

## ORIGINAL RESEARCH

## Infectious Disease

# Characteristics and outcomes of adverse events after COVID-19 vaccination

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## Abstract

**Objectives:** BNT-162b2, mRNA-1273, and Ad26.COVS.2.S vaccines data regarding adverse events (AEs) are scarce. In this report, we aimed to describe fatal and non-fatal possible AEs after COVID-19 vaccine administration.

**Methods:** An observational multicenter study investigating the causes of emergency department visits and hospital admissions within 10 days of COVID-19 vaccination. Patients who received first or second doses of COVID-19 vaccines and presented to the emergency department (ED), as well as those admitted to the hospitals or intensive care units (ICUs) were included. Causes of ED, hospital, and ICU admissions and discharges were collected based on the *International Classification of Diseases, Tenth Revision* (ICD-10) coding system.

**Results:** Between December 2020 and March 2021, 1842 patients visited the ED within 10 days of COVID-19 vaccine administration. The mean age was 70.3 years. Overall, 1221 patients presented after the first dose of the vaccine and 653 after the second dose. Trauma (14.9%), hypertensive emergency/urgency (7.8%), generalized pain and arthralgia (5.7%), and chest pain (4.4%) were the most common causes of presentation to the ED. Of all ED presentations, mortality rate was at 2.2% (41 patients) with a median follow-up time of 68.0 days, versus 2.6% in unvaccinated ED patients. Postvaccination acute hypoxemic respiratory failure (46.3%), septic shock (24.4%), and cardiogenic shock (12.2%) were the most common causes of death.

**Conclusion:** Although reported AEs are not necessarily caused by the vaccination, this study provides further information about possible AEs after COVID-19 immunization, especially those requiring hospital admission. This study also supports prior data that serious AEs post vaccination are much lower than primary COVID-19 infections. Further studies are needed to investigate causalities between vaccines and reported AEs across all age groups.

## KEYWORDS

BNT-162b2 vaccine, COVID-19, hospital admission, mRNA vaccine, mRNA-1273 vaccine, serious adverse events

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## 1 | INTRODUCTION

### 1.1 | Background

After the Food and Drug Administration (FDA) issued Emergency Use Authorization (EUA) of different coronavirus disease 2019 (COVID-19) vaccines, a mass vaccination campaign was needed across the United States and the world to stop the spread of the COVID-19 pandemic.<sup>1</sup> As of mid-April 2021, a total of 222,322,230 vaccine doses had been administered in the United States, and about 91,175,995 people have been fully vaccinated,<sup>2</sup> representing nearly one-fourth of its entire population. Despite efforts for vaccination, there have been high levels of reluctance for COVID-19 vaccination among the public, particularly owing to the safety concerns of these new vaccines given their rapid development and deployment. According to the international survey data, just 49% of the US population was willing to get vaccinated.<sup>3</sup>

### 1.2 | Importance

Adverse events following immunization (AEFI) are common and can range from minor side effects to more severe reactions. Surveillance of AEFI represents a particular challenge in mass vaccination because it involves administering vaccine doses to a large population over a short period of time.<sup>4</sup> As a result, adverse events (AEs) may be more noticeable to the public leading to hesitancy and reluctance. In response to these concerns, the US Centers for Disease Control and Prevention (CDC) implemented a comprehensive safety monitoring system program, which currently includes the Vaccine Adverse Event Reporting System (VAERS), a CDC spontaneous reporting system, and V-safe, an active surveillance system.<sup>5</sup>

### 1.3 | Goals of this investigation

According to the CDC's first month of COVID-19 safety monitoring report, only 9.2% of the population had a reported serious AE.<sup>6</sup> However, the data regarding these AEs are scarce. Given these events can lead to hospitalizations, recognition by health care workers is essential. This study aims to give a detailed description of the patient population who presented to the emergency department within 10 days after first or second dose of COVID-19 vaccination with AEs leading or not to hospital and ICU admissions.

## 2 | METHODS

### 2.1 | Study design and setting

We conducted a multicenter, retrospective, descriptive study across the Cleveland Clinic Enterprise (11 hospitals) in Northeast Ohio between December 11, 2020, the date the FDA issued the first EUA for a COVID-19 vaccine, and March 25, 2021 to investigate the

#### The Bottom Line

This article supports prior research that although the vaccine is associated with adverse events, there are much fewer than seen with primary COVID-19 infections.

causes of ED visits and hospital admissions after COVID-19 vaccine administration.

### 2.2 | Selection of participants

All patients aged 18-years-old and older, who received a COVID-19 vaccine, whether first or second dose and presented to the ED or were admitted to the regular medical floor or ICU within 10 days of vaccine administration, were included in the study. Vaccination status of each of the participants was identified in the immunization section of their electronic medical record. Patients who did not receive the vaccine or had unknown vaccination status were excluded from the study.

### 2.3 | Exposures

AEFI were defined as per the World Health Organization (WHO) and the CDC VAERS definition as any untoward medical occurrence that follows immunization and that does not necessarily have a causal relationship with the usage of the vaccine. Serious AEs (SAEs) or reactions were defined as any untoward medical occurrence that resulted in hospital admission or resulted in death.<sup>4,7,8</sup> It is important to note that AEs reported are not necessarily side effects of the immunization; rather they are health problems that happened after the vaccination that may or may not be caused by the vaccination per the CDC and WHO definitions.<sup>7,8</sup>

### 2.4 | Measurements

Causes of hospital admissions were obtained and classified based on the *International Classification of Diseases, Tenth Revision* (ICD-10) coding system. Demographics and clinical variables were electronically extracted and collected from the electronic health records by dedicated e-research and business analytics teams from the coding and the reimbursement departments. Hypertensive crises were identified in patients presenting with hypertensive urgency and hypertensive emergency. This study was approved by the institutional review board at the Cleveland Clinic health care system.

