

Original article

COVID-19 vaccination is associated with lower mortality and intensive care unit admission among hospitalized patients with COVID-19: A retrospective cohort study

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Abstract

Background: Vaccination has been central to reducing severe coronavirus disease 2019 (COVID-19). However, the association between prior vaccination and outcomes among patients hospitalized with COVID-19 remains clinically relevant.

Objective: This study aimed to investigate the association between COVID-19 vaccination status and mortality and intensive care unit (ICU) admission among hospitalized patients with COVID-19.

Methods: This retrospective single-center cohort study included adults hospitalized with reverse transcription polymerase chain reaction -confirmed COVID-19 between July 2021 and February 2022 who had documented vaccination status and underwent at least one chest computed tomography scan. The exposure of interest was full COVID-19 vaccination. Primary outcomes were mortality and intensive care unit (ICU) admission. Associations were examined using regression models adjusted for age, type 2 diabetes, hypertension, cardiac disease, and pulmonary disease. Exploratory predictor analyses were performed using Least Absolute Shrinkage and Selection Operator (LASSO) regression.

Results: The analytic cohort comprised 167 patients: 69.0% were male, mean age was 58 years (95% CI [55–60]), and 42.0% were fully vaccinated. Full vaccination was associated with lower adjusted relative risk of mortality (RR: 0.46, 95% CI [0.13–0.99]) and ICU admission (RR: 0.59, 95% CI [0.28–0.89]). The adjusted absolute risk difference for ICU admission corresponded to an observational number-needed-to-treat-like estimate of four, which should be interpreted cautiously. In patients younger than 60 years, vaccination was associated with fewer ICU admissions (RR: 0.64, 95% CI [0.32–0.99]).

Conclusion: COVID-19 vaccination was associated with lower mortality and reduced ICU admission among hospitalized patients with COVID-19 in this retrospective single-center cohort. Because of the observational design, selected hospitalized CT-imaged population, and potential residual confounding, these findings should be interpreted as associations rather than proof of causal protection.

Keywords: Computed tomography, COVID-19, hospitalized patients, ICU admission, mortality, SARS-CoV-2, vaccination.

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Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged in late 2019 and rapidly evolved into a global pandemic with profound health, social, and economic consequences. ⁽¹⁾ Although viral evolution and the emergence of new variants complicated pandemic control, vaccination substantially changed the clinical trajectory of COVID-19 by reducing severe disease at the population level. ⁽²⁾

Severe COVID-19 is characterized by complex host–virus interactions. In some patients, dysregulated inflammation and immune activation contribute to acute lung injury and systemic complications. ⁽³⁾ In addition, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can affect multiple organ systems, likely reflecting both direct viral tropism and indirect consequences of inflammation, endothelial dysfunction, and critical illness. ⁽⁴⁾ Clinically, severe disease is often defined by the need for intensive care unit (ICU) admission, mechanical ventilation, vasopressor therapy, or death. ⁽⁵⁾ Beyond the lungs, COVID-19 has been associated with renal, hepatic, pancreatic, vascular, and coagulation abnormalities ⁽⁶⁾

Vaccination reduces symptomatic infection, hospitalization, and mortality in broader populations. ⁽⁷⁾ Less is known, however, about whether vaccination status remains associated with clinical outcomes among patients who are hospitalized despite SARS-CoV-2 infection. This question is important because hospitalized patients represent a selected, high-risk population in whom comorbidity burden, age, variant period, and vaccination history may differ substantially from the general infected population.

We therefore conducted a retrospective single-center cohort study to examine whether COVID-19 vaccination status was associated with ICU admission, mortality, and selected clinical characteristics among hospitalized patients with COVID-19. The primary outcomes were ICU admission and mortality. Secondary outcomes included exploratory clinical, imaging, laboratory, and organ-system parameters, with particular focus on pulmonary, hepatic, renal, pancreatic, and coagulation-related findings.

Materials and methods

Study design and ethics

This retrospective cohort study was approved by the Institutional Research Ethics Board of the Medical Faculty at Albert-Ludwig-University Freiburg (22-1046-retro). Owing to the retrospective design, the Ethics Committee waived the requirement for informed consent. The study was conducted in accordance with the Declaration of Helsinki.

Study population

The study was conducted at a single tertiary-care center and included patients hospitalized with COVID-19 between July 1, 2021, and February 14, 2022. The exposure of interest was COVID-19 vaccination status. The primary outcomes were ICU admission and mortality. Patients were eligible if they were at least 18 years old, had confirmed SARS-CoV-2 infection documented by at least one positive reverse transcription polymerase chain reaction (RT-PCR) test from a nasal or throat swab, had documented vaccination status, and underwent at least one chest computed tomography (CT) scan during hospitalization. Patients were excluded if vaccination status was unknown or incomplete, if they were only partially vaccinated, or if they were younger than 18 years (**Figure 1**).

By design, this cohort was restricted to hospitalized adults who underwent chest CT. This may have selected patients with more severe respiratory disease, suspected pulmonary complications, or other clinical indications for imaging. Therefore, the cohort may not represent all hospitalized patients with COVID-19 or the broader population of individuals with SARS-CoV-2 infection. Because vaccination can reduce the probability of hospitalization, conditioning on hospitalization may also introduce selection or collider bias. All findings should therefore be interpreted as associations within this selected hospitalized CT-imaged cohort.

This cohort partially overlaps with previously reported imaging and acute respiratory distress syndrome (ARDS) analyses from our institution. ⁽⁸⁻¹¹⁾ The present study extends that work by focusing specifically on mortality, ICU admission, and systemic clinical parameters according to vaccination status.

