

Protection Against Severe Clinical Outcomes With Adenovirus or Messenger RNA Severe Acute Respiratory Syndrome Coronavirus 2 Vaccines in Patients Hospitalized With Coronavirus Disease 2019

TO THE EDITOR—Šmíd and colleagues [1] reported that recent severe acute respiratory (syndrome coronavirus 2) SARS-CoV-2 vaccination provides substantial protection against severe outcomes for infection with Delta B.1.617.2 and Omicron B.1.1.529 variants, including hospital admission, use of oxygen therapy and intensive care unit (ICU) admission. In their analysis, most had been vaccinated with the messenger RNA (mRNA) vaccine BNT162b2 (Pfizer/BioNTech), followed by mRNA-1273 (Moderna) and the adenovirus-based vector vaccines ChAdOx1 nCoV-19 (AstraZeneca) and Ad26.CoV2.S (Johnson & Johnson). However, the authors did not analyze the comparative vaccine effectiveness in adenovirus-vectored or mRNA-based vaccines regarding their protection against clinical outcomes in hospitalized patients. The relative efficacy comparing these 2 vaccine platforms has been controversial [2–5]. Data are needed to understand potential differences in vaccine effectiveness, particularly regarding severe clinical outcomes.

We assessed the relationship between previous SARS-CoV-2 vaccination (adenovirus vs mRNA based) in 368 consecutive patients hospitalized with coronavirus disease 2019 (COVID-19) from 1 November 2021 to 31 January 2022. Demographic and clinical characteristics of the study population and types of SARS-CoV-2 vaccine are provided in [Supplementary Table 1](#) and [Supplementary Figure 1](#) in the [Supplementary Appendix](#). Those vaccinated with adenovirus-vectored vaccines were significantly younger and had less severe comorbid conditions and a shorter

median time since primary course vaccination ([Supplementary Table 1](#)).

The study period included a transition from Delta variant (99.6%) in the initial weeks to Omicron BA.1 in the final weeks (92%) in the population area included in the analysis [6]. In this background population, 42 749 persons had received full vaccination with mRNA vaccines (43.7% BNT162b2 and 40.3% mRNA-1273) and 8150 with adenovirus-vectored vaccines (5.9% ChAdOx1 nCoV-19 and 10.1% Ad26.CoV2.S). (The director of the institutional ethics committee waived the need for a specific approval for this study, owing to the analysis of anonymized data without implementation of any specific measures.)

Those vaccinated with ChAdOx1 nCoV-19 adenovirus vaccine were over-represented among patients with hospitalized COVID-19 (18.6%), compared with the general population (5.9% [$P < .001$; McNemar test]). Despite having baseline variables associated with better COVID-19 prognosis, those hospitalized with COVID-19 and vaccinated with adenovirus vaccines had significantly higher rates of pulmonary embolism ($P = .001$), noninvasive mechanical ventilation ($P = .01$), ICU admission ($P < .001$), mechanical ventilation ($P < .001$), and use of extracorporeal membrane oxygenation ($P = .03$; Pearson χ^2 test) ([Supplementary Table 2](#)).

In a Poisson regression analysis adjusted for age, sex, type of primary course vaccination, booster vaccination, number of comorbid conditions, and immune suppression, mRNA-vaccinated patients had an adjusted incidence rate ratio (aIRR) for ICU admission of 0.29 (95% confidence interval, .13–.68) compared with those who had received an adenovirus vaccine, the latter showing no significant difference compared with unvaccinated patients (aIRR, 0.70

[.37–1.37]) ([Figure 1](#)). There were no differences in mortality rates between adenovirus and mRNA vaccines ([Supplementary Table 3](#)). The only factor identified with higher risk of death was age (adjusted mortality rate ratio [aMRR], 1.07 [95% confidence interval, 1.04–1.10]) for every year of age. We did a sensitivity analysis excluding 80 patients who had received a booster (third) dose (>15 days before admission), and results did not change ([Supplementary Figure 2](#) and [Supplementary Table 2](#)).