### 2.5 | Outcomes

The primary outcome was to describe the patient population who presented to the ED within 10 days after first or second dose of

**TABLE 1** Baseline characteristics and outcomes of patients presented after the first dose of the vaccine

| Characteristic                            | Total (%)   | BNT-162b2 vaccine (%) | mRNA-1273 vaccine (%) | Ad26.COVS.2.S vaccine (%) |
|---|-------------|-----------------------|-----------------------|---------------------------|
| Total number, no.                         | 1221 (100)  | 824 (100)             | 354 (100)             | 43 (100)                  |
| Mean age (SD), years                      | 69.8 (17.5) | 73.5 (15.6)           | 60.8 (19.0)           | 69.4 (14.9)               |
| Male sex, no. (%)                         | 515 (42.3)  | 356 (43.2)            | 138 (39.0)            | 21 (48.8)                 |
| Race, no. (%)                             |             |                       |                       |                           |
| White                                     | 1008 (82.6) | 671 (81.4)            | 307 (86.7)            | 30 (69.8)                 |
| African-American                          | 161 (13.2)  | 121 (14.7)            | 28 (7.9)              | 12 (27.9)                 |
| Other                                     | 52 (4.3)    | 32 (3.9)              | 19 (5.4)              | 1 (2.3)                   |
| History of COVID-19 no. (%)               | 115 (9.4)   | 64 (7.8)              | 49 (13.8)             | 2 (4.7)                   |
| Total admitted, no. (%)                   | 487 (39.9)  | 351 (42.6)            | 111 (31.4)            | 25 (58.1)                 |
| Admitted to regular floor no. (%)         | 460 (37.7)  | 332 (40.3)            | 106 (29.9)            | 22 (51.6)                 |
| Admitted to ICU, no. (%)                  | 27 (2.2)    | 19 (2.3)              | 5 (1.4)               | 3 (7.0)                   |
| Mean time to presentation (SD), days      | 4.9 (3.2)   | 5.0 (3.2)             | 4.8 (3.2)             | 4.7 (3.3)                 |
| Admission means length of stay (SD), days | 3.6 (4.2)   | 3.5 (4.1)             | 3.6 (4.2)             | 4.7 (5.3)                 |
| Death events, no. (%)                     | 27 (2.2)    | 20 (2.4)              | 4 (1.1)               | 3 (7.0)                   |

COVID-19 vaccination with AEs leading or not to hospital and ICU admissions.

## 2.6 | Analysis

Descriptive analysis was performed to compare baseline characteristics of patients presenting after the first and the second dose of the vaccines. Continuous variables were reported as mean with SD. We used Kaplan-Meier analysis to report overall survival time (OST) outcomes. Cox proportional hazards analysis was performed to test for the prognostic values of different vaccine types, age, and gender. Hazard ratio (HR) was reported. All statistical calculations were made using STATA Statistics/Data analysis (version 16.1).

## 3 | RESULTS

### 3.1 | Characteristics of study subjects

We identified 153,726 patients who presented to the ED during the study period, only 1842 patients (1.19%) presented within 10 days of COVID-19 vaccine administration, whether first dose or second dose, between December 11, 2020 and March 25, 2021 (Figure S1). Of all vaccinated patients, 757 (41.1%) were male and 1520 (82.5%) patients were white. The mean (SD) age was 70.3 (18.6) years. The mean age of the patients who received mRNA-1273 vaccine (59.1 years) was lower compared to that of patients receiving the other vaccines (75.2 and 69.4 years for patients who received BNT-162b2 and Ad26.COVS.2.S vaccines, respectively). Of all presented patients, only 154 (8.4%) had a history of confirmed COVID-19 infection.

Overall, 1221 patients presented after the first dose of the vaccine and only 653 presented after the second dose of the vaccine. Tables 1 and 2 summarize the baseline characteristics of the patients presenting to the ED after the first (Table 1) and the second (Table 2) doses of the vaccines.

Patients who presented after the first dose had received BNT-162b2 (824, 67.5%), mRNA-1273 (354, 29.0%) and Ad26.COVS.2.S (43, 3.5%) vaccines, respectively. On the other hand, patients who presented after the second dose received BNT-162b2 (455, 70.0%) and mRNA-1273 (195, 30.0%), respectively. The mean time (SD) from the date of vaccines administration to the date of hospital presentation was 4.9 (3.2) and 4.7 (3.1) days after the first and the second doses of the vaccines, respectively.

We identified the causes of ED presentations in 1768 patients (Figure 1). Trauma (14.9%) was the most common cause of all ED visits, followed by hypertensive emergency and urgency (7.8%), generalized pain and arthralgia (5.7%), and chest pain (4.4%). COVID-19 infection post vaccination were identified in 51 patients (2.9% of all patients presenting to the ED).

### 3.2 | Main results

#### 3.2.1 | Characteristics of patients admitted to the hospital

Hospital admissions were required in 487 (39.9%) and 262 (40.3%) patients who presented to the ED after the first and the second doses of the vaccine, respectively. Among all patients admitted, a total of 43 (5.7%) patients were admitted to the ICU. The percentage of ED visits that resulted in hospital admissions increased with age: 35.9% of visits

**TABLE 2** Baseline characteristics and outcomes of patients presented after the second dose of the vaccine

| Characteristic                            | Total (%)   | BNT-162b2 vaccine (%) | mRNA-1273 vaccine (%) |
|---|-------------|-----------------------|-----------------------|
| Total number, no.                         | 650 (100)   | 455 (70.0)            | 195 (30.0)            |
| Mean age (SD), years                      | 72.0 (19.9) | 78.8 (12.5)           | 56.5 (22.0)           |
| Male sex, no. (%)                         | 246 (37.9)  | 186 (40.9)            | 60 (30.8)             |
| Race, no. (%)                             |             |                       |                       |
| White                                     | 535 (82.3)  | 371 (81.5)            | 164 (84.1)            |
| African-American                          | 86 (13.2)   | 70 (15.4)             | 16 (8.2)              |
| Others                                    | 29 (4.5)    | 14 (3.1)              | 15 (7.7)              |
| History of COVID-19 no. (%)               | 44 (6.8)    | 28 (6.2)              | 16 (8.2)              |
| Total admitted, no. (%)                   | 262 (40.3)  | 206 (45.3)            | 56 (28.7)             |
| Admitted to regular floor no. (%)         | 246 (37.8)  | 194 (42.6)            | 52 (26.7)             |
| Admitted to ICU, no. (%)                  | 16 (2.5)    | 12 (2.6)              | 4 (2.1)               |
| Mean time to presentation (SD), days      | 4.7 (3.1)   | 4.8 (3.2)             | 4.5 (3.0)             |
| Admission means length of stay (SD), days | 1.4 (2.8)   | 1.6 (3.1)             | 0.8 (2.2)             |
| Death events, no. (%)                     | 13 (2.0)    | 9 (2.0)               | 4 (2.1)               |

Abbreviation: COVID-19, coronavirus disease 2019.

for patients aged 60–69 years, 45.7% of visits for patients 70–79 years, 52.3% of visits for patients 80–89 years, and 55.0% of visits for patients 90 years and above (Figure 5).

