Effects of COVID-19 Vaccination Status and COVID-19 Complication Risk Score on COVID-19-Related Hospitalization and Mortality of Veterans in Southern California

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Abstract

Introduction
The coronavirus disease of 2019 (COVID-19) related risk factors and vaccines have been identified; however, their impact on hospitalization of veterans due to COVID-19 is not fully known. We aimed to determine effects of the COVID-19 impact score and vaccination status on hospitalization, hospital length of stay (LOS) and mortality of veterans.

Methods
Chart reviews were conducted for 530 veterans with their first COVID-19 positive result at the Veterans Affairs Long Beach Healthcare System from February 11, 2021, to October 11, 2021. Data collection included demographics, comorbidities and outcomes. COVID-19 complication risk scores were calculated for each patient. Multiple logistic and linear regression analyses were conducted to examine the effects of vaccination status, COVID-19 complication risk score and age on patients' outcomes.

Results
Of 530 patients, 173 were vaccinated and 357 were unvaccinated. Logistic regression analyses indicated that veterans with no COVID-19 vaccination, a higher COVID-19 complication risk score or older age were more likely to be hospitalized (OR > 1.024, P ≤ 0.05). Linear regression analyses indicated that Veterans with no COVID-19 vaccination (B = –11.7, P < 0.01) or higher COVID-19 complication risk score (B = 3.9, P < 0.01) had a longer hospitalization. No variable was a significant predictor of patients' mortality.

Conclusion
Veterans with COVID-19 vaccination were less likely to be hospitalized, and those hospitalized had a shorter hospital stay than unvaccinated veterans. Veterans with higher COVID-19 complication risk scores were more likely to be hospitalized and had a longer hospital LOS.

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Introduction

The coronavirus disease of 2019 (COVID-19) pandemic started in December 2019, and in December 2020 the Food and Drug Administration (FDA) issued the first Emergency Use Authorization (EUA) for a COVID-19 vaccine in the U.S. Shortly after, on Jan. 4, 2021, the Veterans Affairs Long Beach Healthcare System (VALBHS) started administering COVID-19 vaccines to the veteran population. The Centers for Disease Control and Prevention (CDC) has published a list of conditions found to increase the risk of severe COVID-19 infection. These include but are not limited to elderly age, immunocompromised state, chronic kidney disease, chronic obstructive pulmonary disease, heart conditions, obesity, sickle cell disease, smoking, Type 2 diabetes mellitus, pregnancy and mental health conditions.[1] The CDC has also published COVID-19 infection data for Los Angeles County. Of the positive COVID-19 cases from May 2021 to July 2021, 71.4% were in unvaccinated patients and these patients had worse outcomes compared to vaccinated and partially vaccinated patients.[2] Unvaccinated patients had a higher incidence of hospitalization, intensive care unit (ICU) admission and mortality ($p < 0.001$).[3]

As of October 2021, 73% of veterans at VALBHS had

received at least one dose of a Moderna, Johnson & Johnson's Janssen or Pfizer COVID-19 vaccine. Although a high proportion of veterans have received a COVID-19 vaccine, both vaccinated and unvaccinated veterans continue to become infected with COVID-19 and some are hospitalized with more severe disease. Published studies indicate that unvaccinated patients had a higher incidence of hospitalization, hospital length of stay and mortality compared to vaccinated patients.[4,5,7-9] Other studies have reported that hospitalized patients with COVID-19 were older, had a higher COVID-19 complication risk score, if calculated, and more chronic medical conditions.[6,7,9] Worth noting is that no single study has evaluated all of these factors together and there is a lack of data on variables that predict hospitalization and clinical outcomes in vaccinated and unvaccinated veterans in Southern California. Therefore, the goal of this study was to evaluate whether being vaccinated against COVID-19 reduces the risk of hospitalization, hospital LOS and mortality in the Southern California veteran population.

