

Letters

RESEARCH LETTER

Binding and Neutralization Antibody Titers After a Single Vaccine Dose in Health Care Workers Previously Infected With SARS-CoV-2

Current shortages in COVID-19 vaccine production and distribution have led some experts to suggest untested regimens.¹ Persons who have had COVID-19 are thought to have protective immunity and memory responses² for at least 6 months; however, neither recall responses nor ideal vaccine dosing regimens have been studied in those previously infected with SARS-CoV-2. We assessed whether health care workers with previous COVID-19 infection could mount recall responses to a single dose of an mRNA-based COVID-19 vaccine.

Methods | Health care workers who had previously enrolled in a hospital-wide serosurvey study,³ conducted from July to August 2020 at the University of Maryland Medical Center, were randomly contacted based on stratification into 3 groups: SARS-CoV-2 IgG antibody-negative (Ab-negative); IgG-positive asymptomatic COVID-19 (asymptomatic); and IgG-positive with history of symptomatic COVID-19 (symptomatic). Participants were vaccinated with either the Pfizer-BioNTech or Moderna vaccine, depending on personal preference and availability. Blood was drawn at days 0 (baseline), 7, and 14 postvaccination in December 2020 and January 2021 (draws could be within 1 day from assigned day). Plasma was tested using enzyme-linked immunosorbent assay (ELISA) for IgG to spike trimer, which was modified from an assay⁴ to give a readout of half-

maximal binding titers. The reciprocal half-maximal binding titers represent the dilution of plasma that achieves 50% of maximal binding of a known control that reaches saturation. Day 0 and 14 samples from vaccinees were also tested for ID₉₉ (the 99% inhibitory dose, the highest dilution at which 99% of cells were protected) by live virus neutralization (presented as reciprocals).⁵ Samples from each day were compared between each prior Ab-positive (asymptomatic or symptomatic) group to the Ab-negative group.

All health care workers provided written informed consent; the study was approved by the University of Maryland institutional review board. Statistical analysis was performed with GraphPad Prism 5 (GraphPad Software). Antibody titers between groups were tested using the 2-tailed Mann-Whitney test, with $P < .05$ considered significant.

Results | Of 3816 health care workers enrolled in the serosurvey study,³ 151 were randomly contacted and 59 volunteers enrolled: 17 in the Ab-negative, 16 in the asymptomatic, and 26 in the symptomatic group (Table). The median age was 38 years for the Ab-negative, 40 years for the asymptomatic, and 38 years for the symptomatic group. The percentage of women was 71% for the Ab-negative, 75% for the asymptomatic, and 88% for the symptomatic group. At 0, 7, and 14 days, median reciprocal half-maximal binding titers were higher in each of the asymptomatic (208, 29 364, and 34 033) and symptomatic (302, 32 301, and 35 460) groups compared with the Ab-negative group (<50, <50, and 924) ($P < .001$ for each). At 0 and 14 days, median reciprocal ID₉₉ virus neutralization titers of each of the asymptomatic (80 and 40 960) and symptomatic (320 and 40 960) groups

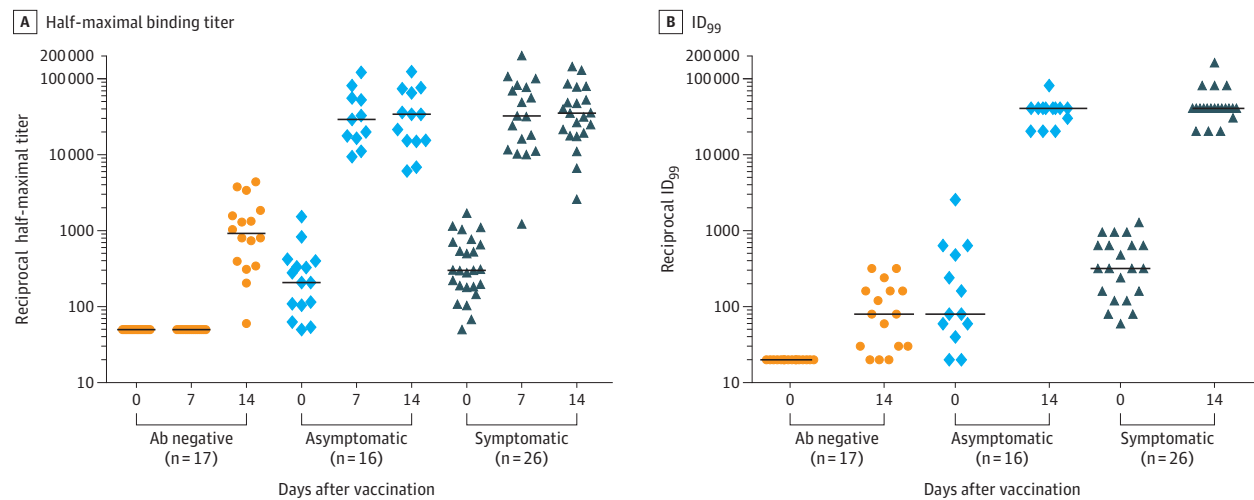
Table. Study Population Baseline Characteristics