CONSORT 2010 Flow Diagramm

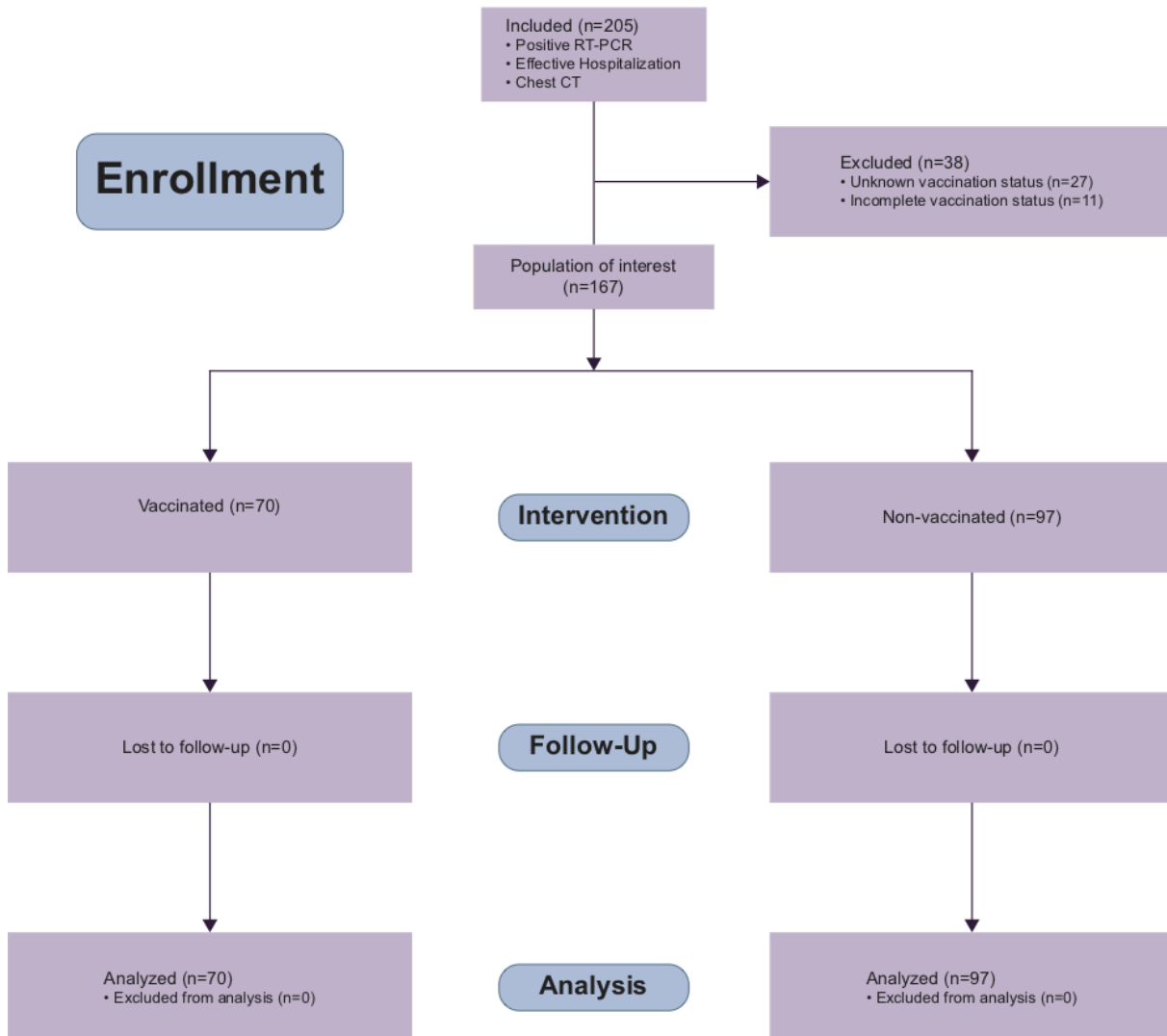


Figure 1. Flow diagram illustrating study participants.

Vaccination classification

Vaccination status was classified as non-vaccinated, partially vaccinated, fully vaccinated, or unknown. Patients with explicit documentation of no COVID-19 vaccination and confirmed SARS-CoV-2 infection were classified as non-vaccinated. Patients who had received only one vaccine dose, or who developed COVID-19 less than 14 days after a second dose, were classified as partially vaccinated. Patients were classified as fully vaccinated if they tested positive for SARS-CoV-2 or developed symptoms at least 14 days after their second vaccine dose. Patients with absent vaccination records or incomplete

documentation of the final vaccination date were classified as unknown.

No vaccine-specific analyses were performed. Vaccines administered in the cohort included ChAdOx1 nCoV-19, BNT162b2, mRNA-1273, and Ad26.COV2.S. Patients who received Ad26.COV2.S as their first vaccine were considered fully vaccinated only if they had also received a second mRNA vaccine dose at least 14 days before the positive RT-PCR test or symptom onset. Booster status and time since last vaccination were not incorporated into the primary models; residual confounding by these factors cannot be excluded.

Data collection

Patients were identified through the electronic hospital information system. Clinical data were extracted from electronic medical records and included vaccination status, age, sex, infection-related variables including variant data where available, symptom onset, anti-SARS-CoV-2 antibodies, symptoms, body mass index (BMI), comorbidities, laboratory parameters, CT findings, COVID-19 treatments, and complications.

Laboratory parameters included C-reactive protein, procalcitonin, D-dimer, partial thromboplastin time (PTT), international normalized ratio (INR), platelet count, creatinine, urea, aspartate aminotransferase (AST), alanine aminotransferase (ALT), partial pressure of oxygen (pO_2), and partial pressure of carbon dioxide (pCO_2). Imaging data included quantitative chest CT lesion scores, as previously described.^(8,9) Treatment and outcome variables included ICU admission, ICU duration, oxygen therapy, non-invasive ventilation (NIV), invasive ventilation, extracorporeal membrane oxygenation (ECMO), sepsis, pulmonary superinfection, coagulopathy, pulmonary embolism, renal failure, and mortality.

Statistical analysis

Baseline differences according to vaccination status were assessed using regression models. Variables that differed between vaccination groups and had sufficient event counts were considered for confounder adjustment. Rare or unevenly distributed variables, defined as variables with fewer than 10 events or unstable model behavior, were not included in the primary multivariable model. Instead, subgroup analyses were performed after excluding patients with these rare characteristics.

For the primary outcomes, mortality and ICU admission, regression analyses were performed with and without adjustment for age, type 2 diabetes, hypertension, cardiac disease, and pulmonary disease. Variant distribution and calendar period were considered potentially important confounders because both may be associated with vaccination status and COVID-19 severity. However, confirmed variant data were sparse and unevenly distributed, limiting stable inclusion in the primary multivariable model. Where feasible, subgroup analyses were performed; otherwise, residual confounding by variant distribution, calendar period, vaccine type, booster status, and time since vaccination was acknowledged.

Additional subgroup analyses were performed after excluding patients with rare characteristics,

including Omicron variant infection, absence of pre-existing disease, immunodeficiency, oncological disease, vascular disease, neurological disease, organ transplantation, and pregnancy. Age-stratified analyses were also performed in patients younger than 60 years and older than 60 years.

Analyses of secondary clinical, imaging, laboratory, and organ-system outcomes were exploratory. For laboratory parameters, analyses were additionally adjusted for duration since symptom onset. No formal adjustment for multiple comparisons was applied; therefore, statistically significant secondary findings should be interpreted cautiously and considered hypothesis-generating.

To identify predictors of ICU admission and mortality, exploratory regularized logistic regression was performed using LASSO regression. Variables selected by LASSO were subsequently examined in logistic regression models, with additional adjustment for vaccination status.

Effect sizes and adjusted effect sizes were reported with bootstrapped 95% confidence intervals (CI). Relative risks (RRs) and adjusted RRs were calculated where feasible; odds ratios (ORs) and adjusted ORs were reported when RR estimation was unstable or inappropriate. For continuous outcomes, Cohen's *d* and adjusted Cohen's *d* were used as effect sizes.⁽¹²⁾ Statistical evidence was inferred from 95% CIs: RRs and ORs were considered statistically significant when the 95% CI did not include 1, and Cohen's *d* was considered statistically significant when the 95% CI did not include 0. NNT-like estimates were calculated from absolute risk differences where applicable and should be interpreted cautiously because of the observational design. Analyses were performed using RStudio version 2023.06.0 + 421.