Methods

Study Design and Subjects

This retrospective, single-center study was conducted at a 360-bed VA hospital located in Southern California. Retrospective chart reviews were conducted for 649 veterans who had a first positive COVID-19 test result from February 11, 2021, to October 11, 2021. Of 649 patients, 119 were excluded from the study for the following reasons: partially vaccinated (n = 29), admitted for an indication other than COVID-19 infection (n = 35), employee (n = 53) and positive for COVID-19 infection after a third COVID-19 vaccine or booster (n = 2). Therefore, a total of 530 patients were included in the study. The patients were divided into two groups: 1) fully vaccinated patients (n = 173) who met the criteria for one of the following: two weeks after a second dose in a two-dose series, such as the Pfizer or Moderna vaccines, or two weeks after a single-dose vaccine, such as Johnson & Johnson's Janssen vaccine and 2) unvaccinated patients (n = 357) who did not receive any FDA-authorized or approved vaccine against SARS-CoV-2.

Data Collection

The Corporate Data Warehouse (CDW) and Computerized Patient Record System (CPRS) were used to identify patients and collect relevant data such as patients' age, gender, weight, height, comorbidities (e.g., diabetes, congestive heart failure, coronary artery disease, etc.), hospital LOS and death. Using the collected information, the COVID-19 complication risk score was calculated for all patients. It is a validated clinical risk score to identify patients with COVID-19 at high risk of hospital admission and in-hospital mortality.[3]

The COVID-19 complication risk score components include: age divided into four categories: < 60 years old (0 points), 60-69 years old (one point), 70-79 years old (two points) and ≥ 80 years old (three points); male sex; coronary artery disease; congenital heart disease; congestive heart failure; end-stage renal disease; end-stage liver disease; chronic pulmonary disease (pulmonary fibrosis/chronic obstructive pulmonary disease/bronchial asthma); diabetes; hypertension; obesity; nursing home residence; pregnancy status; and immunocompromised status (diagnosis of human immunodeficiency virus infection, actively receiving chemotherapy, receiving immunosuppressive agents, carrying a diagnosis of iatrogenic immunosuppression). The maximum score was 15 and each of the 12 items received 1 point if present, except for age as indicated. Patient comorbidities included in the study were as defined by the CDC.

The outcome variables were the incidence of hospitalization, hospital LOS and mortality within 90 days of COVID-19 positive result. This study was approved by the VA Long Beach Healthcare System Research Office as a research study. The procedures followed in this study were in accord with the ethical standards of the institution's committee on human experimentation or with the "World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects," as amended in October 2013.

Statistical Analyses

Chi-squared or Fisher's exact tests were used to compare categorical variables between patients who were admitted or not admitted to the hospital and patients who were alive or deceased within 90 days of a positive COVID-19 result. Unpaired t-tests were conducted to evaluate age and hospital LOS, and Mann-Whitney U tests were conducted to evaluate COVID-19 complication risk scores across groups. Multiple logistic regression analyses were carried out to evaluate whether vaccination status, COVID-19 complication risk score and age predicted hospitalization or death. Multiple linear regression analysis was carried out to evaluate whether vaccination status, COVID-19 complication risk score and age predicted hospital LOS. $P < 0.05$ was considered statistically significant. All statistical analyses were conducted using IBM SPSS Statistics 26 software (IBM Corporation, Armonk, New York).

Results

Baseline Characteristics

Table 1 shows the baseline characteristics of all patients and indicates that vaccinated patients were older than unvaccinated patients. All (100%) of the study participants from the American Indian or Alaska Native ethnicity were unvaccinated, albeit our sample size was small (n = 10).

A greater proportion of the unvaccinated patient group had a history of smoking or other health conditions compared with the vaccinated patient group. Compared with the unvaccinated patient group, vaccinated participants more often had immunocompromising conditions, diabetes, respiratory diseases, renal diseases or cardiovascular disease. In the hospitalized cohort, the proportion of White patients was greater in the vaccinated group compared with the unvaccinated group. In both hospitalized and ambulatory patients, vaccinated individuals had a higher number of comorbidities and a higher COVID-19 complication risk score compared with those who were unvaccinated.

