Effects of vaccination against COVID-19 on the evolution of critically ill patients☆

Efectos de la vacunación contra la COVID-19 en la evolución de los pacientes críticos

To the Editor,

In December 2019 an alert went off on a novel disease caused by a new type of coronavirus called SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2).[1] The economic and health impact of the COVID-19 pandemic has been tremendous. Measures to mitigate the pandemic have focused on social distancing and barrier measures.[2] However, the development of vaccines has been the main therapeutic tool to control this pandemic.[3] In Spain, the 5th wave has brought already vaccinated patients—whether totally or partially—to the intensive care units (ICU) together with unvaccinated patients. Therefore, now we have a new kind of patient, one whose disease progression we simply cannot anticipate. The objective of this study is to assess the effects of vaccination in the evolution of patients with SARS-CoV-2-induced pneumonia admitted to the ICU setting.

The study period (5th wave) went from July 2 2021 through September 8 2021. This period was defined by the interval in which the 14-day cumulative incidence exceeded 150 cases/100 000 inhabitants, which according to the directives coming from the Spanish Ministry of Health (SMH), is categorized as a high-risk epidemiological situation.[4] The diagnosis of SARS-CoV-2 infection was achieved through the polymerase chain reaction (PCR) test in samples from nasopharyngeal exudates (82%), bronchoaspiration (11%) or bronchoalveolar lavage (BAL) (7%). Complete vaccination was defined, according to the SMH strategic plan, as patients who had received the booster shot 7 (Comirnaty®) and 14 days (Spikevax® and Vaxzevria®) before. In the case of the Janssen® vaccine, 14 days after the single dose mark.[5] Quantitative variables were expressed as median and interquartile range (IQR). Categorical variables were expressed as count (percentage). For quantitative variable comparison purposes, the ANOVA test (analysis of variance) was used with post hoc studies to show inter-group differences. For categorical variable comparison purposes the chi-square test was used with Fisher approximation should the applicability conditions not be met. *P* values <.05 were considered statistically significant. Data were obtained from the registry of COVID-19 patients from our center intensive care unit after obtaining the approval of the local research ethics committee.

The total number of patients admitted during this period was 76, 50 (65.8%) out of whom remained unvaccinated, 11 (14.5%) partially baccinated, and 15 (19.7%) vaccinated with the booster shot. Among the patients actually vaccinated the following vaccines were used: Comirnaty® (developed by BioNTech and Pfizer) in 53.9% (14/26), Spikevax® (developed by Moderna) in 3.9% (1/26), Vaxzevria® (developed by AstraZeneca) in 23.1% (6/26), and COVID-19 Vaccine Janssen® (developed by Janssen, a company from Johnson&Johnson) in 19.2% (5/26). The reasons to refuse vaccination was not having been called for vaccination in 54% of the cases (27/50), voluntary rejection in 20% (10/50), and unvoluntary rejection (work or health issues) in 26% of the cases (13/50). Table 1 shows the baseline characteristics and severity scores used among the different groups. Table 2 compares the ventilation received by the different groups, the complications that occurred, and patient progression. All patients died at the ICU, but none at the hospital regular wards after ICU discharge. Table 3 SMH (supplementary data, Appendix) shows the mortality rate at the ICU setting of patients standardized by age (whether 55 years old or more).

As far as we know today, vaccination protects against the infection and when it happens, the chances of developing severe forms of the disease are much lower.[6] This has been essential to reduce pressure to the healthcare system at both the hospital and the ICU settings. Also, it has changed the profile of the patients who are admitted with severe disease due to SARS-CoV-2.[7,8] However, we still don't know what the evolution of vaccinated patients who have been admitted to the ICU due to SARS-CoV-2 induced severe pneumonia will be.

In Spain, at the beginning of the study period, nearly 18 million adult people had already received their vaccines with the booster shot too.[9] In our cohort, unvaccinated patients were younger with a median age of 51.5 years (IQR, 35.8—60) compared to partially (median, 62; IQR, 44—67) and fully vaccinated patients (median, 57; IQR, 49—68), *P* = .045. Both the mortality rate and the ICU stay were similar with a median of 22 days (IQR, 14—27) for vaccinated patients compared to 25 days (IQR, 14–36) for those unvaccinated. Severity scores showed a tendency—that was not statistically significant—to being higher in unvaccinated patients. After adjusting the results by age we could see the in patients under 55 no deaths were reported among partially or fully vaccinated patients while in unvaccinated patients, the mortality rate reported was 6.3% (table 3 SMH).

The rate of IMV among vaccinated patients with the booster shot was 93% compared to 78% among unvaccinated patients while the days on IMV were 7 (IQR, 1—10) in patients with their booster shots compared to 8 (IQR, 1—20) among unvaccinated patients. The prone position maneuver was required by 57% of the fully vaccinated patients compared to 64% of unvaccinated patients. Regarding evolutionary complications, there is a tendency towards less pulmonary thromboembolism and renal failure (defined by assessments > II in the Acute Kidney Injury Network classification). Regarding infections, no herpes simplex virus (HSV)

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Table 1 Baseline characteristics and severity scores of unvaccinated patients, partially vaccinated patients, and patients vaccinated with the booster shot.

