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COVID-19 vaccine effectiveness in patients with non–dialysis-dependent chronic kidney diseases: findings from a population-based observational study from British Columbia, Canada

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Patients with chronic kidney disease (CKD) are considered to be a high-risk group for contracting severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (coronavirus disease 2019 [COVID-19]) infection and postinfection complications. Recent research investigating the COVID-19 vaccine effectiveness (VE) in a population with CKD mostly involved patients receiving kidney replacement therapy, including kidney dialysis or transplantation.[1–5] Little is known about the VE in non–dialysis-dependent patients with CKD.

In British Columbia (BC), Canada, 1 in 10 individuals has some form of kidney disease.[6] These patients have a wide range of estimated glomerular filtration rate (eGFR), an indicator of the severity of kidney disease. The province had prioritized patients with CKD to receive COVID-19 vaccines, including a third dose first administered in October 2021. However, the COVID-19 VE among this nondialysis population with CKD is unknown. In addition, researchers want to know if the VE varies by the CKD disease stage based on eGFR. Our objective was to investigate the effectiveness of Health Canada–approved COVID-19 vaccines in a population-based cohort of non–dialysis-dependent patients with CKD from BC. We also looked into the COVID-19 VE by eGFR category.

RESULTS

The study sample included 18,850 patients with CKD who were followed up by nephrologists in BC (Supplementary Figure S1). Median age was 74 years, and 53% were men. Median follow-up time was 382 days, resulting in a cumulative follow-up time of 16,311 person years. By the end of follow-up, half of the study sample received their third dose, and a substantial proportion (33%) received 2 doses. Only 797 (4%) received 1 dose, and 2418 (13%) patients did not receive any vaccine (Table 1; Supplementary Table S1 presents patient characteristics by vaccination status).

There were 454 incident cases of COVID-19 infection, of which 42 were attributable to 1 dose, 122 to 2 doses,

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Table 1 | Patient characteristics

Variables	Overall study cohort
No. (%) of patients	18,850 (100)
Age at index date, yr	74 (64–82)
Male sex	9999 (53)
Race	
White	7881 (42)
Oriental Asian	1197 (6)
East-Indian Asian	1759 (9)
Indigenous	311 (2)
Others	7702 (41)
CKD vintage, yr	2.35 (0.34–5.73)
Etiology of kidney disease	
Glomerulonephritis	1756 (9)
Polycystic kidney disease	627 (3)
Diabetic nephropathy	3509 (19)
Others	12,958 (69)
Comorbidities	
Diabetes	9490 (50)
CVD-related comorbidities	8170 (43)
Respiratory disease	4980 (26)
Baseline eGFR, ml/min per 1.73 m^2	29 (21–40)
eGFR categories, ml/min per 1.73 m^2	
<15	1428 (8)
15–30	7121 (38)
30–60	6598 (35)
≥60	1463 (8)
Missing	2240 (12)
On immunosuppressive medication	1653 (9)
Long-term care	847 (4)
Study follow-up time, d	382 (279–382)
Cumulative follow-up, person years	16,311
No. of COVID-19 doses at the end of study follow-up	
No vaccine	2418 (13)
1 Dose	797 (4)
2 Doses	6129 (33)
3 Doses	9506 (50)
Time between COVID-19 vaccine doses, d	
From index date to first dose	110 (97–125)
From first dose to second dose	75 (64–87)
From second dose to third dose	162 (146–173)

CKD, chronic kidney disease; COVID-19, coronavirus disease 2019; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate.
Data are given as n (%) or median (interquartile range).

and 22 to 3 doses of vaccine exposure. The remaining 268 infections occurred during the prevaccination person-time (Supplementary Figure S2). After adjusting for age, sex, race, vintage, and etiology of CKD, comorbidities, including diabetes, cardiovascular disease–related disorders, and respiratory diseases, baseline eGFR category, baseline history of immunosuppressive medication use, long-term care residence, and monthly background infection rate, compared with prevaccination person-time, the risk of developing COVID-19 infection was 59% (adjusted hazard ratio [aHR], 0.41; 95% confidence interval [CI], 0.28–0.60), 71% (aHR, 0.29; 95% CI, 0.21–0.40), and 78% (aHR, 0.22; 95% CI, 0.13–0.38) less among patients with CKD who received 1, 2, and 3 doses, respectively (Figure 1a and Supplementary Table S2).