Results

Study cohort and baseline characteristics

The analytic cohort included 167 hospitalized adults with RT-PCR-confirmed COVID-19, documented vaccination status, and at least one chest CT scan. Overall, 69.0% of patients were male, the mean age was 58 years (95% CI [55–60]), and 42.0% were classified as fully vaccinated.

Baseline characteristics differed between vaccinated and non-vaccinated patients (**Table 1**). Vaccinated patients were older and had a higher burden of pre-existing disease, including type 2 diabetes, hypertension, cardiac disease, pulmonary disease, oncological disease, vascular disease,

Table 1. Demographic characteristics according to COVID-19 vaccination status. Results highlighted in blue are statistically significant.

	All	Vaccination status (n = 167)		Odds ratio (± 95% CI)
		Non-vaccinated (n = 97)	Vaccinated (n = 70)	
General information				
Age (years) (n = 167)	57.9(55.33–60.36)	51.1(48.12–54.04)	67.2 (63.97–70.59)	1.07 (1.05–1.10)
Sex (n = 167)				1.09 (0.56–2.15)
Male	115 (69.0%)	66 (68.0%)	49 (70.0%)	
Female	52 (31.0%)	31 (32.0%)	21 (30.0%)	
Virus variant (n = 81) **				7.11 (2.09–33.00)
Omicron	18 (22.0%)	3 (8.0%)	15 (37.0%)	
Delta	63 (78.0%)	37 (92.0%)	26 (63.0%)	
Pre-existing conditions				
BMI (n = 129)				0.75 (0.36–1.57)
> 25 kg/m ²	86 (67.0%)	50 (69.0%)	36 (63.0%)	
< 25 kg/m ²	43 (33.0%)	22 (31.0%)	21 (37.0%)	
Pregnancy (n=167)*				
Yes	6 (3.5%)	6 (6.0%)	0 (0.0%)	
No	161 (96.5%)	91 (94.0%)	70 (100.0%)	
Pre-existing diseases (n=167)**				7.75 (2.87–27.14)
Yes	132 (79.0%)	66 (68.0%)	66 (94.0%)	
No	35 (21.0%)	31 (32.0%)	4 (6.0%)	
Immunodeficiency (through disease or medication) (n = 167)**				4.78 (1.96–12.97)
Yes	26 (16.0%)	7 (7.0%)	19 (27.0%)	
No	141 (84.0%)	90 (93.0%)	51 (73.0%)	
Prediabetic metabolism (n = 167)*				0.45 (0.02–3.63)
Yes	4 (2.0%)	3 (3.0%)	1 (1.0%)	
No	163 (98.0%)	94 (97.0%)	69 (99.0%)	
Type 2 diabetes (n = 167)				2.83 (1.29–6.43)
Yes	32 (19.0%)	12 (12.0%)	20 (29.0%)	
No	135 (81.0%)	85 (88.0%)	50 (71.0%)	
Hypertension (n = 167)				4.07 (2.12–7.96)
Yes	66 (40.0%)	25 (26.0%)	41 (59.0%)	
No	101 (60.0%)	72 (74.0%)	29 (41.0%)	
Anemia (n = 167)				1.32 (0.53–3.21)
Yes	23 (14.0%)	12 (12.0%)	11 (16.0%)	
No	144 (86.0%)	85 (88.0%)	59 (84.0%)	
Rheumatological disease (n = 167)*				1.41 (0.37–5.28)
Yes	10 (6.0%)	5 (5.0%)	5 (7.0%)	
No	157 (94.0%)	92 (95.0%)	65 (93.0%)	
Oncological disease (n = 167)**				6.50 (2.59–18.68)
Yes	27 (16.0%)	6 (6.0%)	21 (30.0%)	
No	140 (84.0%)	91 (94.0%)	49 (70.0%)	
Infectious disease (n = 167)*				0.37 (0.05–1.62)
Yes	9 (5.0%)	7 (7.0%)	2 (3.0%)	
No	158 (95.0%)	90 (93.0%)	68 (97.0%)	
Cardiac disease (n = 167)				4.98 (2.50–10.26)
Yes	53 (32.0%)	17 (18.0%)	36 (51.0%)	
No	114 (68.0%)	80 (82.0%)	34 (49.0%)	
Vascular disease (n = 167)**				3.56 (1.48–9.27)
Yes	25 (15.0%)	8 (8.0%)	17 (24.0%)	
No	142 (85.0%)	89 (92.0%)	53 (76.0%)	

Table 1. (Cont.) Demographic characteristics according to COVID-19 vaccination status. Results highlighted in blue are statistically significant.

	All	Vaccination status (n = 167)		Odds ratio ($\pm$ 95% CI)
		Non-vaccinated (n = 97)	Vaccinated (n = 70)	
Pulmonary disease (n = 167)				3.23 (1.56–6.85)
Yes	41 (25.0%)	15 (15.0%)	26 (37.0%)	
No	126 (75.0%)	82 (85.0%)	44 (63.0%)	
Neurological disease (n = 167)**				4.13 (1.58–12.18)
Yes	21 (13.0%)	6 (6.0%)	15 (21.0%)	
No	146 (87.0%)	91 (94.0%)	55 (79.0%)	
Liver disease (n = 167)*				0.57 (0.12–2.15)
Yes	10 (6.0%)	7 (7.0%)	3 (5.0%)	
No	157 (94.0%)	90 (93.0%)	67 (95.0%)	
Renal disease (n = 167)				4.19 (1.93–9.08)
Yes	38 (23.0%)	12 (12.0%)	26 (37.0%)	
No	129 (77.0%)	85 (88.0%)	44 (63.0%)	
Thyroid disease (n = 167)				1.11 (0.51–2.38)
Yes	34 (20.0%)	19 (20.0%)	15 (21.0%)	
No	133 (80.0%)	78 (80.0%)	55 (79.0%)	
Organ transplant (n = 167)**				10.83 (2.85–70.90)
Yes	15 (9.0%)	2 (2.0%)	13 (19.0%)	
No	152 (91.0%)	95 (98.0%)	57 (81.0%)	

Results highlighted in gray are statistically significant. BMI, body mass index; CI, confidence of interval.

neurological disease, immunodeficiency, and organ transplantation. Six pregnancies occurred in the non-vaccinated group and none in the vaccinated group. Because several baseline variables were rare or unevenly distributed, the primary adjusted models included age, type 2 diabetes, hypertension, cardiac disease, and pulmonary disease, while additional subgroup analyses were performed for selected rare characteristics.