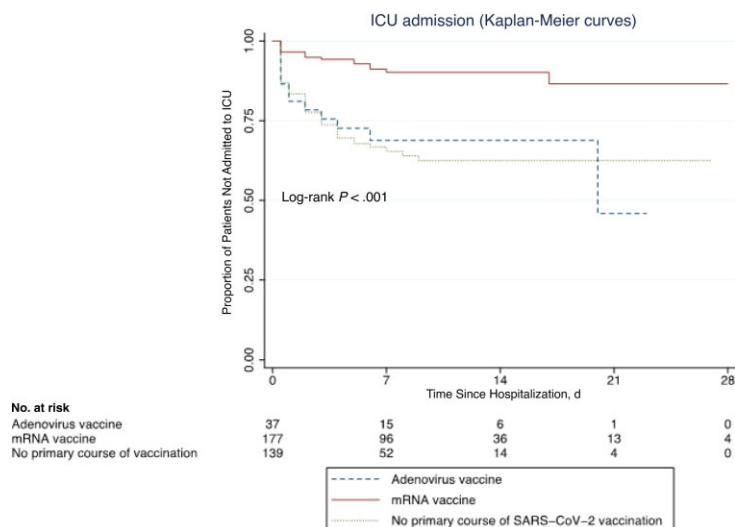
Kaplan-Meier curves showed a shorter time to ICU admission for those with adenovirus versus mRNA vaccines ($P < .001$), with no differences compared with the unvaccinated group ([Figure 1](#)). Similarly, patients who not received a booster (third) vaccine dose had a significantly shorter time to ICU admission ($P < .001$) ([Supplementary Figure 3](#)).

The inclusion of all consecutive patients hospitalized with COVID-19 in our analysis eliminates the possibility of underreporting, acknowledged as a limitation in the study reported by Šmíd et al [1]. These findings have public health implications and suggest a better protection against severe clinical outcomes among persons hospitalized with COVID-19 and vaccinated with SARS-CoV-2 mRNA-based vaccines versus adenovirus-vectored ones.

Supplementary Data

[Supplementary materials](#) are available at *The Journal of Infectious Diseases* online (<http://jid.oxfordjournals.org/>). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

A



B

Risk of ICU admission in patients hospitalized for COVID-19

Variable	Patients, No.	IR per 1000 Person-Days	IRR (95% CI)	aIRR
Total	75	17.3 (13.8–21.7)
Sex				
Female	24	14.9 (10.0–22.2)	1.00 (Reference)	...
Male	51	18.7 (14.2–24.7)	1.26 (.78–2.05)	
Age				
			0.95 (.93–.96)	0.95 (.94–.97)
SARS-CoV-2 vaccination status				
No primary course vaccination	47	27.5 (20.6–36.6)	0.83 (.44–1.57)	0.71 (.37–1.37)
Adenovirus vaccine	12	33.0 (18.7–58.1)	1.00 (Reference)	1.00 (Reference)
mRNA vaccine	16	7.1 (4.3–11.5)	0.21 (.10–.45)	0.29 (.13–.68)
Booster vaccination				
No primary course vaccination and, no booster	47	27.5 (20.6–36.6)	5.70 (2.05–15.82)	...
Primary course vaccine but no booster	24	13.4 (9.0–19.9)	2.77 (.96–7.99)	1.43 (.45–4.48)
Primary course vaccine and booster	4	4.8 (1.8–12.8)	1.00 (Reference)	1.00 (Reference)
Immune suppression				
No	66	18.0 (14.2–23.0)	1.00 (Reference)	1.00 (Reference)
Yes	9	13.2 (6.9–25.5)	0.73 (.37–1.47)	1.43 (.66–3.09)
No. of comorbid condition				
0–2	51	18.6 (14.2–24.5)	1.00 (Reference)	1.00 (Reference)
≥3	24	15.0 (10.1–22.4)	0.81 (.50–1.31)	0.92 (.55–1.53)

Figure 1. A, Kaplan-Meier curves for intensive care unit (ICU) admission by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination: no primary course vaccination, vaccination with adenovirus-vectored vaccine, or vaccination with messenger RNA (mRNA) vaccine. B, Risk for ICU admission among all patients hospitalized with coronavirus disease 2019 (COVID-19), by demographic and clinical variables and vaccination status. Abbreviations: aIRR, adjusted incidence rate ratio; CI, confidence interval; IR, incidence rate; IRR, incidence rate ratio. The aIRRs were adjusted for age, type of primary course vaccination, booster vaccination, immune suppression, and number of comorbid conditions; comorbid conditions included diabetes mellitus type II, chronic lung disease, chronic kidney disease, arterial hypertension, obesity, and human immunodeficiency virus infection.

Notes

Data sharing. Data reported in this study and used for the analyses, with de-identified individual-level data, are available to the scientific community on request with a short description of the analysis proposal.

Potential conflicts of interest. All authors: No reported conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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