-19 vaccines, current data on the vaccine efficacy in individuals with CKD are limited to surrogate endpoints such as antibody titers. As a result, a dedicated study is required to evaluate the effectiveness and safety of COVID-19 vaccines for the CKD population.

In Hong Kong Special Administrative Region, China, a territory-wide vaccination program with BNT162b2 (Comirnaty; BioNTech/Pfizer/Fosun) and CoronaVac (CoronaVac Life Sciences) commenced on March 6, 2021, and February 23, 2021, respectively. BNT162b2 vaccine was the first SARS-CoV-2 mRNA vaccine approved by the US Food and Drug Administration,[2] whereas CoronaVac is an inactivated whole-virion SARS-CoV-2 vaccine using adjuvant aluminum hydroxide.[3] Using territory-wide electronic medical records and vaccination records, we conducted this population-based, retrospective study to evaluate the effectiveness and safety of COVID-19 vaccines in the CKD population.

RESULTS

A total of 144,591 individuals with CKD before the matched first vaccination date were included, and 220 subjects aged below 18 years and 3130 subjects who received different brands of vaccines were excluded (Supplementary Figure S1).

Vaccine effectiveness using a retrospective cohort

After excluding individuals without matched second vaccination date and who died or who contracted COVID-19 before the matched second vaccination date, 28,374 non-vaccinated, 27,129 two-dose BNT162b2 vaccine recipients,

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Table 1 | Vaccine effectiveness of BNT162b2 and CoronaVac against COVID-19 infection, COVID-19–related hospitalization, and COVID-19–related death using a retrospective cohort design

Exposure	Events	Time to events, d, median (IQR)	Follow-up time, person-years	Incidence, 100 person-years, (95% CI)	Adjusted IRR[a]	P value
COVID-19 infection						
Nonvaccinated	4933	157 (34–220)	10,830.67	45.55 (44.28–46.84)	Ref	—
BNT162b2	2714	156.5 (51–201)	10,608.71	25.58 (24.63–26.56)	0.62 (0.59–0.66)	<0.001
CoronaVac	5048	120.5 (26–186)	13,260.88	38.07 (37.02–39.13)	0.96 (0.92–1.00)	0.05
COVID-19 hospitalization						
Nonvaccinated	1488	154 (34–217.25)	11,028.46	13.49 (12.82–14.2)	Ref	—
BNT162b2	293	84 (26–175)	10,767.85	2.72 (2.42–3.05)	0.36 (0.31–0.43)	<0.001
CoronaVac	620	61 (19.75–160)	13,536.92	4.58 (4.23–4.96)	0.56 (0.51–0.63)	<0.001
COVID-19 death						
Nonvaccinated	792	144 (35–211.25)	11,101.85	7.13 (6.65–7.65)	Ref	—
BNT162b2	49	94 (34–196)	10,785.68	0.45 (0.34–0.6)	0.14 (0.10–0.20)	<0.001
CoronaVac	177	80 (29–166)	13,569.68	1.3 (1.12–1.51)	0.30 (0.25–0.36)	<0.001

CI, confidence interval; COVID-19: coronavirus disease 2019; IQR, interquartile range; IRR, incidence rate ratio.
[a]Vaccine effectiveness = (1 – IRR) × 100%.

and 47,640 two-dose CoronaVac vaccine recipients were included in the retrospective cohort study. After inverse probability of treatment weighting with 1% extreme values trimming, we obtained a well-balanced cohort with all standardized mean difference <0.1. The baseline characteristics are shown in Supplementary Table S1.

The incidence rates of the COVID infection in the BNT162b2 (25.58 [95% confidence interval {CI}: 24.63–26.56] per 100 person-years) and CoronaVac group (38.07 [95% CI: 37.02–39.13] per 100 person-years) were lower than that in the nonvaccinated group (45.55 [95% CI: 44.28–46.84] per 100 person-years). The vaccine effectiveness was estimated to be 38% (95% CI: 34%–41%) for BNT162b2 and 4% (95% CI: 0%–8%) for CoronaVac when compared with the nonvaccinated group.

Contrary to the COVID-19 infection, both vaccines demonstrated a reduction in COVID-19–related hospitalization and death. For BNT162b2 recipients, the vaccine effectiveness was 64% (95% CI: 57%–69%) for COVID-19–related hospitalization and 86% (95% CI: 80%–90%) for COVID-19–related death. For CoronaVac, the vaccine effectiveness was 44% (95% CI: 37%–49%) and 70% (95% CI: 64%–75%) for COVID-19–related hospitalization and death, respectively. Table 1 summarizes the results of the vaccine effectiveness for both vaccines.