Primary outcomes: mortality and ICU admission

In unadjusted analysis, vaccination was not significantly associated with mortality (RR: 0.72, 95% CI [0.36–1.31]). After adjustment for age, type 2 diabetes, hypertension, cardiac disease, and pulmonary disease, full vaccination was associated with lower mortality among hospitalized patients with COVID-19 (adjusted RR: 0.46, 95% CI [0.13–0.99]) (Table 2 and Figure 2).

Vaccination was also associated with lower ICU admission in both unadjusted and adjusted analyses. The unadjusted RR for ICU admission was 0.60 (95% CI [0.40–0.83]), and the adjusted RR was 0.59 (95% CI [0.28–0.89]) (Table 2 and Figure 2). The corresponding absolute risk difference translated into an observational NNT-like estimate of four patients; however, this estimate should be interpreted cautiously because vaccination status was not randomly assigned.

Post-hoc sensitivity calculations indicated that, with 167 patients, the study had greater than 80.0% power to detect RRs below 0.73 or above 1.27 for mortality and below 0.79 or above 1.21 for ICU admission.

Subgroup and age-stratified analyses

Subgroup analyses excluding patients with rare or unevenly distributed characteristics generally supported the primary findings (Supplementary Tables 1, 2 and Supplementary Figures 1, 2). For mortality, the direction of association remained similar across most subgroups, although statistical significance was not retained in some analyses, likely reflecting smaller sample sizes and wider confidence intervals. For ICU admission, the association between vaccination and lower ICU admission remained statistically significant across the examined subgroup analyses.

In age-stratified analyses, vaccination was associated with fewer ICU admissions among patients younger than 60 years (RR: 0.64, 95% CI [0.32–0.99]) (Table 3 and Figure 3). Among patients older than 60 years, the association was not statistically significant (RR: 0.68, 95% CI [0.35–1.20]). Vaccination was not significantly associated with mortality in either age stratum.

Table 2. Primary outcome. Mortality and ICU admissions in non-vaccinated and vaccinated hospitalized COVID-19 patients.

	All (n=167)	Vaccination status		<i>P</i> -value	Estimate (± 95% CI)	Risk ratio (± 95% CI)	NNT-like estimate
		Non-vaccinated	Vaccinated				
Mortality (n = 167)				Without correction			
Yes	38 (23.0%)	25 (26.0%)	13 (19.0%)	0.275	−0.42 (−1.19 to 0.32)	0.72 (0.36 to 1.31)	13.2
No	129 (77.0%)	72 (74.0%)	57 (81.0%)	With correction			
				0.07	−0.86 (−1.83 to 0.04)	0.46 (0.13 to 0.99)	
ICU (n = 167)				Without correction			
Yes	79 (47.0%)	55 (57.0%)	24 (34.0%)	0.0045	−0.92 (−1.56 to −0.29)	0.60 (0.40 to 0.83)	4.46
No	88 (53.0%)	42 (43.0%)	46 (66.0%)	With correction			
				0.0091	−1.03 (−1.84 to −0.29)	0.59 (0.28 to 0.89)	

Results highlighted in gray are statistically significant. Results were adjusted for age, type 2 diabetes, hypertension, cardiac disease, and pulmonary disease. CI, confidence of interval; ICU, intensive care unit. NNT-like estimates are point estimates derived from absolute risk differences.

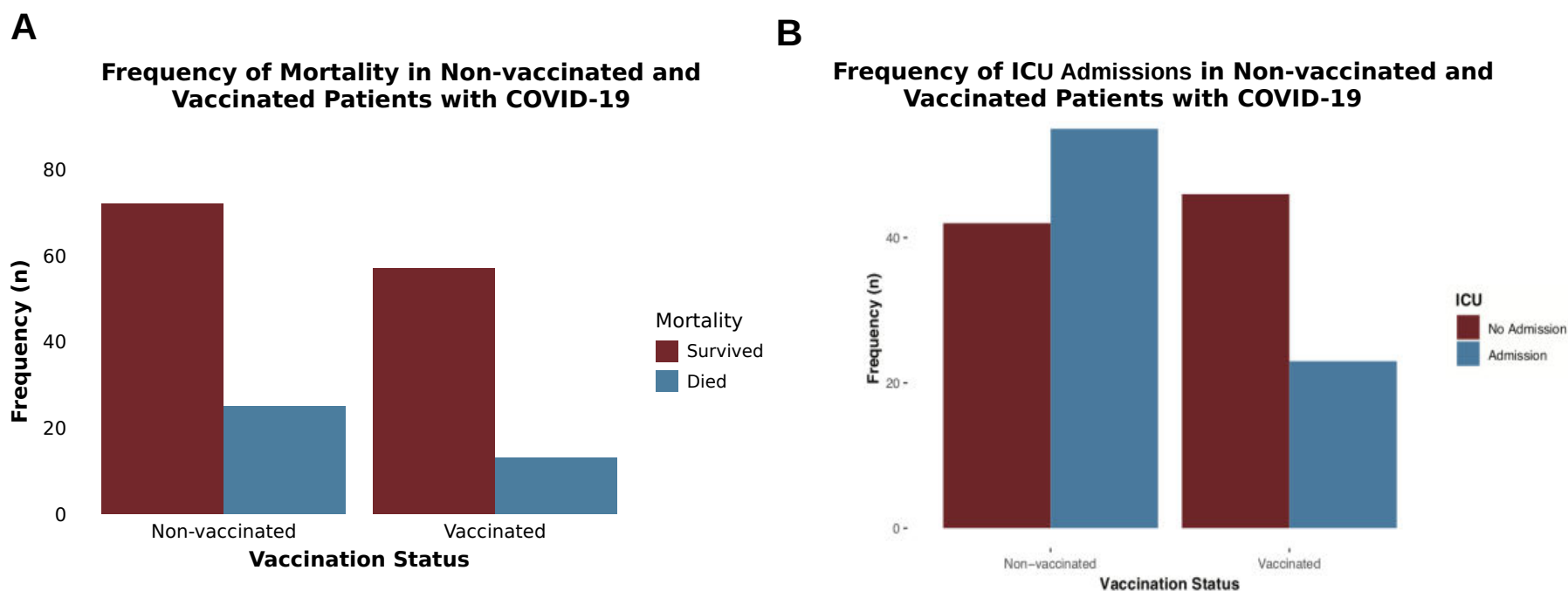


Figure 2. Frequency of (A) mortality and (B) ICU admission in non-vaccinated and vaccinated hospitalized COVID-19 patients. ICU, intensive care unit.

Table 3. Secondary outcome. Mortality and ICU admissions among non-vaccinated and vaccinated COVID-19 hospitalized patients, stratified by young and elderly subgroups.