Compared with prevaccination person-time, the risk of developing the secondary outcome of COVID-19–related hospitalization or death was 53% (aHR, 0.47; 95% CI, 0.28–0.77), 84% (aHR, 0.16; 95% CI, 0.10–0.27), and 90% (aHR, 0.10; 95% CI, 0.04–0.28) less among patients with CKD vaccinated with 1, 2, and 3 doses, respectively (Figure 1b and Supplementary Table S3).

In a sensitivity analysis including only patients with prevalent CKD as of December 14, 2020 (N = 15,242), both the magnitude and directionality of the COVID-19 VE was similar to the hazard ratio estimates obtained from the primary analysis (Supplementary Tables S4 and S5).

The interaction between baseline eGFR category and COVID-19 vaccine exposure was not statistically significant ($P = 0.75$). However, we found that the risk of developing the COVID-19 infection was less in patients with CKD with eGFR <30 ml/min per 1.73 m^2 compared with those with eGFR ≥30 ml/min per 1.73 m^2 (Supplementary Figure S3). For exposure to 3 doses (booster dose), the risk was 83% less in eGFR category of <30 ml/min per 1.73 m^2 compared with 73% decreased risk in patients with eGFR ≥30 ml/min per 1.73 m^2. The aHRs (95% CIs) were 0.17 (0.08–0.36) and 0.27 (0.14–0.52), respectively. The VE was similar by age ($P = 0.83$), sex ($P = 0.84$), presence of comorbidities ($P = 0.13$), and baseline history of immunosuppressive medication use ($P = 0.47$) (Supplementary Figures S4–S7).

DISCUSSION

To the best of our knowledge, this is the first observational study investigating the COVID-19 VE among non–dialysis-dependent patients with CKD using population-based registry data from BC. We found that compared with prevaccination person-time, 2 or 3 doses of COVID-19 vaccines were highly effective in preventing incident COVID-19 infection (≥71%) as well as COVID-19–related hospitalization and death (≥84%). One dose was ≥53% effective. The reduced effectiveness in the study population compared with the efficacies reported in seminal randomized controlled trials appeared to be biologically plausible. Approximately 10% of the study sample were on immunosuppressive medication that could play a role in reducing vaccine effects. Patients with CKD produce lower antibody titers, and a lower sustained humoral response that might result in lower protection after vaccination.[7] Our findings are consistent with the literature investigating the COVID-19 VE among other populations with CKD (e.g., 69%–79% efficacy in preventing reverse transcriptase polymerase chain reaction–confirmed COVID-19 infection among maintenance dialysis population).[1,8]

The counterintuitive findings of lower VE among patients with higher eGFR could be due to several reasons. First, the proportion of individuals who were on immunosuppressive medications at baseline was more than double in the eGFR category of ≥30 versus <30 ml/min per 1.73 m^2. Second, patients with CKD with higher eGFR values may feel less vulnerable, which would impact their health behavior in taking precautions against contracting COVID-19 infection. In contrast, patients with CKD with lower eGFR may have been monitored more closely, resulting in better protection.