Table 1. Baseline Characteristics of All Patients[a]

Baseline Characteristics	Unvaccinated Patients N = 357	Vaccinated Patients N = 173	Test Values ($X^2/t/U$ value)	*P* Value
Age, mean (±SEM), yrs	47.1 (± 0.9)	60.1 (± 1.3)	1.967	<0.001
Male, N (%)	315 (88.2)	160 (92.5)	3.841	0.132
Race				
American Indian or Alaska Native, N (%)	10 (2.8)	0 (0)	3.841	0.026
Asian, N (%)	24 (6.7)	9 (5.2)	3.841	0.497
Black or African American, N (%)	68 (19.0)	26 (15.0)	3.841	0.256
Native Hawaiian or other Pacific Islander, N (%)	13 (3.6)	8 (4.6)	3.841	0.587
White, N (%)	166 (46.5)	95 (54.9)	3.841	0.069
Declined/unknown/not answered, N (%)	76 (21.3)	35 (20.2)	3.841	0.779
BMI, mean (± SEM), kg/m^2	29.7 (± 0.3)	30.1 (± 0.5)	1.967	0.443
Number of comorbidities, median (IQR)	2 (1, 3)	3 (2, 4)	19810	<0.001
Obese, N (%)	140 (39.2)	78 (45.1)	1.967	0.344
Current smoker, N (%)	49 (13.7)	12 (6.9)	1.965	0.010
Diabetes, N (%)	29 (8.1)	36 (20.8)	1.969	<0.001
Immunocompromised, N (%)	0 (0)	8 (4.6)	1.974	0.004
Respiratory disease, N (%)	24 (6.7)	33 (19.1)	1.970	<0.001
Renal disease, N (%)	16 (4.5)	19 (11.0)	1.970	0.014
Liver disease, N (%)	15 (4.2)	10 (5.8)	1.968	0.447
Cardiovascular disease, N (%)	73 (20.4)	77 (44.5)	1.968	<0.001
Cerebrovascular disease, N (%)	8 (2.2)	5 (2.9)	1.968	0.665
Mental health disorder, N (%)	96 (26.9)	49 (28.3)	1.967	0.731
Neurological condition, N (%)	3 (0.8)	3 (1.7)	1.970	0.420
Other, N (%)	154 (43.1)	59 (34.1)	1.967	0.044
COVID-19 complication risk score, median (IQR)	2 (1, 3)	3 (2, 5)	17529	<0.001

[a]BMI: body mass index; IQR: interquartile range; other comorbidities: includes HIV (treated or not advanced), overweight (BMI ≥25 and <30), sickle cell disease, and substance use disorder.

Table 2. Logistic Regression Analysis of Variables Predicting Hospitalization[a]

Predictors	Beta Coefficient	Odds Ratio (95% confidence interval)	*P* value
Unvaccinated	1.34	3.82 (1.89-7.77)	<0.001
COVID-19 complication risk score	0.39	1.48 (1.17-1.87)	0.001
Age	0.02	1.02 (1.00-1.05)	0.05

[a]Unvaccinated: Did not receive COVID-19 vaccine.

Hospitalization

Of 63 hospitalized patients, 46 were unvaccinated, and 17 were vaccinated. Although a higher proportion of unvaccinated patients (12.9%) were hospitalized than that of vaccinated patients (9.8%), the difference was not significant per a univariate chi-square test. The average age of hospitalized patients was not greater than those not hospitalized (P = 0.05). The median COVID-19 complication risk score of hospitalized patients (4 units) was greater than those not hospitalized. The multiple logistic regression model showed 0.177 Nagelkerke r2 value. Vaccination status and COVID-19 complication risk score significantly predicted hospitalization in the logistic regression model, whereas age did not.

While keeping age and the COVID-19 complication risk score constant, the unvaccinated patients were 3.82 times more likely to be hospitalized than vaccinated patients. Every unit increase in COVID-19 complication risk score or each 1-year increase in age increased the patients' odds of hospitalization by 1.48 and 1.02 times, respectively, while other variables were kept constant in the model (Table 2). Multicollinearity did not exist among predictors in this model (variance inflation factor [VIF] < 2.4).