	All (n=167)	Vaccination status		Risk ratio (± 95% CI)	NNT -like estimate
		Non-vaccinated	Vaccinated		
Mortality in patients < 60 years (n = 95)					
Yes	23 (24.0%)	19 (27.0%)	4 (17.0%)	0.643 (0.11 to 1.45)	9.9
No	72 (76.0%)	52 (73.0%)	20 (83.0%)		
Mortality in patients > 60 years (n = 72)					
Yes	15 (21.0%)	6 (23.0%)	9 (20.0%)	0.84 (0.33 to 2.54)	28.47
No	57 (79.0%)	20 (77%)	37 (80.0%)		
ICU in patients < 60 years (n = 95)					
Yes	51 (54.0%)	42 (59.0%)	9 (38.0%)	0.64 (0.32 to 0.99)	4.61
No	44 (46.0%)	29 (41.0%)	15 (62.0%)		
ICU in patients > 60 years (n = 72)					
Yes	28 (39.0%)	13 (50.0%)	15 (33.0%)	0.68 (0.35 to 1.20)	5.75
No	44 (61.0%)	13 (50.0%)	31 (67.0%)		

Results highlighted in gray are statistically significant. CI, confidence of interval; ICU, intensive care unit. NNT-like values are point estimates derived from absolute risk differences.

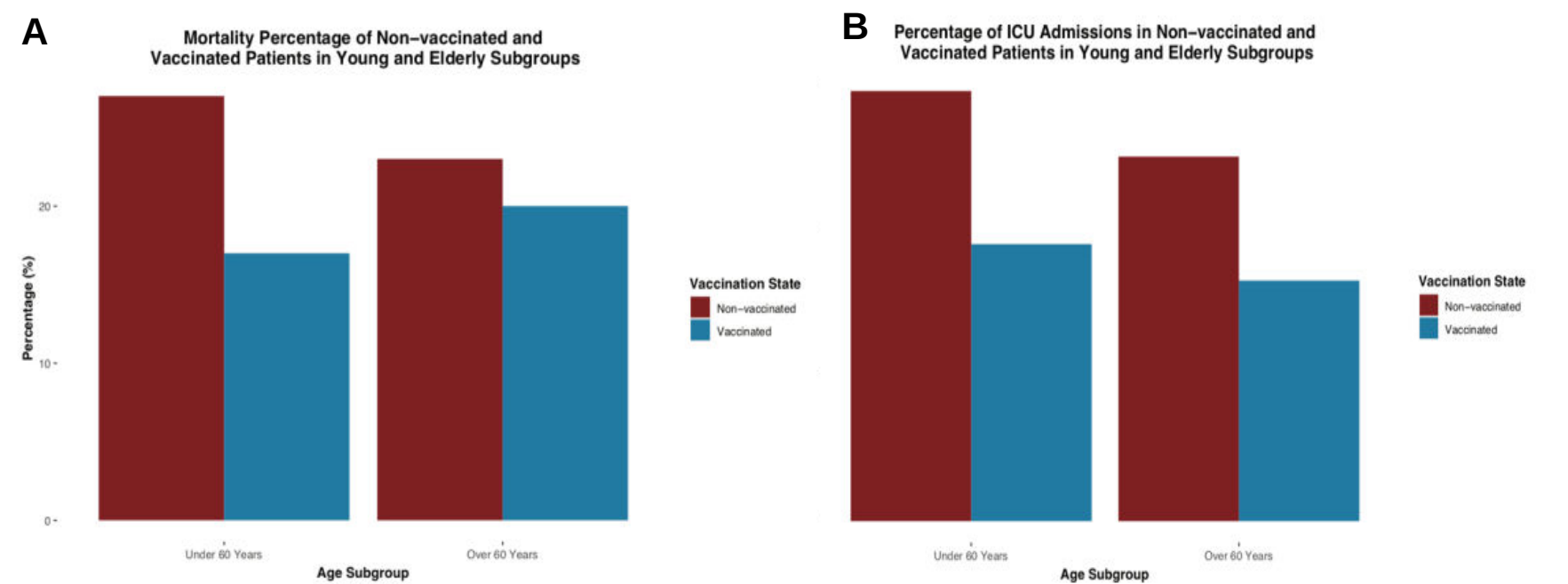


Figure 3. Proportions of (A) mortality and (B) ICU admissions among non-vaccinated and vaccinated hospitalized COVID-19 patients, stratified by young and elderly subgroups. ICU, intensive care unit.

Exploratory secondary outcomes

Exploratory analyses of clinical, imaging, laboratory, and organ-system parameters are shown in **Table 4**. After adjustment, vaccinated patients had lower risks of dyspnea, oxygen therapy, non-invasive ventilation, invasive ventilation, ECMO, ICU admission, sepsis, and coagulopathy. Vaccinated patients also had fewer CT lung lesions, shorter ICU duration, lower PCT, AST, and ALT values, and higher anti-SARS-CoV-2 antibody positivity.

Several unadjusted associations, including lower oxygen requirement, lower high-flow oxygen use, fewer tracheotomies, lower pCO₂, and higher creatinine and urea values, were no longer statistically significant after adjustment. Because these secondary analyses were exploratory and not corrected for multiple comparisons, they should be interpreted as hypothesis-generating.

Exploratory predictor analyses

In LASSO-based exploratory predictor analyses for mortality, type 2 diabetes and vascular disease were selected for further modeling. Type 2 diabetes was associated with higher mortality, and this association persisted after adjustment for vaccination status (adjusted OR: 3.02, 95% CI [1.24–7.34])(**Table 5**). Vascular disease was associated with lower odds of mortality after adjustment (adjusted OR: 0.27, 95% CI [0.04–0.99]), a counterintuitive finding that should be interpreted cautiously because of sparse events and possible residual confounding.

For ICU admission, LASSO selected type 2 diabetes, pregnancy, immunodeficiency, vascular disease, vaccination status, and age. After adjustment for vaccination status, type 2 diabetes remained associated with higher odds of ICU admission (adjusted OR: 3.09, 95% CI [1.33–7.57]), while vascular disease remained associated with lower odds of ICU admission (adjusted OR: 0.27, 95% CI [0.08–0.75]) (**Table 6**). All pregnant patients were admitted to the ICU, but the small number of cases precluded stable estimation of an OR and confidence interval (**Figure 4**).

Discussion

This retrospective single-center cohort study found that full COVID-19 vaccination was associated with lower adjusted risks of ICU admission and mortality among hospitalized patients with COVID-19 who underwent chest CT. The association was more consistent for ICU admission than for mortality and was observed despite vaccinated patients being older and having more comorbidities. However, because this was an observational study in a selected hospitalized CT-imaged cohort, the findings should be interpreted as associations rather than evidence of causal protection.

These findings are consistent with prior evidence that vaccination reduces severe COVID-19 outcomes, including hospitalization and mortality, in broader populations.^(7,13) The present study adds data from a distinct clinical setting: patients who were hospitalized despite SARS-CoV-2 infection. Within this high-risk group, vaccination status remained associated with lower severity after adjustment for key measured confounders. These findings are also consistent with reported cardioprotective effects of COVID-19 vaccination in hospitalized patients, although cardiovascular outcomes were not specifically evaluated in our cohort.⁽¹¹⁾ The observational NNT-like estimate of four for ICU admission suggests a potentially meaningful absolute difference, but this value should not be interpreted as an interventional NNT because treatment assignment was not randomized.