These findings were generally consistent among all subgroups, except for those aged below 65 years, on dialysis or transplant. The vaccine effectiveness against the COVID-19 infection was smaller among CoronaVac recipients in these subgroups. There was also an increased risk of COVID-19–related hospitalization in dialysis patients who received CoronaVac (Supplementary Figure S2, Supplementary Tables S2–S4).

Vaccine safety using modified self-controlled case series

After excluding individuals who contracted the COVID-19 infection, a total of 20,344 incident adverse event of special interest cases were included in the modified self-controlled case series (SCCS) analysis. Among them, 11,574 individuals were nonvaccinated, 2589 received BNT162b2, and 6181 received CoronaVac.

The incidence rate of any adverse events of special interest after the first dose of vaccine is 34.28 (95% CI: 29.81–39.23) and 38.39 (95% CI: 34.81–42.23) per 10,000 doses of BNT162b2 and CoronaVac, respectively. Compared with the baseline period, no increased risk of overall adverse event of special interest was observed in any risk period for both BNT162b2 (incidence rate ratio [95% CI]: first dose: 0.86 [0.69–1.08]; second dose: 0.96 [0.76–1.22]; third dose: 0.60 [0.33–1.10]) and CoronaVac (incidence rate ratio [95% CI]: first dose: 0.76 [0.64–0.91]; second dose: 0.86 [0.71–1.05]; third dose: 0.74 [0.36–1.54]) (Table 2, Supplementary Table S5).

DISCUSSION

Our study demonstrated that both BNT162b2 and CoronaVac were effective against severe outcomes after the COVID-19 infection by reducing hospitalization and mortality and safe with no increased risk of adverse events of special interest observed during the study period. These results are consistent with the findings among the general population in Hong Kong.[4]

For both BNT162b2 and CoronaVac, the vaccine effectiveness against the infection is substantially lower than the one for more severe outcomes as this is more likely to be affected by time since vaccination. A recent study from Qatar on waning vaccine protection found that the effectiveness against the COVID-19 infection peaked in the first month after the second dose and dropped drastically after 6 months (from 77.5% to 17.3%).[5] However, the effectiveness against severe outcomes was maintained at 88.9% 6 months after the second dose.

Table 2 | Adjusted incidence rate ratio of any AESI after BNT162b2 and CoronaVac vaccines using modified SCCS

Period	Events	Follow-up time, person-years	IRR (95% CI)	P value	Events	Follow-up time, person-years	IRR (95% CI)	P value
		BNT162b2				CoronaVac		
Baseline	13,948	15,262.14	—	—	17,331	18,842.38	—	—
Day 0 after first dose	2	7.09	—	—	0	16.92	—	—
Days 1–13 after first dose	44	89.42	0.65 (0.46–0.90)	0.010	124	213.45	0.67 (0.54–0.84)	0.001
Days 14–27 after first dose	56	58.95	1.20 (0.90–1.59)	0.211	131	204.12	0.82 (0.66–1.02)	0.074
Days 1–27 after first dose	100	148.37	0.86 (0.69–1.08)	0.207	255	417.57	0.76 (0.64–0.91)	0.002
Day 0 after second dose	2	5.60	—	—	2	10.85	—	—
Days 1–13 after second dose	41	68.26	0.84 (0.61–1.16)	0.290	84	122.85	0.84 (0.64–1.10)	0.205
Days 14–27 after second dose	54	62.72	1.15 (0.86–1.53)	0.344	70	96.68	0.83 (0.63–1.07)	0.154
Days 1–27 after second dose	95	130.98	0.96 (0.76–1.22)	0.757	154	219.52	0.86 (0.71–1.05)	0.141
Day 0 after third dose	0	1.56	—	—	0	1.59	—	—
Days 1–13 after third dose	8	17.91	0.58 (0.26–1.29)	0.181	7	18.36	0.73 (0.29–1.82)	0.498
Days 14–27 after third dose	8	14.37	0.70 (0.32–1.53)	0.370	6	14.23	0.66 (0.27–1.62)	0.362
Days 1–27 after third dose	16	32.29	0.60 (0.33–1.10)	0.101	13	32.59	0.74 (0.36–1.54)	0.424

AESI, adverse event of special interest; CI, confidence interval; IRR, incidence rate ratio; SCCS, self-controlled case series.

