

Evaluation of COVID-19 Vaccines in Primary Prevention Against Infections and Reduction in Severity of Illness Following the Outbreak of Sars-Cov-2 Omicron Variant in Shanghai

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Background

- In the first half of 2022, a major COVID-19 outbreak occurred, driven by the severe acute respiratory syndrome coronavirus 2(SARS-CoV-2) Omicron variant, spreading quickly at the community level.
- During this outbreak in Shanghai, multiple rounds of mass PCR testing in conjunction with antigen self-tests were implemented to ensure that no cases were left unidentified.
- Based on real-world, large-scale population data, we reviewed the clinical and demographic profiles of COVID-19 patients and healthy controls in Shanghai to investigate whether the vaccination protected people against SARS-CoV-2 infections and its impact on the severity level and disease outcomes.

Objective

To evaluate COVID-19 vaccines in primary prevention against infections and lessening the severity of illness following the most recent outbreak of the SARS-CoV-2 Omicron variant in Shanghai.

Methods

- To investigate whether inactivated vaccines were effective in protecting against COVID-19 infections, we estimated the odds ratio (OR) of the vaccination in COVID-19 cases vs. matched community-based healthy controls. To evaluate the potential benefits of vaccination in lowering the risk of symptomatic infection (vs. asymptomatic), we estimated the relative risk (RR) of symptomatic infections among diagnosed patients. We also applied the multivariate stepwise Logistic regression analyses to measure the risk of disease severity (symptomatic vs. asymptomatic and moderate/severe vs. mild) in COVID-19 patient cohort with vaccination status as an independent variable while controlling for potential confounding factors.

Results

Demographics and baseline characteristics

- The initial search identified 175,432 patients, after the database construction and cleaning, a total of 153,544 COVID-19 patients were included in the data analysis with the exclusion of the categorization of COVID-19 severity missing (n = 19,876) and the vaccination information missing or not specified (n = 2,012). The cleaning of the data from the NECC Fangcang hospital is illustrated in the flow chart (Figure 1). In addition, we recruited 228 community-based healthy controls with 456 cases matched from the COVID-19 patient cohort following the PSM. After matching, the cases and controls had nearly identical demographic profiles (mean age: 36.8 vs. 36.8; female gender: 43.9% vs. 44.7%; married: 64.9% vs. 66.2%).