In exploratory age-stratified analyses, vaccination was associated with fewer ICU admissions among patients younger than 60 years, whereas the association was not statistically significant among older patients. This pattern should be interpreted cautiously because subgroup analyses were limited by sample size and were not designed to prove differential vaccine effectiveness by age. Biologically, severe COVID-19 may involve both direct viral injury and dysregulated host inflammation.^(14–16) Vaccination has been associated with reduced viral load and robust humoral immune responses^(17,18), which may plausibly reduce downstream inflammatory complications. Nevertheless, mechanistic conclusions cannot be drawn from the present clinical dataset.

Table 4. Secondary outcome. Clinical characteristics of vaccinated and non-vaccinated hospitalized COVID-19 patients.

	All	Vaccination status		Without correction Effect size ($\pm$ 95% CI)	With correction Adjusted effect size ($\pm$ 95% CI)
		Non-vaccinated	Vaccinated		
Dyspnea (n = 165)*				0.84 (0.71 to 0.97)	0.69 (0.36 to 0.96)
Yes	138 (84.0%)	86 (90.0%)	52 (75.0%)		
No	27 (16.0%)	10 (10.0%)	17 (25.0%)		
Coughing (n = 150)*				1.11 (0.83 to 1.45)	1.09 (0.78 to 1.38)
Yes	90 (60.0%)	50 (57.0%)	40 (63.0%)		
No	60 (40.0%)	37 (43.0%)	23 (37.0%)		
Fever (n = 149)*				1.12 (0.86 to 1.44)	1.16 (0.96 to 1.40)
Yes	93 (62.0%)	51 (59.0%)	42 (67.0%)		
No	56 (38.0%)	35 (41.0%)	21 (33.0%)		
Oxygen Therapy (n = 153)*				0.83 (0.70 to 0.98)	0.54 (0.22 to 0.90)
Yes	127(83.0%)	80 (89.0%)	47 (75.0%)		
No	26 (17.0%)	10 (11.0%)	16 (25.0%)		
Oxygen (L/min; n = 110)**	4.20 (3.42 to 5.03)	4.38 (3.35 to 5.50)	4.00 (2.84 to 5.30)	-0.39 (-0.48 to -0.29)	-0.22 (-0.64 to 0.18)
High flow (n = 147)*				0.64 (0.32 to 0.98)	0.66 (0.25 to 1.16)
Yes	43 (29.0%)	29 (35.0%)	14 (22.0%)		
No	104 (71.0%)	55 (65.0%)	49 (78.0%)		
NIV (n = 153)*				0.59 (0.33 to 0.92)	0.59 (0.26 to 0.98)
Yes	56 (37.0%)	39 (44.0%)	17 (26.0%)		
No	97 (63.0%)	49 (56.0%)	48 (74.0%)		
Intubation (n = 165)*				0.32 (0.14 to 0.52)	0.30 (0.08 to 0.62)
Yes	54 (33.0%)	44 (46.0%)	10 (14.0%)		
No	111 (67.0%)	52 (54.0%)	59 (86.0%)		
ECMO-ECLS (n = 165)*				0.13 (0.00 to 0.36)	0.29 (0.00 to 0.84)
Yes	25 (15.0%)	23 (24.0%)	2 (3.0%)		
No	140 (85.0%)	74 (76.0%)	66 (97.0%)		
Tracheotomy (n = 163)*				0.45 (0.13 to 0.96)	0.64 (0.15 to 1.43)
Yes	25 (15.0%)	19 (20.0%)	6 (9.0%)		
No	138 (85.0%)	75 (80.0%)	63 (91.0%)		
Quantitative score of chest CT lesions (n = 167)**	7.31 (6.6 to 8.0)	8.43 (7.5 to 9.2)	5.75 (4.8 to 6.7)	-0.60 (-0.92 to -0.29)	-0.38 (-0.74 to -0.02)
ICU Admission (n = 167)*				0.60 (0.40 to 0.83)	0.59 (0.28 to 0.89)
Yes	79 (47.0%)	55 (57.0%)	24 (34.0%)		
No	88 (53%)	42 (43%)	46 (66%)		
ICU duration (days; n = 158)**	8.30 (6.01 to 10.95)	12.27 (8.69 to 16.01)	2.77 (1.31 to 4.65)	-0.63 (-0.84 to -0.42)	-0.44 (-0.67 to -0.19)
pO₂ (mmHg; n = 151)**	54.4 (50.1 to 59.1)	54.3 (49.8 to 59.0)	54.6 (47.3 to 63.8)	0.00 (-0.38 to 0.35)	0.00 (-0.35 to 0.33)
pCO₂ (mmHg; n = 156)**	43.0 (40.9 to 45.1)	45.0 (42.0 to 48.3)	40.2 (37.4 to 43.3)	-0.36 (-0.68 to -0.03)	-0.28 (-0.61 to 0.05)

Table 4. (Cont.) Secondary outcome. Clinical characteristics of vaccinated and non-vaccinated hospitalized COVID-19 patients.