Patients admitted after the first dose of the vaccine received BNT-162b2 vaccine (351 patients), mRNA-1273 vaccine (111 patients), and Ad26.COVS vaccine (25 patients), respectively. Hypertensive emergency and urgency (10.5%), trauma (5.6%), sepsis (5.3%), COVID-19 infection post vaccination (4.5%), and ischemic/hemorrhagic strokes (4.3%) were the most common identified reasons for admissions. Figure 2 summarizes the primary causes of admission after the first dose of the vaccine.

Patients admitted after the second dose of the vaccine received BNT-162b2 vaccine (206 patients) and mRNA-1273 vaccine (65 patients) respectively. Hypertensive emergency and urgency (13.5%), sepsis (4.8%), trauma (4.4%), cancer and cancer-related complications (4.4%), chest pain (4.0%), and acute coronary syndrome/angina (4.0%) were the most common identified causes. Figure 3 summarizes the primary causes of admission after the second dose of the vaccine.

The mean length of stay in the hospital was higher in the patients admitted after the first dose (3.6 days) as compared to the patients admitted after the second dose (1.4 days) of the vaccine. Among all patients admitted, only 43 (5.7%) patients needed ICU admission, which constitutes 2.3% of all patients presenting to the ED.

### 3.2.2 | Outcomes

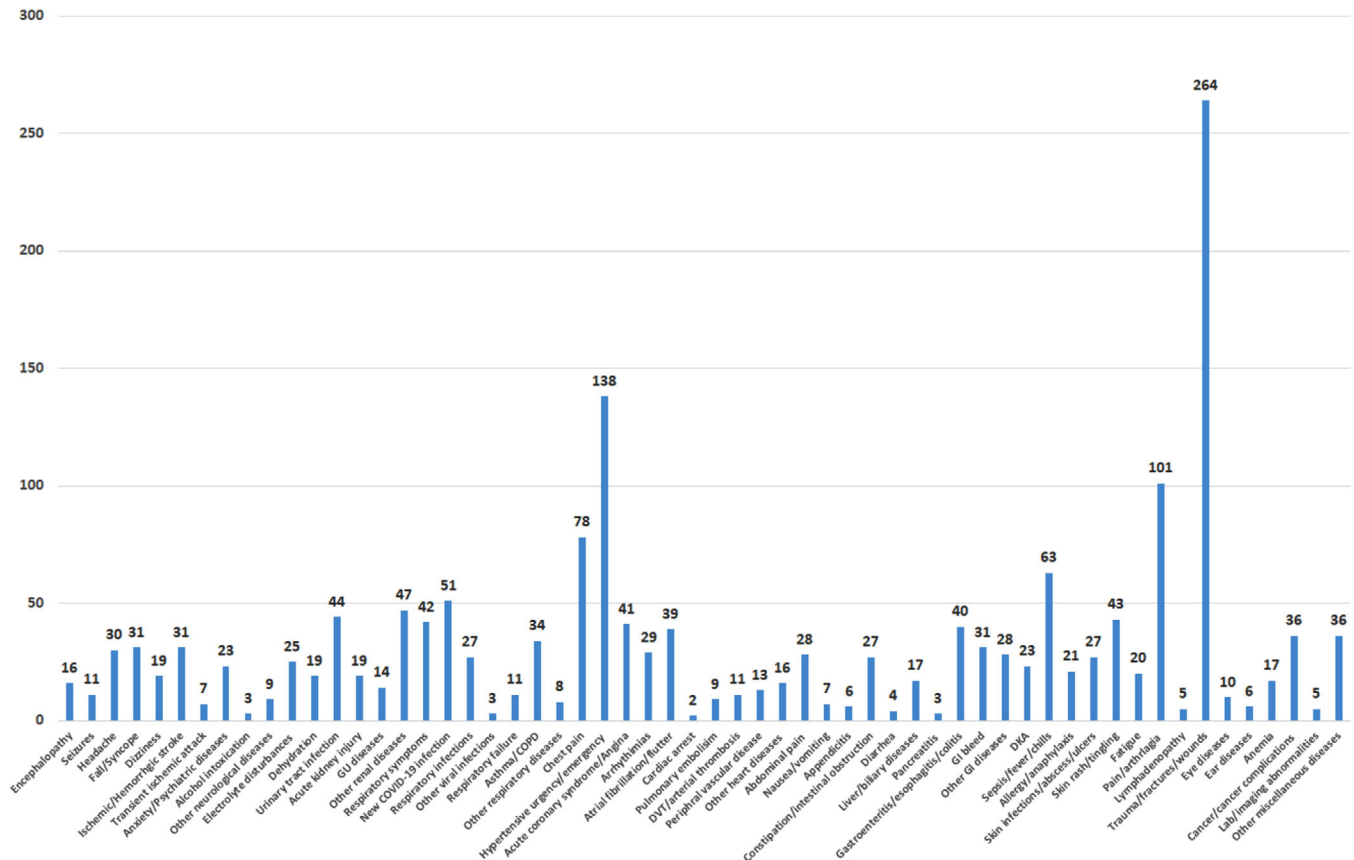
Of all presented patients, we observed 4002 death events (2.6%). Overall 3961 (2.6%) and 41 (2.2%) death events were observed during the follow-up period in the non-vaccinated and vaccinated patients, respectively. The median follow-up time was 68.0 days. Clinical char-

acteristics and types of vaccine given for patients who died are shown in Table 3. The median age of vaccinated patients who died was 81.0 years and 24 (58.5%) patients were male. Among the patients who expired, 29 (70.7%) patients received BNT-162b2 vaccine, 8 patients (19.5%) received mRNA-1273 vaccine, and 3 (7.3%) patients received Ad26.COVS. The type of the vaccine given was not known in 1 patient. Acute hypoxemic respiratory failure (19 patients, 46.3%), septic shock (10 patients, 24.4%), and cardiogenic shock (5 patients, 12.2%) were the most common causes of death. Three patients presented to the ED with cardiac arrest, and all died.