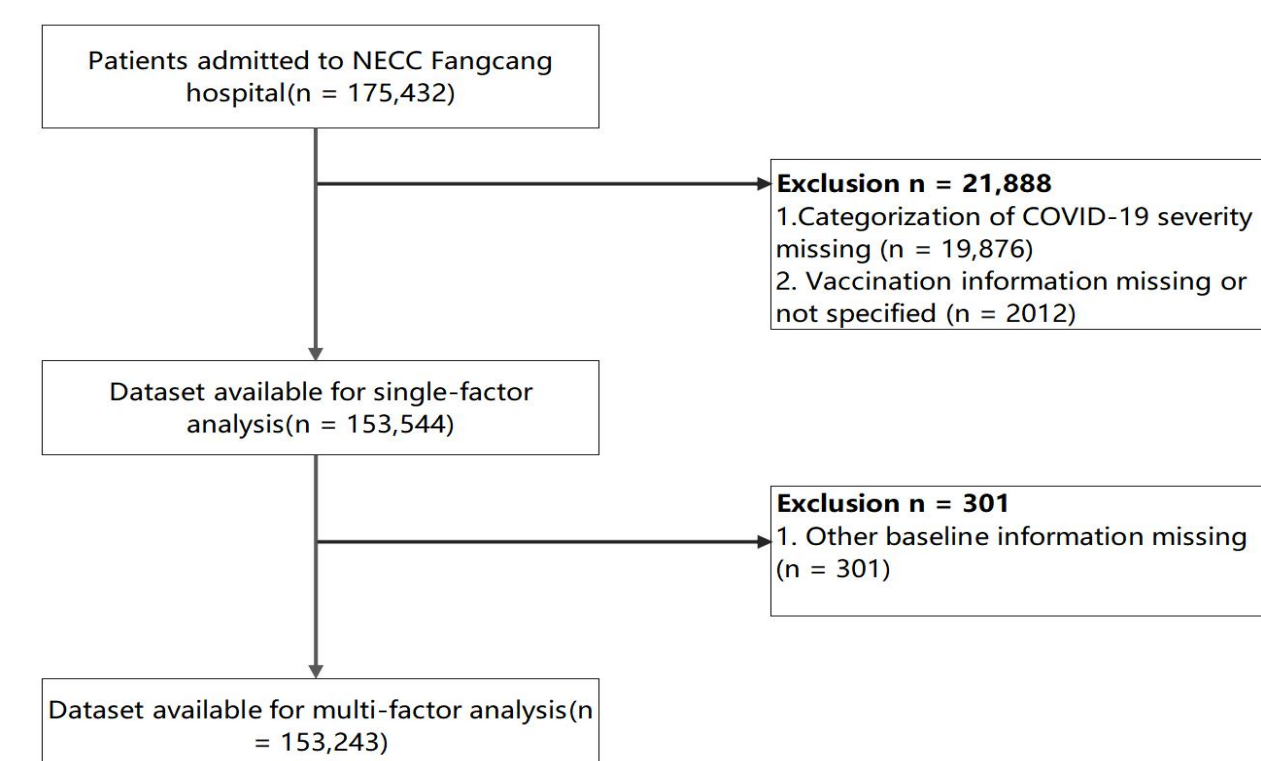


Figure 1: Flow chart of NECC Fangcang hospital data cleaning

Results

Single-factor analysis

- Of the 153,544 COVID-19 patients, the mean age was 41.59 years (SD = 15.53) and 90,830 (59.2%) were males. Of the entire patient cohort, 118,124 (76.9%) had been vaccinated and among them, 5,088(3.3%), 47,532 (31.0%%), and 65,504 (42.7%) received one dose, two doses, and three doses (three doses mean the 1st booster after completion of the primary series of 2 vaccinations), respectively. A vast majority of infected persons were asymptomatic (93.3%). Of the 10,319 symptomatic patients, 10,031(97.2%), 281(2.7%), and 7(0.1%) experienced mild, moderate, and severe infections, respectively. Of the 288 moderate/severe symptomatic patients,158(54.9%) had been vaccinated, which was at a lower rate than those vaccinated in the entire patient cohort (76.9%).

Table 1 Baseline characteristics

| Overall (n = 153,544) | |
|--------------------------------------|----------------|
| Sex, n (%) | |
| Male | 90,830 (59.2) |
| Female | 62,714 (40.8) |
| Age,mean (SD) | 41.59 (15.53) |
| Age ≥ 60, n (%) | 20,666 (13.5) |
| 60-69 | 17157(83.0) |
| 70-79 | 3280(15.9) |
| ≥ 80 | 229(1.1) |
| Marital status, n(%) | |
| Married | 91,919 (59.9) |
| Unmarried | 56,029 (36.5) |
| Others ^a | 5,595 (3.6) |
| Days of admission, mean (SD) | 6.68 (3.23) |
| Vaccination, n (%) | 118,124 (76.9) |
| Doses administered, n (%) | |
| 0 | 35,420 (23.1) |
| 1 | 5,088 (3.3) |
| 2 | 47,532 (31.0) |
| 3+ | 65,504 (42.7) |
| Underlying conditions, n (%) | |
| Hypertension | 13,411 (8.7) |
| Diabetes | 4,557 (3.0) |
| Allergy | 3,356 (2.2) |
| | 2,770 (1.8) |
| Stroke | 898 (0.6) |
| Arrhythmia | 2,390 (1.6) |
| Heart failure | 822 (0.5) |
| Peripheral vascular disease | 1,390 (0.9) |
| | 274 (0.2) |
| Post-operation | 365 (0.2) |
| | 228 (0.1) |
| Categorization upon admission, n (%) | |
| Asymptomatic | 143,225 (93.3) |
| Mild | 10,031 (6.5) |
| Moderate | 281 (0.2) |
| Severe | 7 (0.0) |
| Moderate/Severe | |
| ed, n (%) | 158(54.9) |
| Unvaccinated, n (%) | 130(45.1) |

- We also obtain the distribution of vaccination status of the cases and controls. There was no evidence indicating that the vaccination provided primary prevention against infections(Table 2). Of the 456 cases, 427 (93.6%) had a history of the vaccination and among 228 controls, 216 (94.7%) had received COVID-19 vaccines (OR = 0.82, p = 0.613)