	All	Vaccination status		Without correction Effect size ($\pm$ 95% CI)	With correction Adjusted effect size ($\pm$ 95% CI)
		Non-vaccinated	Vaccinated		
Mortality (n = 167)*				0.72 (0.36 to 1.31)	0.46 (0.13 to 0.99)
Yes	38 (23.0%)	25 (26.0%)	13 (19.0%)		
No	129 (77.0%)	72 (74.0%)	57 (81.0%)		
Sepsis (n = 165)*				0.40 (0.10 to 0.82)	0.42 (0.08 to 0.94)
Yes	28 (17.0%)	22 (23.0%)	6 (9.0%)		
No	137 (83.0%)	75 (77.0%)	62 (91.0%)		
C-reactive protein (mg/L; n = 144)**	102.0 (87.0 to 116.0)	98.0 (81.0 to 117.0)	106.0 (84.0 to 131.0)	0.09 (−0.23 to 0.43)	0.00 (−0.32 to 0.31)
Procalcitonin (μg/L; n = 140)**	0.78 (0.53 to 1.09)	1.01 (0.63 to 1.48)	0.47 (0.30 to 0.71)	−0.32 (−0.54 to −0.05)	−0.37 (−0.73 to −0.05)
Pulmonary superinfection (n = 159)*				0.86 (0.60 to 1.19)	0.81 (0.47 to 1.12)
Yes	78 (49%)	48 (52%)	30 (45%)		
No	81 (51%)	44 (48%)	37 (55%)		
D-Dimer (mg/L; n = 138)**	4.82 (3.54 to 6.26)	5.78 (4.14 to 7.91)	3.41 (2.18 to 5.07)	−0.30 (−0.58 to 0.02)	−0.19 (−0.48 to 0.12)
PTT (sec; n = 160)**	36.6 (34.5 to 39.2)	37.0 (34.0 to 40.6)	36.1 (33.2 to 39.9)	−0.06 (−0.36 to 0.25)	−0.23 (−0.55 to 0.09)
INR (n = 160)**	1.16 (1.09 to 1.26)	1.15 (1.05 to 1.29)	1.19 (1.10 to 1.30)	0.12 (−0.17 to 0.48)	0.00 (−0.29 to 0.38)
Platelets (tsd/μL; n = 167)**	234.7 (218.6 to 252.5)	246.9 (225.6 to 269.5)	217.8 (194.5 to 241.1)	−0.27 (−0.59 to 0.04)	−0.21 (−0.56 to 0.13)
Coagulopathy (n = 165)*				0.31 (0.00 to 0.98)	0.26 (0.00 to 0.88)
Yes	12 (7.0%)	10 (10.0%)	2 (3.0%)		
No	153 (93.0%)	87 (90.0%)	66 (97.0%)		
Pulmonary artery embolism (n = 160)*				1.02 (0.45 to 1.83)	1.18 (0.41 to 2.32)
Yes	32 (20%)	19 (20%)	13 (20%)		
No	128 (80%)	75 (80%)	53 (80%)		
Creatinine (mg/dL; n = 166)**	1.37 (1.19 to 1.58)	1.09 (0.95 to 1.30)	1.76 (1.42 to 2.15)	0.55 (0.23 to 0.83)	0.33 (−0.03 to 0.66)
Urea (mg/dL; n = 162)**	59.9 (48.5 to 62.1)	46.5 (38.1 to 56.7)	66.3 (57.4 to 76.7)	0.48 (0.11 to 0.88)	0.26 (−0.06 to 0.64)
Renal failure (n = 166)*				0.95 (0.59 to 1.42)	0.70 (0.27 to 1.30)
Yes	60 (36%)	36 (37%)	24 (35%)		
No	106 (64%)	61 (63%)	45 (65%)		
AST (U/L; n = 141)**	68.3 (59.4 to 94.3)	78.0 (64.0 to 94.3)	56.3 (46.3 to 66.9)	−0.36 (−0.64 to −0.07)	−0.40 (−0.69 to −0.12)
ALT (U/L; n = 140)**	49.6 (42.7 to 56.5)	60.2 (51.5 to 71.5)	35.9 (28.8 to 44.2)	−0.59 (−0.89 to −0.28)	−0.45 (−0.73 to −0.17)
De Ritis ratio (n=139)**	1.61 (1.45 to 1.76)	1.48 (1.31 to 1.64)	1.77 (1.52 to 2.04)	0.32 (−0.01 to 0.65)	−0.01 (−0.33 to 0.27)
COVID-19 antibody positivity (n = 112)*	—	—	—	1.52 (1.08 to 2.21)	1.38 (1.08 to 1.95)

Results highlighted in gray are statistically significant.

* Risk Ratio and adjusted Risk ratio were used as effect size.

** Cohen's d and adjusted Cohen's d were used as effect sizes.

Laboratory analyses were additionally adjusted for duration since symptom onset.

For COVID-19 antibody positivity, only effect estimates were available in the source table.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CI, confidence of interval; ECMO-ECLS, extracorporeal membrane oxygenation and extracorporeal life support; ICU, intensive care unit; INR, international normalized ratio; NIV, non-invasive ventilation; NNT, number needed to treat; pCO₂, partial pressure of carbon dioxide; pO₂, partial pressure of oxygen; PTT, partial thromboplastin time.

Table 5. Secondary outcome. Predictive risk factors for mortality in non-vaccinated and vaccinated hospitalized COVID-19 patients.

		Mortality		Without correction for vaccination status Odds ratio ($\pm$ 95% CI)	With correction for vaccination status Adjusted odds ratio ($\pm$ 95% CI)
		Survived	Deceased		
Age	57.8 (55.3 to 60.4)	57.4 (54.6 to 60.5)	59.2 (54.4 to 64.5)	1.00 (0.98 to 1.02)	1.01 (0.99 to 1.04)
Type 2 diabetes (n = 167)				2.51 (1.07 to 5.76)	3.02 (1.24 to 7.34)
Yes	32 (19.0%)	20 (16.0%)	12 (32.0%)		
No	135 (81.0%)	109 (84.0%)	26 (68.0%)		
Vascular disease (n = 167)				0.25 (0.03 to 0.92)	0.27 (0.04 to 0.99)
Yes	25 (15.0%)	23 (18.0%)	2 (5.0%)		
No	142 (85.0%)	106 (82.0%)	36 (95.0%)		

Results highlighted in gray are statistically significant. CI, confidence of interval.

Table 6. Secondary outcome. Predictive risk factors for ICU admissions in non-vaccinated and vaccinated patients who are hospitalized with COVID-19.

		ICU admission		Without correction for vaccination status Odds ratio ($\pm$ 95% CI)	With correction for vaccination status Adjusted odds ratio ($\pm$ 95% CI)
		No ICU	ICU		
Age	57.8 (55.3 to 60.4)	60.3 (56.7 to 63.7)	55.0 (51.5 to 58.4)	0.98 (0.96 to 0.99)	0.99 (0.97 to 1.01)
Pregnancy (n = 167)				Not estimable*	Not estimable*
Yes	6 (3.5%)	0 (0.0%)	6 (8.0%)		
No	161 (96.5%)	88 (100.0%)	73 (92.0%)		
Immunodeficiency (n = 167)				0.35 (0.13 to 0.85)	0.46 (0.16 to 1.16)
Yes	26 (16.0%)	19 (22.0%)	7 (9.0%)		
No	141 (84.0%)	69 (78.0%)	72 (91.0%)		
Type 2 diabetes (n = 167)				2.14 (1.01 to 4.85)	3.09 (1.33 to 7.57)
Yes	32 (19.0%)	12 (14.0%)	20 (25.0%)		
No	135 (81.0%)	76 (86.0%)	59 (75.0%)		
Vascular disease (n = 167)				0.23 (0.07 to 0.60)	0.27 (0.08 to 0.75)
Yes	25 (15.0%)	20 (23.0%)	5 (6.0%)		
No	142 (85.0%)	68 (77.0%)	74 (94.0%)		

Results highlighted in gray are statistically significant. CI, confidence of interval; ICU, intensive care unit. *Complete separation: all 6 pregnant patients were admitted to the ICU; conventional ORs and 95% CIs could not be estimated reliably.