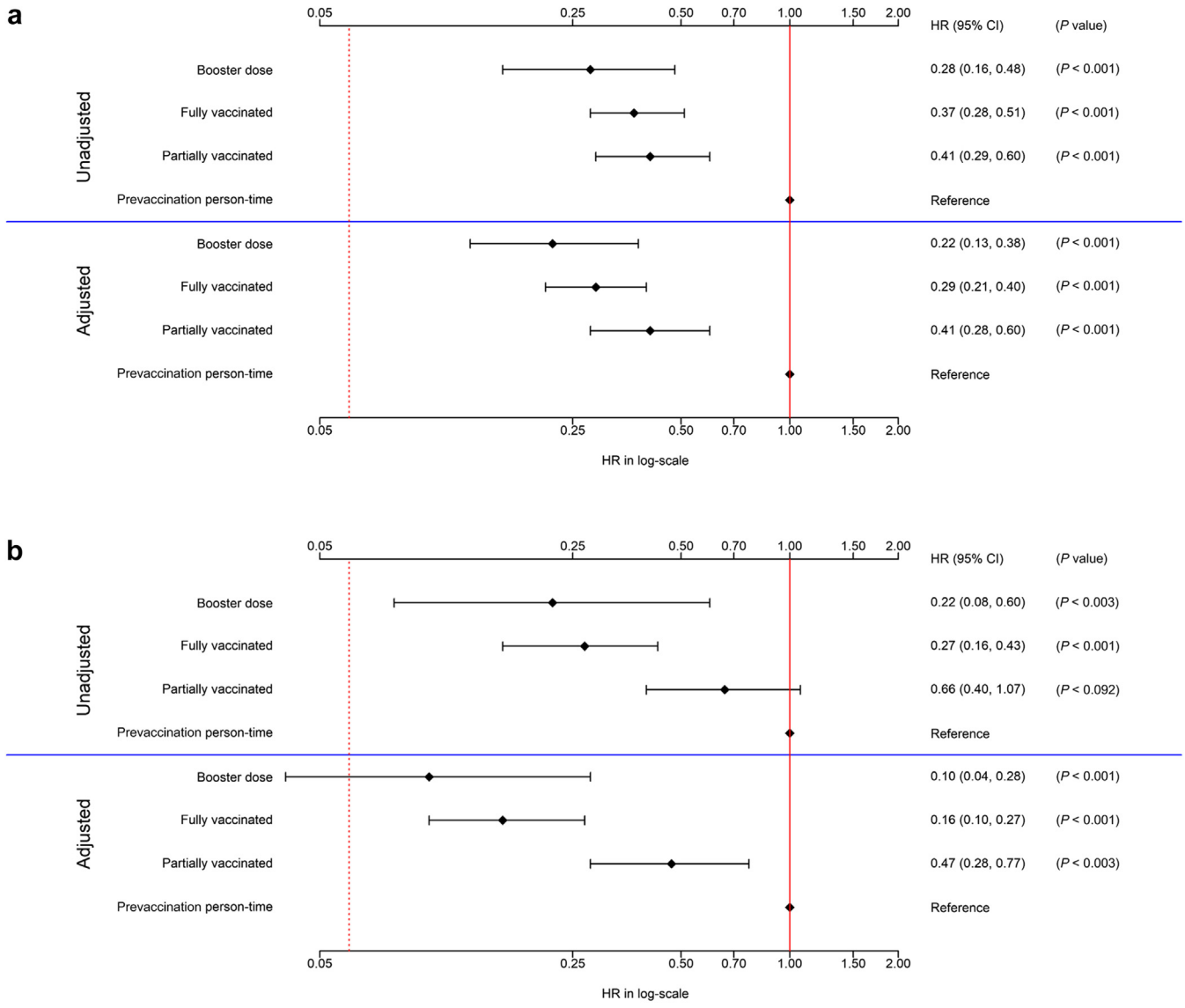

Figure 1 | Results from the Cox regression analysis using time-dependent coronavirus disease 2019 (COVID-19) vaccine exposure. (**a**) Primary outcome: severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (COVID-19) infection. (**b**) Secondary outcome: composite of COVID-19–related hospitalization or death. The solid line indicates the hazard ratio (HR) of 1. All the HRs associated with COVID-19 vaccine exposures appeared to be protective against COVID-19 infection and COVID-19–related severe outcomes. The dotted line indicates the efficacy of COVID-19 vaccine reported in seminal randomized control trials. In line with the hypothesis, the COVID-19 vaccine effectiveness among nondialysis patients with chronic kidney disease appeared to be less than what was reported in general population. CI, confidence interval.

Symptom information was not recorded in the health administrative data in BC. As such, we adopted a full cohort analysis strategy over a test-negative design that enabled us to include the entire nondialysis population with CKD who were registered in the Patient Records and Outcome Management Information System (PROMIS). In the primary analysis, we modeled the COVID-19 vaccine exposure in a time-dependent manner and adjusted for the monthly background infection rate at the health authority level as a time-varying covariable. In addition, VE estimates from the sensitivity analysis, including the patients with prevalent CKD, were similar to the results obtained from the primary analysis, which demonstrates the robustness of the study findings.