Table 2 Distribution of vaccination status for both cases and controls

| Vaccination Status | Case Group (infected patients) | Control Group (healthy community residents) | Total | OR | P value |
|--------------------|--------------------------------|---|-------|------|---------|
| Vaccinated | 427 | 216 | 643 | 0.82 | 0.613 |
| Unvaccinated | 29 | 12 | 41 | | |
| Total | 456 | 228 | 684 | | |

- To evaluate the efficacy of vaccination in patients infected with SARS-CoV-2, we used the symptom status of patients upon admission grouped by vaccination status. As is shown in Table 3, the inactivated vaccines appeared to offer a small but significant protection against symptomatic infections. Among 118,124 vaccinated patients, 7,787 (6.6%) had COVID-19-related symptoms compared to 2,532 (7.1%) patients with symptomatic infections among 35,420 unvaccinated patients (RR = 0.92, p<0.001).

Table 3 Occurrence of any COVID-19 related clinical symptoms by vaccination status

| | Vaccinated | Unvaccinated | Total | RR | P value |
|--------------|------------|--------------|---------|------|---------|
| Symptomatic | 7,787 | 2,532 | 10,319 | 0.92 | <0.001 |
| Asymptomatic | 110,337 | 32,888 | 14,3225 | | |
| Total | 118,124 | 35,420 | 153,544 | | |

Multivariate analysis

- A multivariate stepwise logistic regression analysis was applied to evaluate the significant independent predictors for symptomatic SARS-CoV-2 infections upon controlling potential confounding factors. The results showed that receiving inactivated vaccines helped reduce symptomatic infections by 7% (OR = 0.93, 95% CI: 0.88-0.97) (Table 4). 1 dose, 2 doses of vaccination, and the presence of coronary artery disease were also associated with a lower risk of symptomatic infections (OR = 0.83, 95% CI:0.73- 0.94; OR =0.90, 95% CI:0.85-0.95; OR = 0.82, 95% CI: 0.69-0.97, respectively) (Appendix Table 4A &Table 4). Female gender, older age (≥ 60 years), and post-operation were significantly associated with increased risk of symptomatic infections (OR = 1.23, 95% CI:1.18 - 1.28; OR = 1.13, 95% CI:1.06 - 1.20; OR=2.31, 95% CI:1.70 - 3.15; respectively)

Table 4: Stepwise logistic regression analysis of the factors that influenced the presence of symptoms after the patients were infected with SARS-CoV-2

| Influencing factors | OR (95%CI) | P value |
|-----------------------------|-------------------|---------|
| Vaccination | 0.93 (0.88, 0.97) | 0.002 |
| Female | 1.23 (1.18, 1.28) | <0.001 |
| Age ≥ 60 years | 1.13 (1.06, 1.20) | <0.001 |
| Unmarried | 1.03 (0.92, 1.15) | 0.606 |
| Married | 1.10 (0.99, 1.23) | 0.082 |
| Diabetes | 0.92 (0.81, 1.03) | 0.160 |
| Coronary artery disease | 0.82 (0.69, 0.97) | 0.022 |
| Peripheral vascular disease | 0.83 (0.65, 1.06) | 0.140 |
| Post-operation | 2.31 (1.70, 3.15) | <0.001 |
| Renal disease | 1.54 (0.99, 2.39) | 0.055 |

- Finally, to further assess whether the factors associated with moderate/severe infections (vs. mild) in patients with symptomatic infections, another stepwise logistic regression analysis was performed. After adjusting for potential confounding factors, inactivated COVID-19 vaccines significantly reduced moderate/severe infections by about half (OR = 0.48, 95% CI: 0.37 - 0.61). Female gender was also associated with a lower risk of moderate/severe illness (OR = 0.77, 95% CI: 0.60 - 0.97)

Table 5: Stepwise logistic regression analysis of the factors associated with moderate/severe illness in patients with symptomatic infections

| Influencing factors | OR (95%CI) | P value |
|-------------------------|--------------------|---------|
| Vaccination | 0.48 (0.37, 0.61) | <0.001 |
| Female | 0.77 (0.60, 0.97) | 0.030 |
| Age ≥ 60 years | 3.14 (2.43, 4.04) | <0.001 |
| Coronary artery disease | 1.68 (0.93, 3.05) | 0.087 |
| Malignant tumors | 4.15 (1.50, 11.47) | 0.006 |

Conclusions

Inactivated COVID-19 vaccines helped provide small but significant protection against symptomatic infections and halved the risk of moderate/severe illness among symptomatic patients. The vaccination was not effective in blocking the community spread of the SARS-CoV-2 virus.