Clinical and virological assessment on effects of COVID-19 vaccination and oral antivirals among elderly patients during omicron waves in Hong Kong

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Background

COVID-19 vaccines and oral antivirals (molnupiravir and nirmatrelvir-ritonavir) reduce the health impact of SARS-CoV-2 infections through modifying the host immunity and suppressing viral replications. Population-level clinical and virological outcomes may reflect individual immune responses to the virus among patients with COVID-19 who received these pharmaceutics in comparison with those not receiving such interventions, and may inform optimal implementation of control measures especially for high-risk populations during the post-pandemic era.

Objectives

This study aimed to evaluate the clinical and virological outcomes in relation to patients' demographic and clinical characteristics including vaccination and use of oral antivirals, aiming to highlight the possible protective effects of both interventions in different aspects.

Methods

We analyzed healthcare data for inpatients with COVID-19 admitted into public hospitals over omicron waves in Hong Kong during February 25 - December 31, 2023, to evaluate occurrence of in-hospital mortality and temporal patterns of viral shedding in relation to patients' vaccination status and antiviral treatments considering the demographic and other clinical factors.

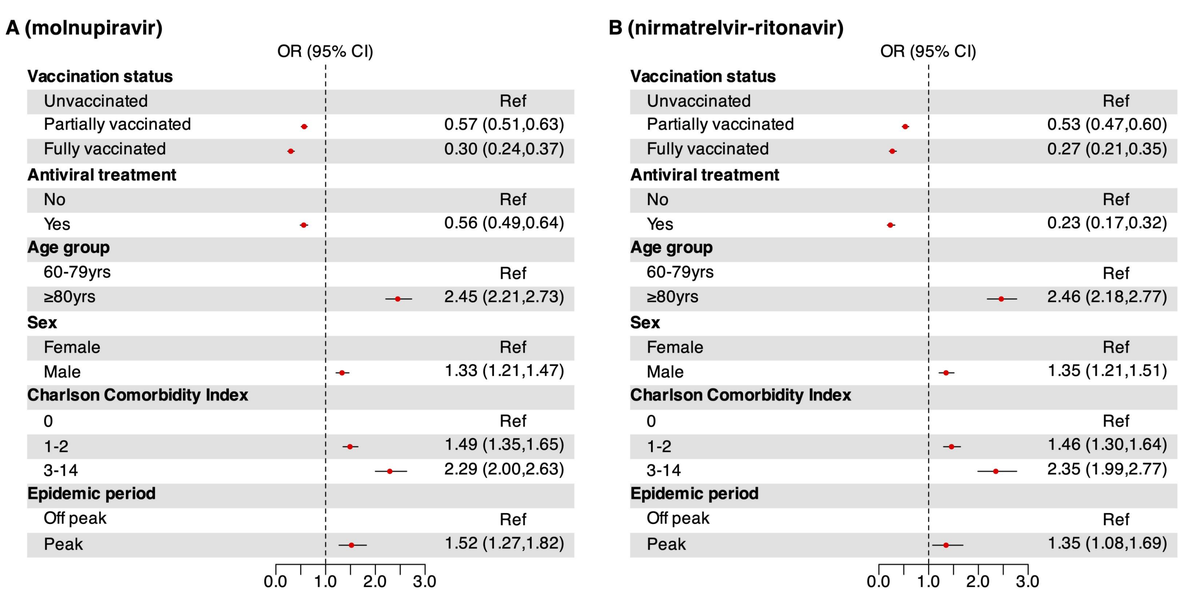

Figure 1. Associations estimated from the logistic regression model between (A) molnupiravir and (B) nirmatrelvir-ritonavir and the risk of in-hospital mortality adjusting for vaccination status and other potential confounders.

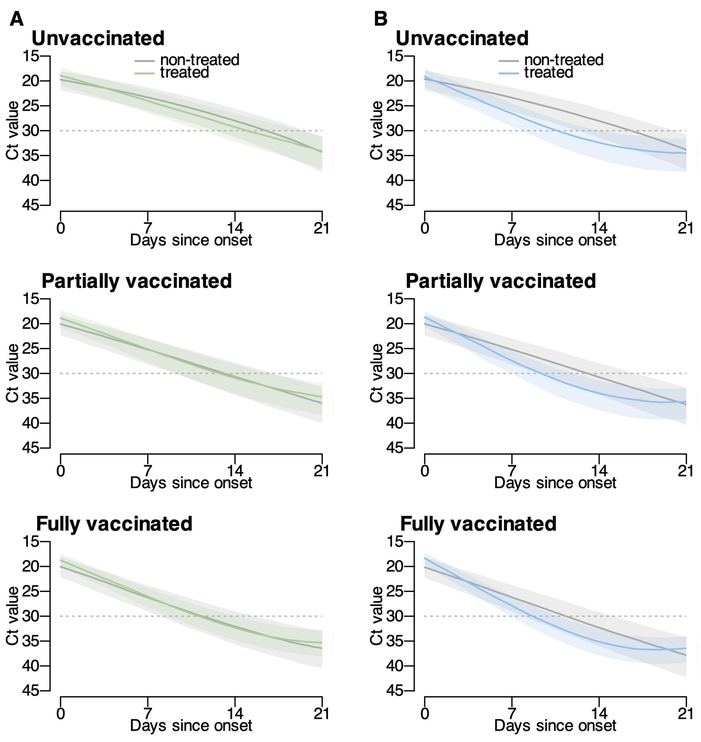

Figure 2. Trajectory of viral shedding since symptom onset estimated from random-effects models[1] between (A) molnupiravir and (B) nirmatrelvir-ritonavir, stratified by vaccination status.

