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Research Letters

Highly Effective Naturally Acquired Protection Against COVID-19 Persists for at Least 1 Year: A Meta-Analysis

To the Editor:

The current massive COVID-19 immunization campaign has initiated a change in the course of the pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The duration of postvaccination protection can be estimated from longer-term monitoring of the persistence of naturally acquired protection (since November 2019). Therefore, this rapid meta-analysis was conducted to evaluate the reinfection rates in post–COVID-19 patients as the primary endpoint to predict protection not only in the general population but also in vulnerable long-term care (LTC) recipients.

Methods

A search of the relevant literature was carried out in the MEDLINE, EMBASE, Web of Science, MedRxiv, and BioRxiv databases on June 7 and August 20, 2021, to identify any original studies on reinfections in post–COVID-19 patients. Eligible studies had to include the measure of association of acquired SARS-CoV-2 infection in post–COVID-19 individuals with previously uninfected ones. Key findings [ie, numbers of infected and reinfected individuals, measures of association including the 95% confidence intervals (95% CIs), viral variant of concern, follow-up period of $\geq$180 days, etc] were extracted.

This was a rapid and pragmatic meta-analysis to estimate reduction in the risk of reinfection in post–COVID-19 patients, expressed by the efficacy of naturally acquired protection, that is, (1 − measure of association) × 100%. Given the nonhomogeneity of the studies identified, the outcome was assessed using the random effects model (DerSimonian-Laird method). Analysis were performed using Stata, version 17 (StataCorp, College Station, TX), at a significance level of $\alpha = 0.05$ with a 2-tailed 95% CI. The protocol of this study was not registered.

Results

A total of 15 eligible publications were identified to assess the risk of reinfection in post–COVID-19 patients. These publications reported the results of cohort studies conducted in the general population (8 studies), in the population of health care workers (6) or in the military (1) including either only adults or individuals regardless of age (ie, also children and adolescents). The mean or median age of the study populations ranged from 19 to 59 years. Among the 10,123,319 subjects enrolled in the studies (42.8% of males), 67,124 were polymerase chain reaction (PCR)–positive (4), seropositive (7), or PCR/seropositive (4) with documented reinfection in 0.6% of cases beyond 60-120 days after complete resolution of the first infection. The mean follow-up time for reinfection was 234 days (range, 180-360 days) between March 2020 and May 2021.

The pooled efficacy of naturally acquired immunity determined using a random effects method achieved 87.1% (95% CI 82.4%, 90.6%) against any PCR-confirmed COVID-19 independently of the presence or absence of symptoms (Figure 1).[1–15] Publication bias, the effect of small studies, as well as omission of studies were not found. If the meta-analysis had included only adjusted measures of association (9 studies), the pooled efficacy would have achieved 85.0% (95% CI 77.0%, 90.2%). When considering only symptomatic reinfections (4 studies), the efficacy of naturally acquired protection increased to 91.7% (95% CI 84.6%, 95.5%).

Discussion

This meta-analysis confirmed a high (87%) level of protection acquired after COVID-19. When assessing the efficacy in symptomatic patients only, their 92% level of protection was close to that seen postvaccination.

As naturally acquired immunity to SARS-CoV-2 infection can dramatically reduce the risk of reinfection within at least 1 year, one may reasonably expect that vaccine-induced protection could confer a similar level of protection against COVID-19 for the first year.

Unfortunately, only 3 studies investigated the impact of SARS-CoV-2 variants of concern (B.1.1.7) on the risk of reinfection, making it impossible to quantitatively assess the efficacy of naturally acquired immunity against new variants.[1,6,8] The current more frequent failure of postvaccination protection, especially against the Delta variant, should also be taken very seriously as an issue related to post–COVID-19 protection.

Although all the studies were designed and conducted as cohort ones, the risk of bias was not the same across the studies as documented by the different pooled efficacies from adjusted and unadjusted measures of association. The published outcomes ranged between 69% and 98%, and the lower limit of the 95% CI was higher than 47%. One may assume that the efficacy results obtained from studies with a moderate or high risk of bias did not critically impact the final pooled efficacy in this meta-analysis. It should not be forgotten that the level of protection afforded by naturally acquired immunity depends on disease severity.[16] Therefore, the effectiveness determined from cohort studies could be skewed as a result of not taking into account mild or subclinical primary infections.

Although no study focused specifically on LTC recipients, they could be protected against reinfections the same as the general population in the context of current vaccination.[17]

The author declares no conflicts of interest.