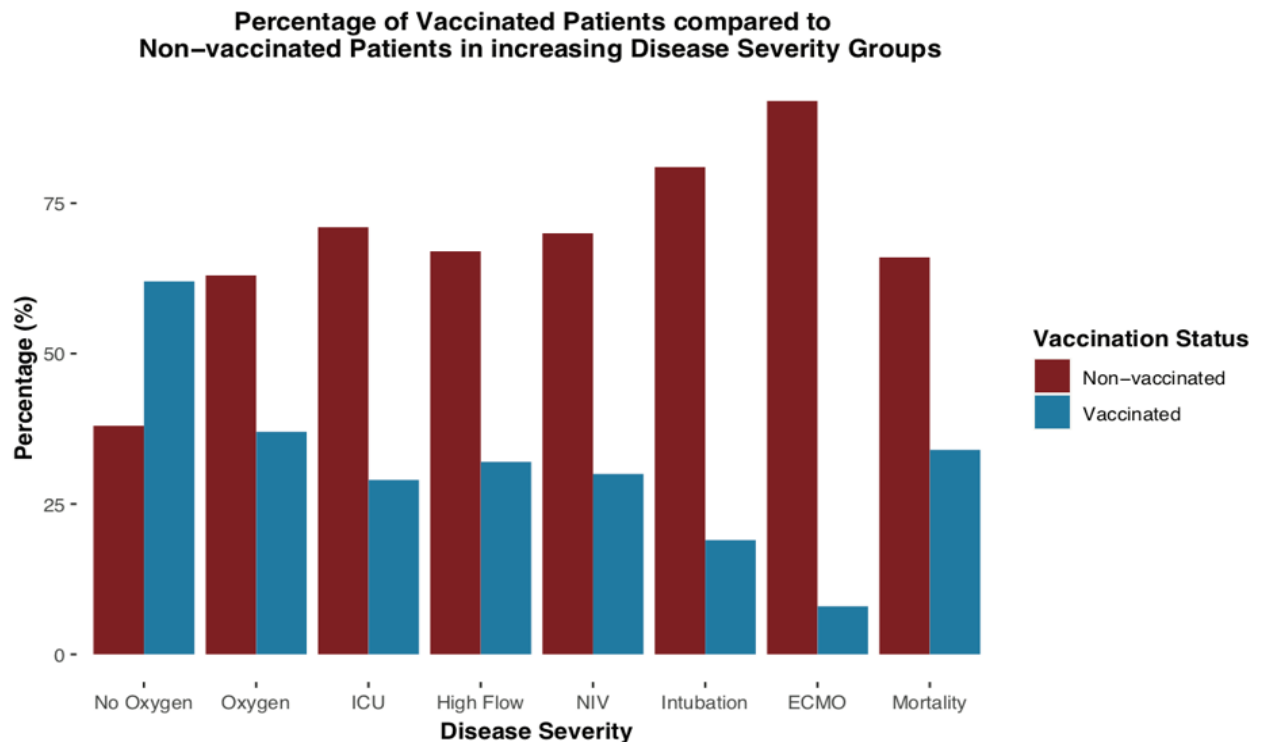


Figure 4. Distribution of vaccination status within clinical severity categories among hospitalized patients with COVID-19. Percentages are calculated within each clinical severity category. Categories may overlap because oxygen therapy, non-invasive ventilation, invasive ventilation, and extracorporeal membrane oxygenation are not mutually exclusive unless otherwise specified. ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; NIV, non-invasive ventilation.

Exploratory predictor analyses identified type 2 diabetes as a risk factor for both mortality and ICU admission, consistent with previous reports and plausible mechanisms involving impaired immune response, increased inflammation, and altered ACE2- and furin-related pathways.^(19,20) Pregnancy was also associated with ICU admission, although all pregnant patients in this cohort were non-vaccinated and the number of cases was small, precluding stable effect estimation. Conversely, vascular disease and immunodeficiency were associated with lower odds of selected severe outcomes in some models. These counterintuitive findings may reflect small numbers, treatment-selection effects, residual confounding, or competing-risk mechanisms and should not be interpreted as protective causal effects.

Secondary analyses suggested associations between vaccination status and several clinical and organ-system parameters, including less dyspnea, reduced need for oxygenation and ventilatory support, fewer chest CT lesions, shorter ICU duration, lower PCT values, less coagulopathy, and lower AST and ALT levels. These findings are biologically plausible given the pulmonary tropism of SARS-CoV-2, endothelial and coagulation abnormalities in severe COVID-19, and reported extrapulmonary involvement of the liver and kidney.^(6, 21–24) However, these secondary outcomes were exploratory and not adjusted

for multiple comparisons; they should therefore be considered hypothesis-generating.

The pulmonary findings should also be interpreted in the context of partial overlap with previous imaging and ARDS analyses from our institution.^(8–10) The present study differs by focusing on mortality, ICU admission, and systemic clinical parameters according to vaccination status.

This study has several limitations. First, the retrospective single-center design limits causal inference and generalizability. Second, inclusion required hospitalization and at least one chest CT scan, which may have enriched the cohort for patients with respiratory symptoms, suspected complications, or more severe disease. Third, because vaccination affects the probability of hospitalization, restricting the analysis to hospitalized patients may introduce selection or collider bias. Fourth, residual confounding remains possible despite adjustment for measured variables. In Germany, vaccination prioritization initially favored older and high-risk individuals, which likely contributed to the older age and higher comorbidity burden observed among vaccinated patients. Fifth, variant distribution, calendar period, vaccine type, booster status, and time since vaccination could not be fully modeled because of limited sample size and sparse data. Sixth, rare characteristics such as pregnancy and organ transplantation could not be

analyzed robustly. Finally, multiple secondary outcomes were examined without correction for multiple comparisons.

Strengths of the study include RT-PCR-confirmed COVID-19, documented vaccination status, detailed clinical and laboratory phenotyping, availability of chest CT data, adjustment for major measured confounders, and sensitivity analyses addressing rare characteristics.

Conclusion

COVID-19 vaccination was associated with lower ICU admission and mortality among hospitalized patients with COVID-19 in this retrospective single-center cohort. The association appeared more consistent for ICU admission than for mortality and was most evident among patients younger than 60 years. Because the study was observational and restricted to hospitalized patients who underwent chest CT, the findings should not be interpreted as definitive evidence of causal protection. Secondary clinical, laboratory, imaging, and organ-system findings should be considered exploratory and hypothesis-generating.

Author contributions

JM, PA, and EA contributed substantially to the study concept and design, data acquisition, literature review, and data analysis and interpretation. JM, PA, KMP, and EA contributed substantially to data acquisition. JM drafted the manuscript. JM, PA, KMP, LB, MS, PD, JK, GT, SU, TW, HJB, DS, SR, MP, CLS, FB, and EA revised the manuscript critically for important intellectual content. All authors approved the final version submitted for publication and take responsibility for all statements made in the published article.

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Conflict of interest statement

All authors have completed and submitted the International Committee of Medical Journal Editors Uniform Disclosure Form for Potential Conflicts of Interest. All authors declare that they have no conflicts of interest.

Data sharing statement

The datasets used and analyzed during the current study are available for non-commercial purposes from the corresponding author upon reasonable request.

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