Results

Vaccination was found to be associated with a lower mortality risk, and the risk for individuals that were fully vaccinated was prominently lower than that for those who were partially vaccinated (Figure 1). Treatment with either molnupiravir or nirmatrelvir-ritonavir demonstrated significant effects in reducing in-hospital mortality (OR: 0.56, 95% CI: 0.49-0.64 for treatment with molnupiravir and 0.23 (0.17-0.32) for nirmatrelvir-ritonavir respectively; Figure 1), and insignificant interactive effects were found between vaccination and oral antiviral treatments.

Majority of individuals included in the analyses for clinical severity were tested with Ct values from RT-qPCR during admission, and around 30-40% of individuals with Ct values were tested more than twice, providing sufficient longitudinal Ct values for the construction of individual viral shedding patterns over time. It was shown that vaccination and treatment with nirmatrelvir-ritonavir were associated with pronouncedly faster viral clearance particularly in the unvaccinated patients compared with the vaccinated counterparts (Figures 2-3). Only a marginal relationship with the change of viral burden was observed in patients treated with molnupiravir (Figure 3).

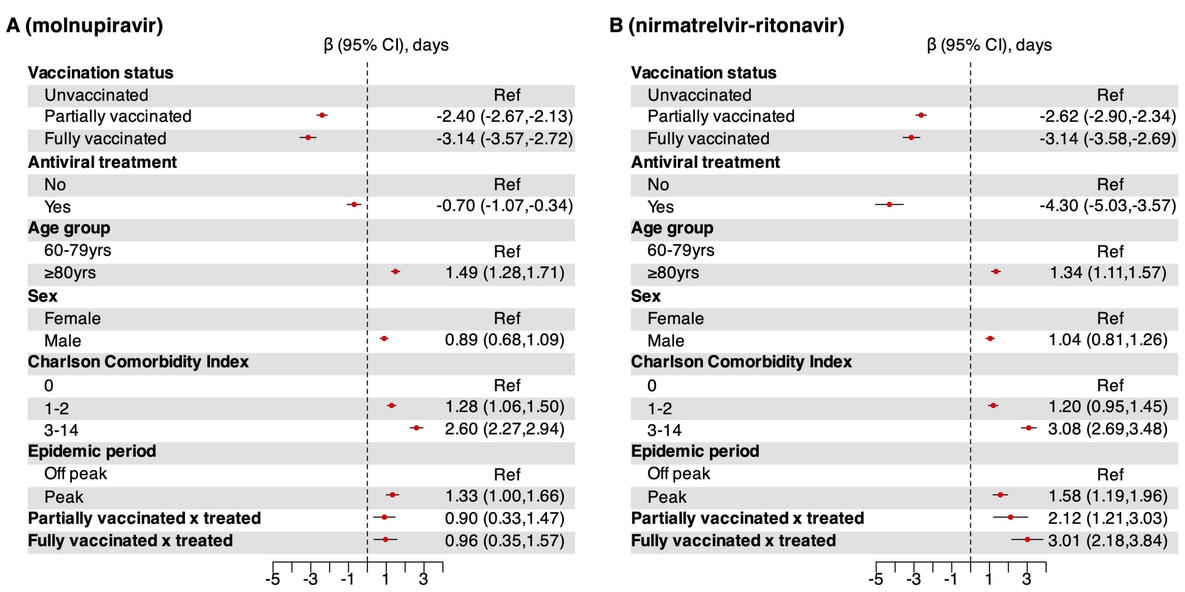

Figure 3. Associations estimated from the linear regression model between (A) molnupiravir and (B) nirmatrelvir-ritonavir and the duration of effective viral shedding (based on the trajectory of daily viral burden since onset estimated from random-effects models[1]), adjusting for vaccination status and other potential confounders.

Conclusion

Our study demonstrates that both COVID-19 vaccines and oral antivirals were independently associated with a better clinical outcome and faster viral clearance, especially nirmatrelvir-ritonavir. Further studies may be needed to investigate the interactive effect between vaccination and nirmatrelvir-ritonavir on viral kinetics to explore underlying mechanisms of immune responses to the viral infection.

References

[1] Lin Y, Wu P, Tsang TK, et al. Viral kinetics of SARS-CoV-2 following onset of COVID-19 in symptomatic patients infected with the ancestral strain and omicron BA.2 in Hong Kong: a retrospective observational study. Lancet Microbe 2023; 4(9): e722-e31.

Acknowledgements

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