The VE observed in this study is most likely against the pre-Omicron variants, including Alpha and Delta, given the time period sampled. We anticipate that 3% to 7% of the study outcomes could be due to Omicron variant, which might have insignificant impact on the VE estimates (Supplementary Figure S8). Approximately 2% of the study sample received ChAdOx1 vaccine. As such, it can be safely assumed that the VE estimated in this study was the efficacy of mRNA vaccines predominantly against Alpha and Delta variants.

This study has numerous strengths. First, the registry-based, large cohort of nondialysis patients with CKD makes our findings to be generalizable to this population. Second,

we identified COVID-19 cases confirmed by reverse transcriptase polymerase chain reaction testing using patient-level clinical data. The study sample was multicultural in nature. Access to the patient-level data on immunosuppressive medication use allowed us to investigate if VE varies by exposure to these medications. Our study had a few limitations of observational studies based on administrative data. For example, we did not have access to the variant data. We created the study cohort using PROMIS database. We might have missed non-dialysis patients with CKD who were not registered in PROMIS during the study period. However, the large sample of patients with CKD in PROMIS represents the majority of the patients with CKD in BC, under the care of nephrologists. In addition, inability to compare the VE with non-CKD population was a limitation. Future studies may consider conducting similar analyses using health administrative data.

In conclusion, the Health Canada–approved COVID-19 vaccines (namely, mRNA vaccines) were highly effective in preventing incident COVID-19 infection and COVID-19–related hospitalizations and death among non–dialysis-dependent patients with CKD. We observed a dose-response relationship in which higher doses provided better protection. Future research is necessary to investigate if the vaccines would produce similar results for the newer variants, including Omicron.

DISCLOSURE

MJO is a contracted medical lead at Ontario Renal Network, Ontario Health. He is the owner of Oliver Medical Management, Inc., which licenses the Dialysis Management Analysis and Reporting System software. He has received honoraria for speaking from Baxter Healthcare and has participated on advisory boards for Amgen and Janssen. All the other authors declared no competing interests.

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SUPPLEMENTARY MATERIAL

Supplementary File (Word)

Supplementary Methods.

Supplementary References.

Appendix S1. Regrouping the self-reported race recorded in PROMIS database.

Appendix S2. List of cardiovascular diseases (CVDs) included in the composite CVD-related comorbidities.

Appendix S3. Calculating monthly background coronavirus disease 2019 (COVID-19) infection rate.

Appendix S4. Covariables selected a priori.

Figure S1. Cohort derivation.

Table S1. Patient characteristics by coronavirus disease 2019 (COVID-19) vaccination status as of the end of follow-up.

Figure S2. Distribution of primary outcome of coronavirus disease 2019 (COVID-19) infection by time-dependent COVID-19 vaccine exposure.

Table S2. Detailed results of the multivariate Cox model for the primary outcome of the coronavirus disease 2019 (COVID-19) infection.

Table S3. Detailed results of the multivariate Cox model for the secondary outcome of coronavirus disease 2019 (COVID-19)–related hospitalization or death.

Table S4. Results from the Cox regression analysis, including patients with prevalent chronic kidney disease (CKD) as of December 14, 2020 (N = 15,242).

Table S5. Detailed results of the multivariate Cox model for the primary outcome of the coronavirus disease 2019 (COVID-19) infection, including only patients with prevalent chronic kidney disease (CKD) as of December 14, 2020 (N = 15,242).

Figure S3. Results from the Cox regression analysis for coronavirus disease 2019 (COVID-19) vaccine exposure by baseline estimated glomerular filtration rate (eGFR) category.

Figure S4. Results from the Cox regression analysis for coronavirus disease 2019 (COVID-19) vaccine exposure by baseline age category.

Figure S5. Results from the Cox regression analysis for coronavirus disease 2019 (COVID-19) vaccine exposure by sex.

Figure S6. Results from the Cox regression analysis for coronavirus disease 2019 (COVID-19) vaccine exposure by baseline comorbidities.

Figure S7. Results from the Cox regression analysis for coronavirus disease 2019 (COVID-19) vaccine exposure by baseline history of immunosuppressive medication use.

Figure S8. Pandemic wave and distribution of coronavirus disease 2019 (COVID-19) variants in British Columbia from December 2020 to December 2021.

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