The median time to death from the date of vaccines administration was 26.0 days. In the Cox hazard regression model there was no significant difference in OST between patients who received BNT-162b2, mRNA-1273, or Ad26.COVS vaccines (HR: 0.957, 95% CI: 0.520 to 0.1.758), (Figure 3). Mean OST in female patients was significantly higher than in male patients (HR: 0.472, 95% CI: 0.251 to 0.889).

## 4 | LIMITATIONS

Our study had some limitations that require careful interpretations. First, the study design was descriptive in nature, and we did not compare the rate of side effects and causes of admissions with a control group of patients who did not receive the vaccine, except the historical data available from similar urban medical centers ED population studies. Second, the rate of side effects reported in our cohort population presenting to the ED might not be generalizable to the general population because of the older median age population that constituted our cohort. Third, as expected with any mass vaccination, the identification of AEs related to the vaccine administration is challenging and will require larger population studies and careful

**Causes of emergency department visits in all patients who presented within ten days of vaccination**


**FIGURE 1** Causes of emergency department visits in all patients who presented within 10 days of vaccination. Other neurological diseases: ataxia, amyotrophic lateral sclerosis, acute transverse myelitis, carpal tunnel syndrome, and aphasia. Genitourinary (GU) diseases including GU infections, vaginal bleeding, ovarian cysts, and vaginal ulcers. Other renal diseases: nephrolithiasis, hydronephrosis, hematuria, renal colic, renal cysts, glomerulonephritis, chronic kidney disease, benign prostatic hyperplasia, urinary retention, and urinary incontinence. Other respiratory diseases: atelectasis, pleural effusion, pyothorax, and bleeding from tracheostomy stoma. Other heart diseases: congestive heart failure, valves stenosis, valves regurgitation, dilated cardiomyopathy, and Takotsubo syndrome. Other gastrointestinal diseases including inguinal hernia, anal abscess, Crohn's disease, gastrostomy malfunction, achalasia, hemorrhoid, vascular disease of the intestine, and sialadenitis. Abbreviations: COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; DKA, diabetic ketoacidosis; DVT, deep vein thrombosis; GI, gastrointestinal; GU, genitourinary

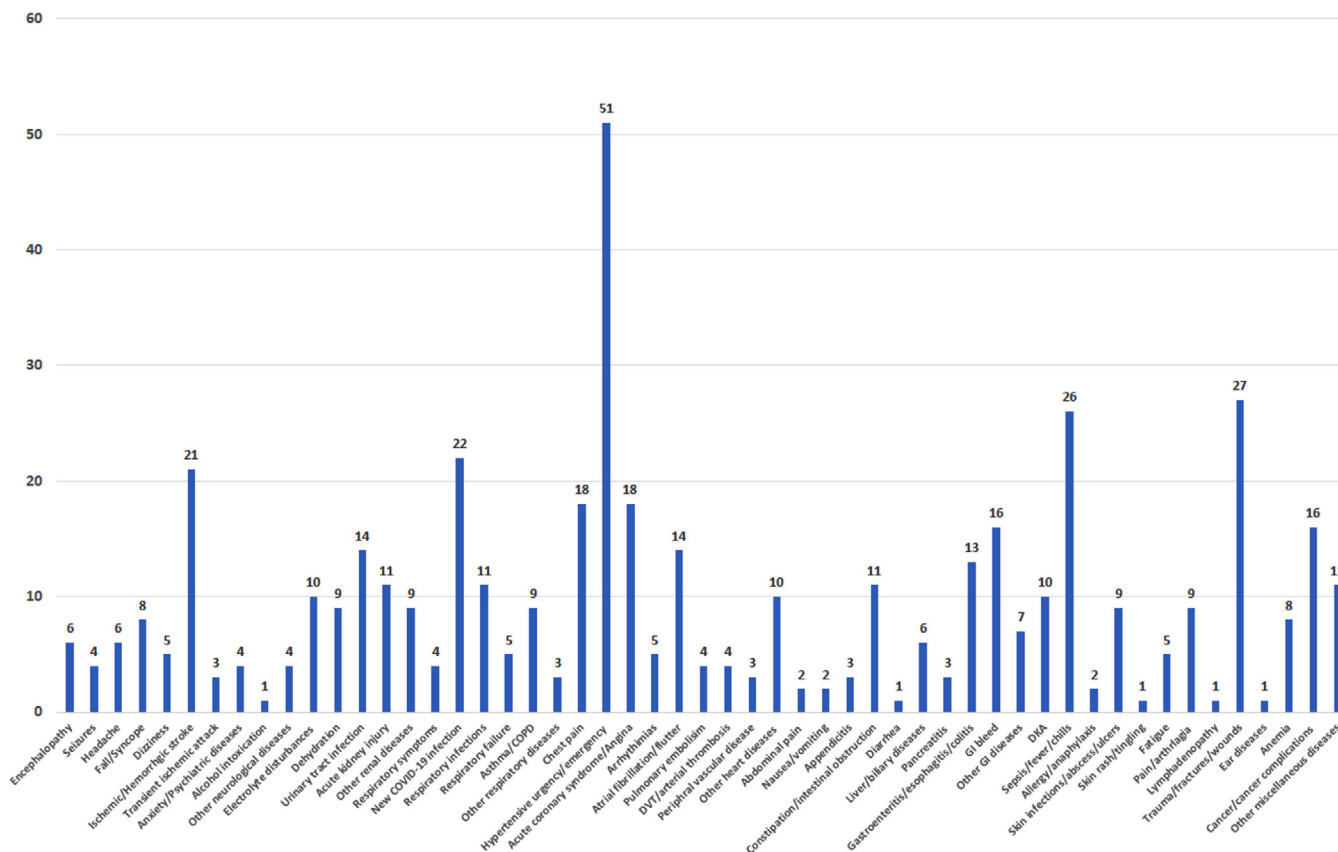
interpretation to identify the AEs specifically related to different types of vaccine.