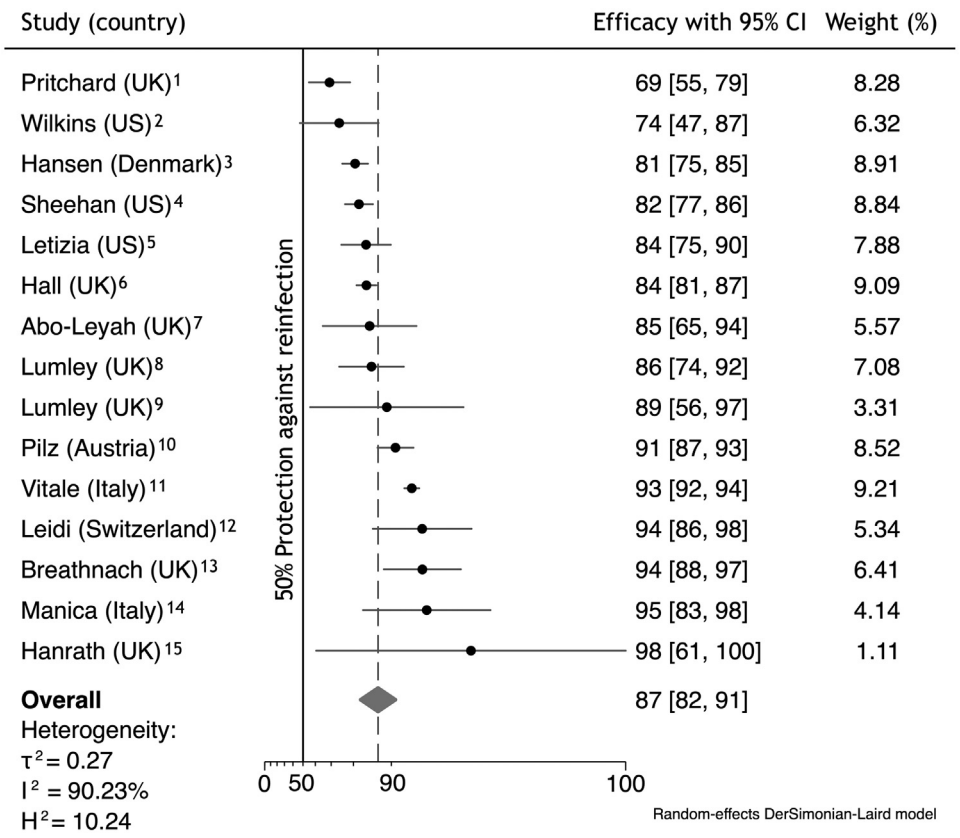

Fig. 1. Forest plot of efficacy of naturally acquired protection after COVID-19 against any reinfection (results are from a meta-analysis). H^2, heterogeneity; I^2, inconsistency; τ^2, variance; UK, United Kingdom; US, United States of America. Particulars of the forest plot: the diamonds indicate overall efficacy, with lateral points indicating the 95% CI; the dashed lines indicate the point of pooled efficacy.

In conclusion, the persistence of post–COVID-19 protection suggests a similarly durable post-vaccination efficacy within the first year. Even if naturally acquired protection against COVID-19 can reduce the risk of reinfections no less than vaccination, the risk of impact of new circulating variants, especially the Delta variant should by no means be underestimated.

Supplementary Data

Supplementary data related to this article can be found online at https://doi.org/10.1016/j.jamda.2021.08.042.

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Marek Petráš, PhD, Prof
Department of Epidemiology and Biostatistics
Third Faculty of Medicine
Charles University
Prague
Czech Republic

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Functional Outcomes of Severe COVID-19 Patients After a Post-Acute Care Hospitalization

To the Editor:

Patients hospitalized for severe coronavirus disease 2019 (COVID-19) may present with persistent symptoms and functional impairment for months after infection.[1,2] A proportion of those patients may need further hospitalization for rehabilitation or proper care transition.[3] However, little is known about outcomes after such hospitalizations.[4] We assessed long-term outcomes of patients admitted to a post-acute care facility (PACF) after a severe COVID-19 hospitalization.

Our study evaluated a cohort of patients with severe COVID-19 treated at a 60-bed private PACF in Brazil. Data were collected at PACF admission, discharge, and follow-up by telephone. Functional status was assessed by modified Barthel Index (20-100 points).[5] Mental health symptoms and quality of life were assessed by the Hospital Anxiety and Depression Scale (HADS) and the EQ-5D-3L score, respectively. Categorical variables with repeated measures were compared with Friedman test and a P value $<.05$ was considered significant. This study was approved by the institutional review board (Hospital das Clinicas da Faculdade de Medicina da Universidade de Sao Paulo (HCFMUSP), number 43277021.7.0000.0068), and informed consent was obtained from participants.

We report the first 100 patients admitted at the PACF after severe COVID-19 from April 2020 to April 2021. Follow-up was performed until June 8, 2021.