	Unvaccinated (N = 50) (65.8%)	Incomplete vaccination (N = 11) (14.5%)	Complete vaccination (N = 15) (19.7%)	*P*
Baseline characteristics				
Male sex	32 (64)	7 (63.6)	11 (73.3)	.789
Age	51.5 (35.8–60)	62 (44–67)	57 (49–68)	.045
BMI	31.5 (29.4–35.3)	29.3 (26.8–42)	30 (28.4–33.6)	.918
Charlson Comorbidity Index	1 (0–3)	2 (0–5)	2 (0–4)	.399
Immunosuppression	8 (16)	5 (45.45)	4 (26.67)	.082
Severity scores (at admission)				
Total SOFA	4 (3–6)	4 (3–4)	4 (3–6)	.413
Respiratory SOFA	3 (3–4)	4 (3–4)	3 (3–4)	.645
APACHE II	9 (7–12)	8 (5–10)	11 (9–12)	.227
SAPS II	23 (17–31.5)	29 (23–36)	27 (22–42)	.529
PSI	70.5 (52.8–93.2)	68 (48–98)	84 (63–118)	.438
ARDS severity				
Mild	4 (8)	0	2 (13.3)	
Moderate	28 (56)	3 (27.3)	8 (53.3)	
Severe	18 (36)	7 (63.7)	5 (33.3)	.160

Quantitative variables are expressed as median (interquartile range). Categorical variables are expressed as count (percentage).
APACHE, Acute Physiology and Chronic Health Evaluation; ARDS, acute respiratory distress syndrome; BMI, body mass index; PSI, Pneumonia Severity Index; SOFA: Sepsis related Organ Failure Assessment.

Table 2 Respiratory support, evolutionary complications, and clinical outcomes in unvaccinated patients, partially vaccinated patients, and patients vaccinated with the booster shot.

	Unvaccinated (N = 50) (65.8%)	Incomplete vaccination (N = 11) (14.5%)	Complete vaccination (N = 15) (19.7%)	*P*
Ventilation				
IMV	39 (78)	8 (81.8)	13 (92.9)	.501
Days on IMV	8 (1–20)	9 (4.5–18)	7 (1–10)	.487
Prone position	32 (64)	7 (63.6)	8 (57.1)	.894
Tracheostomy	13 (27.1)	2 (20)	2 (18.2)	.772
ECMO	5 (10.2)	0	1 (6.7)	.820
Evolutionary complications				
Confirmed PTE	7 (14.6)	4 (40)[a]	1 (9.1)	.114
Acute kidney injury	11 (23.4)	1 (10)	2 (18.2)	.621
Nosocomial infection	20 (41.7)	5 (50)	4 (36.4)	.815
Infection due to HSV	4 (8.3)	0	0	.395
Aspergillosis	4 (8.3)	2 (20)	2 (18.2)	.438
Disease progression				
IVU stay	11 (7–23)	10 (7–23)	10 (9–15)	.617
Hospital stay	25 (14.2–35.7)	20.5 (15.5–36.3)	22 (14–27)	.590
High mortality at the ICU setting	9 (18)	3 (27.3)	2 (13.3)	.658

Quantitative variables are expressed as median (interquartile range). Categorical variables are expressed as count (percentage).
ECMO, extracorporeal membrane oxygenation; HSV, herpes simplex virus; ICU, intensive care unit; IMV, invasive mechanical ventilation; PTE, pulmonary thromboembolism.
[a] *P* values <.05 between the unvaccinated group and the group of patients without the booster shot.

infections were reported among patients with, at least, one vaccination shot while in unvaccinated patients, this infection occurred in 8% of the cases (with a CRP diagnosis on BAL). Confirmed or probable COVID-19 associated pulmonary aspergillosis (CAPA)[10] occurred in 8% of unvaccinated patients, and in 18% of the patients vaccinated with the booster shot.

The group of vaccinated patients without the booster shot shows common and hybrid characteristics compared to the fully vaccinated and unvaccinated patients. The limitations of this study have to do with its sample size, which complicates the process of drawing definitive conclusions. However, at the same time, the immediacy of the epidemiological process we are still going through empowers us to say that severe infection due to SARS-CoV-2 in a fully vaccinated patient can have different evolutionary characteristics and complications we should know. Another limitation is not knowing the type of virus variant, which can affect both the

immune response and the response to the infection given by the cohort. Future studies with larger samples should help us understand these findings much better.

Although the 5th wave has brough the pandemic under control largely thanks to the effect vaccines have had, we should mention that no major differences were seen in the ICU evolution of vaccinated and unvaccinated patients. However, most patients (66%) admitted during this period had never reveived the vaccine shots. Also, unvaccinated patients were younger and no deaths were reported among patients under 55 years who had received, at least, one shot of the vaccine.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.medin.2021.12.009.

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G. Morales Varas*, M. Sánchez Casado, R. Padilla Peinado, F. Morán Gallego, M. Buj Vicente, A. Rodríguez Villamizar

Unidad de Cuidados Intensivos, Servicio de Medicina Intensiva, Complejo Hospitalario Universitario de Toledo, Toledo, Spain

Corresponding author.
E-mail address: guillermo.moralesvaras@gmail.com (G. Morales Varas).

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