## 5 | DISCUSSION

As of late April 2021,  $\approx$  235 million of the US population have been vaccinated,<sup>2</sup> and many others are waiting to get vaccinated. Safety of COVID-19 vaccines under EUA is one of the most discussed and pivotal points leading to hesitance in the general population.<sup>1,9</sup> The present study describes the AEFI observed after COVID-19 vaccines that led to ED presentations, hospital admissions, ICU admissions and deaths. Over 100,000 doses of COVID-19 vaccines were administered across the Cleveland Clinic Enterprise from December 2020 through March 2021 from the total of 360,862 doses given in Cuyahoga County.<sup>10</sup> The total number of vaccine doses given in the state of Ohio until March 25 was 3,218,372 doses.<sup>10</sup> Based on the previous numbers and based

on the Cleveland Clinic hospitals and enterprise market share in the state of Ohio at 13.8%,<sup>11</sup> we can estimate a total of 13,348 statewide prevalence of AEFI that required ED presentation, which is  $\approx$ 0.415% of all those who received the COVID-19 vaccine in the state of Ohio. Regarding race/ethnicity, our cohort was predominantly white (82.5%). As of June 14, 2021, the CDC reports of demographic characteristics of people receiving COVID-19 vaccination in the United States showed that among the vaccinated group, nearly 61.0% were white, 9.0% were African American, 15.0% were Hispanic, and 6.0% were Asian, and 8.0% reported multiple or other races. Based on the 2019 demographic US Census Bureau, Cleveland area population comprised 48.8% African American and 40.0% white races. Our results are highlighting possible racial disparities in the administration of COVID-19 vaccines.<sup>12,13</sup>

Approximately 40% of the patients presenting with AEFI to the ED required hospital admission per our emergency physician's medical decision, and around 2.3% of the studied cohort required a higher

**Causes of hospital admissions in all patients who presented after the first dose of vaccine administration.**


**FIGURE 2** Causes of hospital admissions in all patients who presented after the first dose of vaccine administration. Other neurological diseases: ataxia, acute transverse myelitis, and aphasia. Other renal diseases: nephrolithiasis, hydronephrosis, renal colic, glomerulonephritis, chronic kidney disease, and urinary retention. Other respiratory disease: pleural effusion, pyothorax, and bleeding from tracheostomy stoma. Other heart diseases: congestive heart failure, valves stenosis, valves regurgitation, dilated cardiomyopathy, and Takotsubo syndrome. Other gastrointestinal diseases including inguinal hernia, anal abscess, Crohn's disease, achalasia, and vascular disease of the intestine. Abbreviations: COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; DKA, diabetic ketoacidosis; DVT, deep vein thrombosis; GI, gastrointestinal

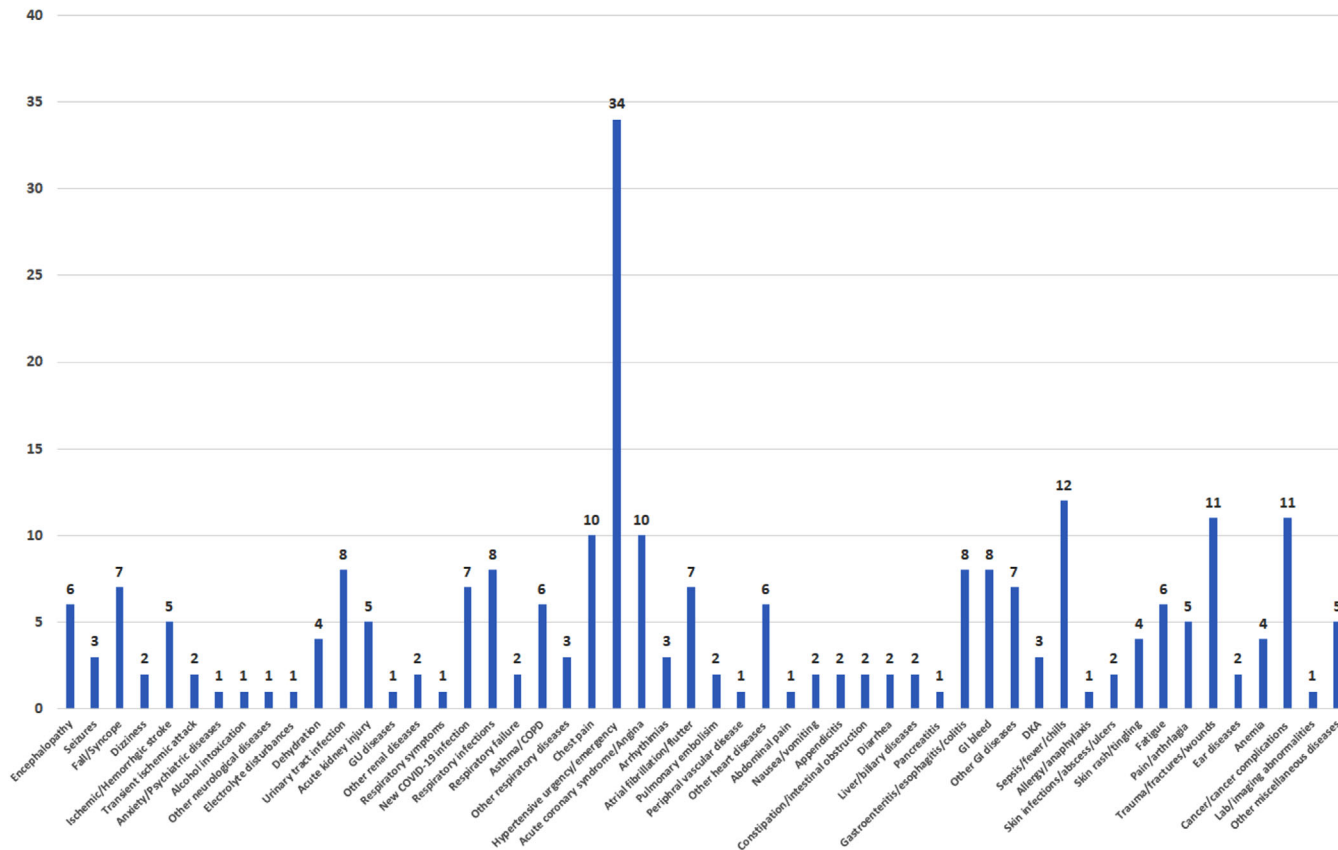
level of care, such as an ICU admission. Previous reports by the FDA from the different vaccine trials described SAEs. The reported proportion of SAEs was 1% in the mRNA-1273 vaccine, < 0.5% in the BNT-162b2 vaccine, and 0-4% in the Ad26.COV2.S vaccine.<sup>14-16</sup> Our estimated numbers confirm a very similar percentage of SAEs at  $\approx 0.415\%$  of all vaccinated people in the state of Ohio per the projections we made based on the Cleveland Clinic market share in the state of Ohio. However, it is difficult to have an accurate estimate of the correct AEs rate because the total number of patients vaccinated cannot be easily and firmly concluded.