Patients were admitted to the PACF from 12 different hospitals, with a median (interquartile range) of 33 (23-42) days from symptom onset. The mean age was 65 ± 15 years, and 63 (63%) were male. Mean Charlson Comorbidity Index was 2.5 ± 1.9, and 86 (86%) were independent for all activities of daily living before hospitalization. Patients were hospitalized for 32 (24-42) days before transition to PACF, and 91 (91%) were admitted in the intensive care unit, 79 (79%) received invasive mechanical ventilation, and 3 (3%) received extracorporeal membrane oxygenation during the original hospitalization.

At admission to the PACF, 41 (41%) patients were in use of tracheostomy tube, 52 (52%) with tube feeding, 63 (63%) needed oxygen supplementation, and 5 (5%) were mechanically ventilated. Median PACF length of stay was 28 (15-46) days. Nine (9%) patients were readmitted to an acute care hospital due to clinical deterioration and 12 (12%) patients died during PACF hospitalization.

Table 1
Functional Status, Burden of Symptoms, and Quality of Life at Follow-up (n = 79)

Characteristics	Value
MBI*, mean ± SD	43.4 ± 12
EQ-5D-3L score†, mean ± SD	0.69 ± 0.27
HADS‡ anxiety, mean ± SD	3.55 ± 4.62
HADS depression, mean ± SD	3.13 ± 5.28
Prolonged symptoms, n (%)	
Dyspnea	19 (23)
Cough	38 (46)
Pain	40 (48)
Fatigue	50 (60)
Anosmia	6 (7)
Headache	20 (24)
Perceived quality of life as compared to before COVID-19, n (%)	
Much worse	18 (22)
Worse	29 (35)
Similar	15 (18)
Better	20 (24)
Much better	1 (1)

HADS, Hospital Anxiety and Depression Scale; MBI, modified Barthel Index.
*Modified Barthel Index (20-100, with 20 being complete dependence and 100 being complete independence).
†EQ-5D-3L health state index scores generally range from less than 0 (where 0 is a health state equivalent to death; negative values indicate a state worse than death) to 1 (perfect health).
‡HADS is assessed in 2 dimensions: anxiety and depression. Each dimension scores from 0 to 21 (higher scores indicating greater chance of symptoms). A score ≥9 is usually interpreted as a cutoff.

At follow-up, for a median (interquartile range) of 54 (40-91) days after PACF discharge and 142 (109-276) days after symptom onset, of the 79 patients discharged alive, 2 (2.5%) died, 12 (15%) were readmitted to an acute care hospital, and 70 (88%) reported at least 1 persistent symptom (Table 1). Of the 45 patients with active work life before hospitalization, 19 (42%) returned to previous level of work during the follow-up period. At follow-up, mean ± SD scores for modified Barthel Index, EQ-5D-3L, and Hospital Anxiety and Depression Scale anxiety and depression subscale scores were 87 ± 27, 0.69 ± 0.27, 3.55 ± 4.62, and 3.13 ± 5.18, respectively. Participants rated perceived quality of life as much worse, worse, similar, better, and much better in 14 (18%), 29 (38%), 15 (19%), 18 (23%), and 1 (1%), respectively. At PACF admission, 70 (88%) were

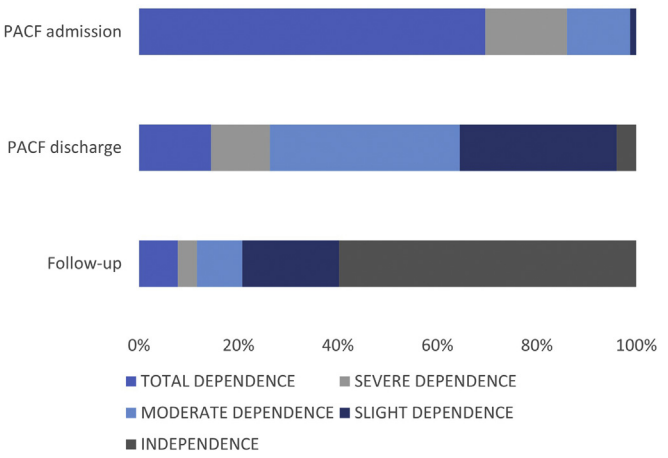

Fig. 1. Functional status, as measured by the modified Barthel Index (MBI) at post-acute care facility (PACF) admission, discharge, and after follow-up ($P < .001$). The MBI was categorized as total dependence if equal to 20; severe dependence, if between 21 and 60; moderate dependence, if between 61 and 90; mild dependence, if between 91 and 99; independence, if equal to 100.[5]

JGRR has received a fee for a lecture on post-acute care of COVID-19 patients by Nestle, unrelated to the present study. The other authors declare no conflicts of interest.