Our subgroup analyses indicated that the vaccines appeared to be less effective to prevent the COVID-19 infection in dialysis, transplant, and younger individuals. This could be attributed to several reasons. Younger subjects are generally more active and may have a higher rate of social contact. Patients on hemodialysis require frequent hospital or hemodialysis center visits, while those younger individuals may still be employed. Notably, these results were also consistent with the current data on COVID-19 vaccination efficacy in individuals with CKD using the immunogenicity data. In a recent meta-analysis, Ma et al.[6] reported a significant reduction in antibody response in patients with renal replacement therapy, leading to reduced protection against the COVID-19 infection.

In addition, we also observed an increased risk of COVID-19 hospitalization among individuals on dialysis. For patients on hemodialysis with the COVID-19 infection, admission may be mandatory to keep the dialysis schedule, irrespective of the COVID-19 severity. In fact, there was no increased risk of mortality despite the higher rate of infection and hospitalization in these patients, indicating that the vaccines remained effective against mortality despite the increased hospitalization rate.

Our study has several strengths. We used a retrospective cohort study to evaluate vaccine effectiveness, whereas modified SCCS to assess vaccine safety. A cohort design enabled us to examine multiple outcomes for a given exposure and calculate the incidence rate over time.[7] The use of territory-wide electronic records reduced the risk of selection, recall, and misclassification biases in the cohort study. At the same time, with the increasing vaccine coverage, SCCS remains the most appropriate method to evaluate the safety by eliminating confounding by all time-independent variables. This study applied the modified SCCS method to avoid the violation of the assumption on the event-dependent exposure as well as event-dependent censoring of observation of SCCS. Our findings provide more information about vaccine effectiveness and safety, which are the core elements affecting vaccine uptake in Hong Kong.[8]

This study is subject to several limitations. First, we defined the COVID-19 infection as SARS-CoV-2 polymerase chain reaction positive, whereas a positive rapid antigen test was regarded as the COVID-19 infection in Hong Kong after March 7, 2022. As a result, we may have underestimated the overall incidence of the COVID-19 infection that affects the estimation of the vaccine effectiveness. However, our results may have underestimated the vaccine effectiveness instead, because vaccinated individuals presumably have a higher rate of social contact and lower adherence to safety measures.[9] Furthermore, polymerase chain reaction tests remain to be the gold standard to confirm the diagnosis, and our results are consistent in COVID-19–related hospitalization and death. Secondly, our study did not consider the waning of vaccine protection over time, which may underestimate the vaccine effectiveness as well. Our subgroup analysis with subjects receiving the booster dose demonstrated that the vaccine is more effective against the COVID-19 infection and severe outcomes than in the main analysis. Lastly, our dataset does not contain information with regard to the SARS-CoV-2 variants. Vaccine effectiveness toward different variants could not be evaluated in this study.

In conclusion, we found that both mRNA (BNT162b2) and inactivated (CoronaVac) vaccines were effective against the severe outcomes of the COVID-19 infection, namely, hospitalization and mortality. Both vaccines were less effective in protecting individuals from the COVID-19 infection. No safety concerns were identified. With these findings, vaccination is strongly encouraged for individuals with CKD.

SUPPLEMENTARY MATERIAL

Supplementary File (Word)
Supplementary Methods.
Supplementary References.
Figure S1. Flowchart for inclusion and exclusion in the retrospective cohort and self-controlled case series (SCCS) design.
Figure S2. Vaccine effectiveness of BNT162b2 and CoronaVac against coronavirus disease 2019 (COVID-19) infection, COVID-19–related hospitalization, and COVID-19–related death across subgroups.
Figure S3. Observation timeline of individuals in the modified self-controlled case series.
Table S1. Baseline characteristics in retrospective cohort design.
Table S2. Incidence rate ratio of BNT162b2 and CoronaVac against coronavirus disease 2019 (COVID-19) infection in subgroups using a retrospective cohort design.
Table S3. Vaccine effectiveness of BNT162b2 and CoronaVac against coronavirus disease 2019 (COVID-19)–related hospitalization in subgroups using a retrospective cohort design.
Table S4. Vaccine effectiveness of BNT162b2 and CoronaVac against coronavirus disease 2019 (COVID-19)–related death in subgroups using a retrospective cohort design.
Table S5. Adjusted incidence rate ratio (IRR) of adverse events of special interest (AESIs) after BNT162b2 and CoronaVac using modified self-controlled case series (SCCS).
Table S6. Definitions of chronic kidney disease (CKD) using *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM).
Table S7. Definitions of adverse events of special interest (AESIs).

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