	No. (%)		
	Ab-negative (n = 17)	Asymptomatic (n = 16)	Symptomatic (n = 26)
Age, median (range), y	38 (29-55)	40 (25-72)	38 (23-59)
Sex			
Male	5 (29)	4 (25)	3 (12)
Female	12 (71)	12 (75)	23 (88)
Race/ethnicity ^a			
Black or African American	2 (12)	5 (31)	5 (19)
White	12 (71)	9 (56)	18 (69)
Asian	3 (18)	2 (13)	3 (14)
Vaccine (by manufacturer)			
Pfizer-BioNTech	10 (59)	6 (37)	13 (50)
Moderna	7 (41)	10 (63)	13 (50)
Days symptomatic, median (range)		0 (0-2)	10 (3-34)
Hospitalization		0	4 (15)
Months from COVID-19 PCR+ to vaccination, median (% PCR tested) [range]		9.0 (44) [6.5-9.7]	8.0 (73) [6.0-10.3]
Months from COVID-19 IgG+ to vaccination, median (range)		6.2 (4.8-7.1)	6.1 (3.8-7.2)

Abbreviation: PCR, polymerase chain reaction.

^a Race/ethnicity data derived from self-report. This variable was of research interest because individuals of different race/ethnicity may react differently to vaccine.

Figure. Anti-SARS-CoV-2 Antibody Responses After a Single Dose of Vaccine in Health Care Workers



After COVID-19 vaccination, plasma was drawn at 0, 7, and 14 days; IgG binding titers against spike trimer were measured by enzyme-linked immunosorbent assay and live virus neutralization was assessed at days 0 and 14. A, IgG spike trimer half-maximal titers. By 7 days and continuing through 14 days following vaccination, both groups of health care workers with prior infection (asymptomatic and symptomatic) who received a single vaccine dose

developed higher peak IgG titers than the antibody (Ab)-negative group. B, Live virus neutralization ID₉₉ (the 99% inhibitory dose, the dilution at which 99% of cells were protected). At 14 days, both groups of health care workers with prior infection (asymptomatic and symptomatic) who received a single vaccine dose developed higher neutralization titers than the Ab-negative group. Horizontal black lines represent median values.

were higher than the Ab-negative group (<20 and 80) ($P < .001$ for each) (Figure).

Discussion | Health care workers with previous COVID-19 infection, based on laboratory-confirmed serology testing, had higher antibody titer responses to a single dose of mRNA vaccine than those who were not previously infected. Antibody titers started peaking at 7 days and achieved higher titers and neutralization in 14 days compared with Ab-negative volunteers. Limitations of the study are the small sample size, lack of demonstration of vaccine efficacy, and potential bias introduced by those enrolling not being representative of the larger original population. Given the ongoing worldwide vaccine shortages, the results inform suggestions for a single-dose vaccination strategy for those with prior COVID-19 or placing them lower on the vaccination priority list.⁶

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Discriminant Accuracy of the SOFA Score for Determining the Probable Mortality of Patients With COVID-19 Pneumonia Requiring Mechanical Ventilation

The COVID-19 pandemic has raised concern regarding the capacity to provide care for a surge of critically ill patients that might require excluding patients with a low probability of short-term survival from receiving mechanical ventilation.¹ A survey identified 26 unique COVID-19 triage policies, of which 20 used some form of the Sequential Organ Failure Assessment (SOFA) score.²

However, studies performed in 2016 and 2017 have shown only moderate discriminant accuracy of the SOFA score for predicting survival in intensive care unit (ICU) patients with sepsis and an area under the receiver operating characteristic curve (AUROC) of 0.74 to 0.75.^{3,4} We hypothesized that the SOFA score might be less accurate in patients requiring mechanical ventilation for COVID-19 pneumonia because such patients generally have severe single-organ dysfunction and less variation in SOFA scores.