Hospital LOS

Although the average hospital LOS was longer in unvaccinated patients (mean ± SEM, 12.3 ± 2.3 days) than that in vaccinated patients (7.8 ± 1.3 days), the difference was not significant per a univariate t-test. The multiple linear regression model showed 0.147 r2 value.

Table 3. Linear Regression Analysis of Variables Predicting Hospital Length of Stay[a]

Predictors	Beta Coefficient	Standard Error	*t*-Value	*P* value
Unvaccinated	11.7	4.5	2.58	0.013
COVID-19 complication risk score	3.9	1.4	2.78	0.007
Age	– 0.2	0.1	– 1.22	0.227

[a]Unvaccinated, did not receive vaccine against COVID-19.

Table 4. Logistic Regression Analysis of Variables Predicting Mortality[a]

Predictors	Beta Coefficient	Odds Ratio (95% confidence interval)	*P* Value
Unvaccinated	1.52	4.57 (0.64-32.65)	0.130
COVID-19 complication risk score	0.57	1.77 (0.93-3.39)	0.083
Age	0.02	1.02 (0.97-1.09)	0.527

[a]Unvaccinated, did not receive vaccine against COVID-19.

Vaccination status and COVID-19 complication risk scores were significant predictors of hospital LOS in the linear regression model. Unvaccinated patients' hospital LOS was 11.7 days longer than that of vaccinated patients, while other variables were kept constant in the linear regression model. Every unit increase in COVID-19 complication risk score increased hospital LOS by 3.9 days, while other variables were kept constant in the model (Table 3). Age did not affect hospital LOS in this model. Multicollinearity did not exist among predictors in this model (VIF < 2.7).

Mortality

Of 63 hospitalized patients, 13 died within 90 days of a COVID-19 positive test result in the inpatient and outpatient setting. Among those who died, 9 were unvaccinated and 4 were vaccinated. There was no difference between the proportions of unvaccinated and vaccinated patients' mortality per Fisher's exact test (P = 0.74). The average age of deceased patients (mean ± SEM, 72.8 ± 4.3 years) was higher than patients who remained alive 90 days after COVID-19 positive test result (60.1 ± 2.3 years). The deceased patients' median COVID-19 complications risk scores (5 units) were higher than who were alive (3 units). The multiple logistic regression model showed 0.253 Nagelkerke r2 value. However, no variable predicted mortality in the model (Table 4). Multicollinearity did not exist among predictors in this model (VIF < 2.7).

Discussion

Findings from this study indicated that unvaccinated veterans with COVID-19 were 3.82 times more likely to be hospitalized and stay in the hospital for almost 12 days longer than vaccinated veterans. In addition, veterans with higher COVID-19 complication risk scores were more likely to be hospitalized and had a longer hospital stay than did veterans with a lower COVID-19 complication risk score. Finally, no variable significantly predicted mortality in the regression model.

Tenforde et al.[6] reported the association between vaccination status and risk of hospitalization, prolonged hospital LOS and death and the association between age and the number of chronic medical conditions on the risk of hospitalization. They reported that COVID-19 hospitalization was strongly associated with a lower likelihood of vaccination, and vaccinated patients had a shorter hospital LOS than unvaccinated patients. They also reported that among patients hospitalized for COVID-19, vaccinated patients had more chronic medical conditions compared to unvaccinated patients. Finally, they reported that among patients hospitalized

for COVID-19, vaccinated patients were older than unvaccinated patients.

Our study expanded upon Tenforde et al.[6] by also evaluating the association between the COVID-19 complication risk score and the same outcomes and the association between age and risk of prolonged hospital LOS and death. Other studies have evaluated similar outcomes, but none as comprehensive as our study.