Previous reports showed that the rates of ED visits that resulted in hospital admissions are affected by the patient's age group. In the United States and per the CDC data, ED visits among adults ended up with hospital admissions in 19.0% (60-69 years old), 23.0% (70-79 years old), 30.0% (80-89 years old), and 33.0% (90 and over) of all patients presenting to emergency rooms between 2014 and 2017.<sup>12</sup> On the other hand, in an urban academic tertiary center similar in volume and care to our health care system, mean admission rates for patients older than 65 years presenting to the ED was at 47.0%.<sup>11</sup>

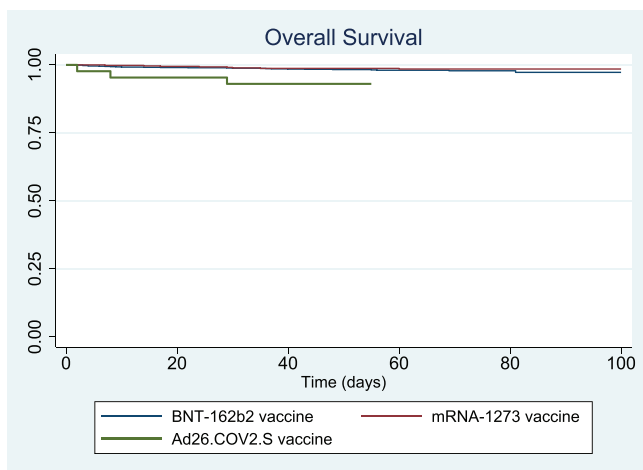
Our reported results showed similar rates compared to similar size urban academic centers; however, there were higher rates of hospital admissions from the ED for all age groups when compared to the CDC national center for health statistics data (Figure 5).

Among the AEs, hypertensive emergency and urgency (11.5%) followed by trauma (5.2%) and sepsis (5.2%) were the most prevalent causes of hospital admissions in our population cohort. Despite neither hypertensive emergency/urgency nor trauma or sepsis were mentioned previously as significantly higher AEs in any of the published vaccine trials, we think that these events truly reflect morbidity in the general population presenting to the ED for this age group and does not represent a frequency above the one expected in the general population. The prevalence of hypertensive emergency and urgency was suggestive of a possible coincidental event rather than a causal relationship to the vaccine.<sup>13</sup> In previous and most recent reports by the Agency for Healthcare Research And Quality (AHRQ) under the Health Care Cost and Utilization Project (HCUP), septicemia was found to be the most common cause of ED hospital admission in 2011 among patients aged 65-84 years.<sup>17</sup>

**Causes of hospital admissions in all patients who presented after the second dose of vaccine administration**



**FIGURE 3** Causes of hospital admissions in all patients who presented after the second dose of vaccine administration. Other neurological diseases: aphasia. Genitourinary diseases: vaginal bleeding. Other renal diseases: nephrolithiasis and renal colic. Other respiratory diseases: pleural effusion and bleeding from tracheostomy stoma. Other heart diseases: congestive heart failure, valves regurgitation, dilated cardiomyopathy. Other gastrointestinal diseases including inguinal hernia, Crohn’s disease, gastrostomy malfunction, and hemorrhoid. Abbreviations: COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; DKA, diabetic ketoacidosis; DVT, deep vein thrombosis; GI, gastrointestinal; GU, genitourinary



**FIGURE 4** Overall survival of patients presented after COVID-19 vaccines administration based on the type of the vaccine given. Abbreviations: COVID-19, coronavirus disease 2019; ED, emergency department

In the following section we report rates of AEs in a purely descriptive analysis. Those rates are not comparable to previous vaccine published trials, given the proportion of AEs in our study are reflective of a percentage out of the ED presenting population cohort. Reported AEs from vaccine trials included all population vaccinated and followed for AEs whether presenting to the ED or not.