Methods | This retrospective study was approved and exempted from the requirement for informed consent by the University of Arizona institutional review board. Data were from patients treated at 18 ICUs in the southwestern US between March 1, 2020, and August 31, 2020. We included consecutive patients aged 18 years or older with a diagnosis of COVID-19 pneumonia and receiving oxygen therapy for 4 hours or longer before undergoing endotracheal intubation. We calculated that a sample size of 640 patients would provide a 95% CI for an AUROC of $\pm 5\%$, assuming an AUROC of 70% and mortality of 25%.

The main outcome variable was hospital mortality or hospice discharge. The SOFA score comprises 0 to 4 points assigned to each of 6 organ systems based on ratio of PaO₂ to fraction of inspired oxygen, Glasgow Coma Scale score, mean arterial pressure, serum creatinine level, bilirubin level, and platelet count. The SOFA score ranges from 0 to 24 points, and higher scores indicate worse organ function. The variables used to calculate SOFA score and describe the patients were collected by electronic medical record review.

The SOFA score was calculated using the worst values observed within 48 hours prior to intubation, which is the point in time when ventilator triage for a patient with COVID-19 pneumonia would theoretically occur. The AUROCs for SOFA score and age (as single variables) were calculated and compared using the χ^2 statistic with a 2-sided $P \leq .05$ as the threshold for significance. Stata version 15 (StataCorp) was used.

Results | Between March 1, 2020, and August 31, 2020, 2546 patients with COVID-19 were admitted to study ICUs. Of

Table. Clinical Characteristics of 675 Study Patients

Characteristics	No. (%) ^a
Age, median (IQR), y	63 (53-72)
Age group, y	
18-44	92 (14)
45-64	267 (40)
65-74	199 (29)
75-84	102 (15)
≥ 85	15 (2)
Sex	
Female	270 (40)
Male	405 (60)
Race/ethnicity ^b	
Non-Hispanic White	259 (38)
Hispanic	286 (42)
Native American	68 (10)
Black	28 (4)
Body mass index, median (IQR) ^c	33 (29-39)
Medications	
Dexamethasone	255 (36)
Remdesivir	326 (48)
Anticoagulants	607 (90)
Norepinephrine	33 (5)
Comorbidities	
Diabetes	413 (61)
Hypertension	500 (74)
Coronary artery disease	134 (20)
Chronic obstructive lung disease	112 (17)
Cancer	67 (10)
Laboratory values, median (IQR)	
C-reactive protein, mg/L	168 (96-260)
D-dimer, $\mu\text{g/mL}$	1.76 (0.93-4.66)
Brain-type natriuretic peptide, pg/mL	461 (180-1328)
Creatinine, mg/dL ^d	0.9 (0.65-1.30)
Bilirubin, mg/dL ^d	0.6 (0.4-0.9)
Ratio of PaO ₂ to FiO ₂ ^d	56 (50-68)
Platelets, $\times 10^3/\mu\text{L}$ ^d	225 (164-299)
Arterial pressure, mean (IQR), mm Hg ^d	74 (64-84)
Glasgow Coma Scale score, median (IQR) ^d	15 (13-15)

Abbreviations: IQR, interquartile range; FiO₂, fraction of inspired oxygen.

SI conversion factors: To convert bilirubin to $\mu\text{mol/L}$, multiply by 17.104; creatinine to $\mu\text{mol/L}$, multiply by 88.4; D-dimer to nmol/L, multiply by 5.476.

^a Unless otherwise indicated.

^b Self-reported at hospital admission and was assessed to aid consideration of the generalizability of the study findings.

^c Calculated as weight in kilograms divided by height in meters squared.

^d Indicates the variables that were incorporated into the Sequential Organ Failure Assessment score.

these, 972 were intubated 4 hours or longer after receiving oxygen, but 297 lacked sufficient data to calculate the SOFA score. The characteristics of the remaining 675 patients appear in the **Table**.

The median SOFA score was 6 (interquartile range, 4-8). Respiratory SOFA subscores were 3 to 4 in 83.5% of patients. The other SOFA subscores were 0 to 1 in 72.1% of patients for