Our findings regarding the effects of vaccination status on hospital admission and hospital LOS are largely consistent with the literature.[4,5,7-9] A previous study conducted in England in patients aged 70 years or older revealed that unvaccinated patients had a higher incidence of hospitalization compared to vaccinated patients.[4] A study conducted in Israel found adjusted estimates of vaccine effectiveness at 7 days or longer after the second dose were 97.2% against COVID-19-related hospitalization.[7] Moghadas and colleagues[8] further showed that vaccination markedly reduced both non-ICU and ICU hospitalizations due to COVID-19 disease in those age 65 years and older, 63.5% and 68.6% respectively.

The current results confirm the published reports that COVID-19 vaccination reduces the risk of hospitalization and extend these findings to the veteran population in Southern California. These findings regarding the effects of the COVID-19 complication risk score and other comorbidities on hospital admission and hospital LOS are largely consistent with the literature.[9] Another study showed that when compared to unvaccinated COVID-19 patients, vaccinated patients had a higher COVID-19 complication risk score and were more likely to be immunocompromised and have diabetes, hypertension, coronary artery disease and chronic kidney disease.[10] Thus, our results add to the growing literature showing the negative impact of comorbidities on COVID-19–related hospitalization.

The current study did not detect a significant effect of age on hospitalization or hospital LOS. These findings are not in agreement with Bosch et al.,[9] who reported that among patients hospitalized due to COVID-19, vaccinated patients were on average 9.5 years older than unvaccinated patients. In contrast, our study showed that the effectiveness of COVID-19 vaccination overcame age barriers in predicting hospitalization. The discrepant findings are likely due to differences among the study populations and methodologies used in these studies. Our study also expanded upon the current published research by evaluating the effect of age on hospital LOS.

While our findings showing the effects of vaccination status on hospitalization and hospital LOS are mostly concordant with the reported studies, our findings regarding mortality differ.[4-8] A previous study conducted in England in patients 70 years or older revealed that unvaccinated patients had a higher incidence of mortality compared with vaccinated patients 21 days after a positive COVID-19 test result.[4] In agreement with these findings, a separate study in Qatar revealed that unvaccinated patients had a nearly threefold higher rate of death compared with their vaccinated counterparts, and 1 factor associated with death over a 12-week follow-up period was age.[5] Further, Tenforde et al.[6] reported that death due to COVID-19 was strongly associated with a lower likelihood of vaccination. Also, a study conducted in Israel found adjusted estimates of vaccine effectiveness at 7 days or longer after the second dose were 96.7% against COVID-19–related death. Moghadas and colleagues[8] also showed that vaccination markedly reduced chances of death from COVID-19 disease in those 65 years and older. In contrast with these published reports, our results indicate no relationship between patients' COVID-19 vaccination status and mortality.

Notably, our study's mortality sample size was small (i.e., only 13 of 63 hospitalized patients died), which could be an important reason for our discordant results. In addition, the discrepant findings could be due to the differences between study populations, methodologies, and measures for mortality (e.g., days after a COVID-19 positive test) used in these studies.

Limitations

This study has several limitations. This study was a retrospective, single-center study with a small sample size with the highest proportion of race being White; therefore, the current findings may only be generalizable to populations like those studied. The study period was from February 2021 to October 2021, when the alpha and delta variants were the majority COVID-19 variants;[10] therefore, it is possible that the results of this study may not be applicable to other or future variants.[11] Moreover, for patients who received a 2-dose COVID-19 vaccine series, we were not able control for timing of the second vaccine. Although 86% of the fully vaccinated veterans in this study received the 2-dose series as recommended by the FDA, veterans who did not receive it may have differed in immunity. Finally, hospital LOS may have been prolonged due to secondary diagnoses that may or may not have been due to COVID-19 disease and we did not review hospital readmission due to COVID-19 disease.

Conclusion

The predictors of hospitalization and hospital LOS in the veteran population at our institution are generally consistent with the published literature. Being unvaccinated and having greater COVID-19 complication risk score predicted hospitalization and a longer hospital LOS. Our study also found that effectiveness of COVID-19 vaccination overcame age barriers in predicting hospitalization which is a unique finding of this study. Thus, the present study provides additional support to the notion of COVID-19 vaccination effectiveness against COVID-related hospitalization and long duration of stay in the hospital.

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