Among all patients admitted to the hospital in our study, 3.8% presented with acute coronary syndrome and angina and only 1.4% were found to have acute myocardial infarction. Myocardial infarction rates in patients who received mRNA-1273 vaccine were 5 patients, 0.03% in the vaccine arm vs. 3 patients, 0.02% in the placebo arm.<sup>18</sup> Only 3 patients (<0.1%) who received BNT-162b2 vaccine developed acute myocardial infarction compared to 5 (<0.1%) patients in the placebo arm. Coronary artery disease was reported in only 4 cases (2 patients in placebo arm and 2 patients in the vaccine arm).<sup>15,19</sup>

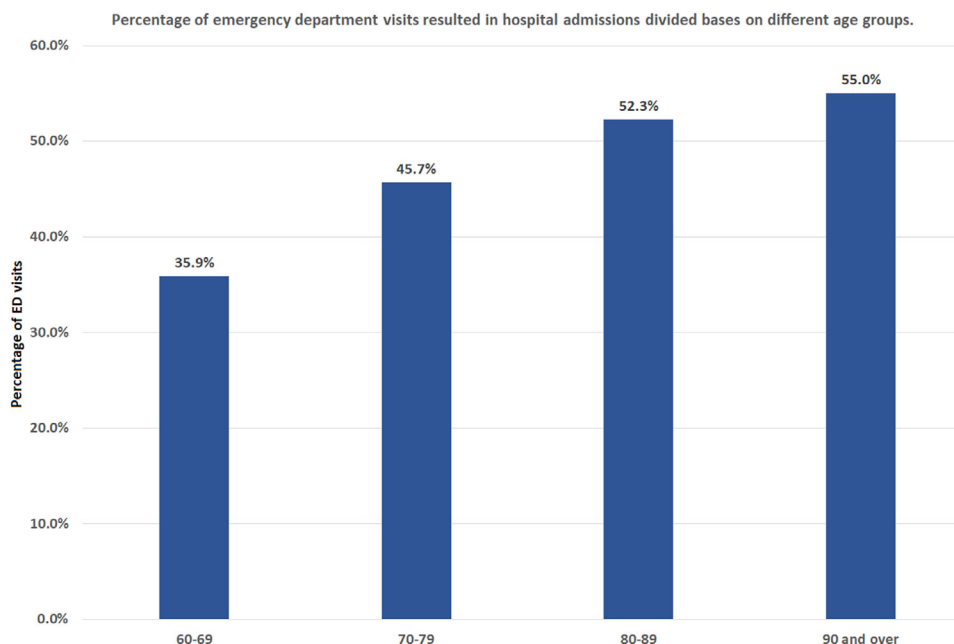
Cerebral vascular accidents (CVA) occurred in 4 patients (0.02%) who received BNT-162b2 vaccine.<sup>19</sup> The rate of CVA was not significantly different between the placebo and the vaccine groups (<0.1% in both groups).<sup>15</sup> CVA was reported in 3 patients (0.02%) who received mRNA-1273 and 1 patient in the placebo arm (0.007%).<sup>14</sup> CVA was

**TABLE 3** Characteristics of patients who died after vaccine

| Number | Gender | Age (years) | Cause of death                  | Past medical history                                     | Vaccine type  |
|--------|--------|-------------|---------------------------------|--|---------------|
| 1.     | Female | 75          | AHRF, AMS                       | SLE  | BNT-162b2     |
| 2.     | Male   | 86          | Small bowel obstruction         | HTN, CKD, hypothyroid, bladder cancer, Parkinson disease | BNT-162b2     |
| 3.     | Female | 90          | AHRF                            | HTN, CAD, CHF, COPD, breast cancer                       | BNT-162b2     |
| 4.     | Female | 70          | AHRF                            | HTN, hypothyroid, lung cancer                            | BNT-162b2     |
| 5.     | Male   | 92          | AHRF, AKI                       | HTN, CHF, CKD, renal cancer                              | Ad26.COVS.2.S |
| 6.     | Male   | 88          | Septic shock, AKI               | HTN, CHF, Afib, CAD, CKD, prostate cancer                | BNT-162b2     |
| 7.     | Male   | 84          | CC                              | HTN, CHF, Afib, COPD, liver cancer                       | BNT-162b2     |
| 8.     | Male   | 90          | Cardiac arrest                  | HTN, CHF, hypothyroid, OSA                               | BNT-162b2     |
| 9.     | Male   | 90          | Septic shock, AKI               | CAD, CHF, CKD  | BNT-162b2     |
| 10.    | Male   | 79          | Cardiac arrest                  | HTN, CAD, DM-2, OSA                                      | BNT-162b2     |
| 11.    | Female | 81          | Cardiac arrest                  | HTN, CHF, CAD, CKD, DM-2, CVA, OSA                       | BNT-162b2     |
| 12.    | Female | 84          | CC                              | CHF, lung cancer, renal cancer                           | BNT-162b2     |
| 13.    | Female | 90          | AHRF                            | HTN, CHF, Afib, CKD                                      | mRNA-1273     |
| 14.    | Female | 74          | Septic shock                    | CAD, Afib, asthma, DM-2                                  | Unknown       |
| 15.    | Male   | 83          | AHRF                            | HTN, IPF   | BNT-162b2     |
| 16.    | Male   | 90          | AHRF, AKI                       | HTN, DM-2, cholangiocarcinoma                            | BNT-162b2     |
| 17.    | Male   | 58          | Septic shock                    | HTN, esophageal cancer                                   | BNT-162b2     |
| 18.    | Female | 75          | Septic shock, cardiogenic shock | HTN, CHF, CAD, COPD, DM-2                                | mRNA-1273     |
| 19.    | Male   | 88          | Septic shock, AHRF              | HTN, CHF, CVA, DM-2, multiple sclerosis                  | Ad26.COVS.2.S |
| 20.    | Male   | 52          | AHRF                            | COPD, lung cancer  | BNT-162b2     |
| 21.    | Male   | 82          | AHRF, AMS                       | CKD, COPD, DM-2, hypothyroid, ulcerative colitis         | BNT-162b2     |
| 22.    | Female | 86          | AHRF, myasthenia gravis crises  | HTN, DM-2, myasthenia gravis                             | BNT-162b2     |
| 23.    | Male   | 75          | AHRF, COVID-19                  | HTN, CKD, lymphoma, Waldenstrom macroglobulinemia        | mRNA-1273     |
| 24.    | Female | 80          | CVA, hemorrhagic shock          | HTN, CHF, Afib, CAD, CKD, DM-2, Parkinson disease        | BNT-162b2     |
| 25.    | Female | 81          | Cardiogenic shock               | HTN, CHF, Afib, CKD, hypothyroid                         | BNT-162b2     |
| 26.    | Male   | 90          | Septic shock, AHRF              | HTN, CAD, Parkinson disease                              | BNT-162b2     |
| 27.    | Male   | 62          | Bowel ischemia/perforation      | CAD, CKD, DM-2, liver cirrhosis                          | BNT-162b2     |
| 28.    | Male   | 94          | Presented expired               | HTN, Afib, CAD, CKD                                      | BNT-162b2     |
| 29.    | Female | 93          | Cardiogenic shock               | HTN, CKD, DM-2   | BNT-162b2     |
| 30.    | Female | 66          | Septic shock, AHRF, acute DVT   | Ovarian cancer, DM-2                                     | BNT-162b2     |
| 31.    | Male   | 79          | AHRF, sepsis                    | CVA, DM-2, OSA   | mRNA-1273     |
| 32.    | Female | 76          | Septic shock, AHRF              | HTN, COPD, Graves disease, lung cancer                   | mRNA-1273     |
| 33.    | Male   | 81          | AHRF                            | HTN, lung cancer   | mRNA-1273     |
| 34.    | Male   | 64          | Septic shock, AKI               | HTN, DM-2, OSA, lymphoma                                 | Ad26.COVS.2.S |
| 35.    | Female | 73          | Cardiac arrest                  | HTN, CHF, DM-2, hypothyroid                              | BNT-162b2     |
| 36.    | Male   | 89          | Cardiogenic shock               | HTN, CHF, Afib, hypothyroid                              | BNT-162b2     |
| 37.    | Male   | 66          | AHRF                            | HTN, CHF, Afib, lung cancer                              | mRNA-1273     |
| 38.    | Male   | 75          | CC                              | HTN, CKD, urethral cancer                                | BNT-162b2     |
| 39.    | Female | 82          | Cardiogenic shock               | HTN, CHF, Afib, CKD, COPD, DM-2                          | mRNA-1273     |
| 40.    | Female | 62          | Cardiac tamponade, AHRF         | Hypothyroid, liver transplant                            | BNT-162b2     |
| 41.    | Male   | 74          | Trauma                          | CVA  | BNT-162b2     |

Abbreviations: Afib, atrial fibrillation; AHRF, acute hypoxic respiratory failure; AMS, altered mental status; AKI, acute kidney injury; CKD, chronic kidney disease; CC, comfort care; CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive lung disease; CVA, cerebrovascular accident; DM-2, diabetes mellitus type 2; DVT, deep vein thrombosis; HTN, hypertension; IPF, idiopathic pulmonary fibrosis; OSA, obstructive sleep apnea; SLE, systemic lupus erythematosus.





**FIGURE 5** Percentage of emergency department visits resulting in hospital admissions divided on the basis of different age groups

the cause of admissions in 3.5% of our studied population. None of our patients had cerebral sinus thrombosis.

In the previously mentioned clinical trials, deep vein thrombosis and pulmonary embolism were not found to be significantly associated with the vaccines; in our cohort 20 patients presented to the ED with either pulmonary embolism, venous thrombosis, or arterial thrombosis, with a rate close to 1.0% of our ED cohort. The rates of pulmonary embolism (0.03%) and deep vein thrombosis (0.01%) were not significantly associated with the mRNA-1273 vaccine group. Venous thrombosis and thrombocytopenia were recently reported in 5 patients after receiving ChAdOx1 nCoV-19 adenoviral vector vaccine.<sup>20</sup> None of the patients who received Ad26.COV2.S in our cohort presented with acute venous thrombosis.

In our cohort, appendicitis was the cause of admission in 5 (0.27%) patients after receiving the vaccine. Appendicitis has been reported at similar rates with the BNT-162b2 vaccine where 8 vaccinated patients developed appendicitis compared to 4 patients (0.02%) in the placebo arm.<sup>19</sup> Also 2 patients (0.01%) who received mRNA-1273 vaccine had appendicitis versus 3 patients (0.02%) in the placebo arm.<sup>14</sup>

Overall, low anaphylaxis rates were reported in our study. Two of our patients (0.11%) presented with anaphylaxis secondary to the vaccine, and both presented after the first dose of the vaccine (1 received mRNA-1273 vaccine and 1 received BNT-162b2 vaccine). In the study published by Shimabukuro et al., 21 patients developed anaphylaxis after receiving the first doses of BNT-162b2 vaccine.<sup>21</sup> In another study, anaphylaxis was confirmed after the first dose in 7 patients who received BNT-162b2 vaccine and 9 patients who received mRNA-1273 vaccine. The CDC had reported a rate of 2.5 cases per million doses.<sup>22</sup>

Of all patients presenting to the ED, only 51 patients (2.9%) were diagnosed with COVID-19 infection post vaccination, of whom 29 patients (56.9%) required hospital admission. This rate is consistent

with the vaccine efficacy reported by the previous clinical trials, although our patient population is not expected to be fully vaccinated within few days of the vaccine administration, because full efficacy is expected after 14 days of vaccination.<sup>14-16</sup> Per Lopez Bernal et al, vaccination with 1 dose of BNT 162b2 was associated with a significant reduction in symptomatic COVID-19 infections in older adults and with further protection against the disease. A second dose of BNT162b2 was associated with further protection against symptomatic disease.<sup>23</sup> These findings support that full vaccination with 2 doses of vaccine is more beneficial as compared to a single dose.

The mortality rate in our cohort was 2.2% during the follow-up period. Our cohort mortality rate is lower compared to the general population as reported by previous studies. One prospective study from a similar size urban academic medical center that included 10,737 patients found that the mortality rate at 1 month after an ED visit was 8.3% in patients aged 65 years and above and 17.2% at 6 months.<sup>24</sup>

Only 2 patients (0.01%) who received BNT-162b2 vaccine died (1 from cardiac arrest and 1 from arteriosclerosis) compared to 4 patients (0.02%) in the placebo arm.<sup>15</sup> Similarly, only 2 patients (0.01%) who received mRNA-1273 vaccine died (1 from cardiac arrest and 1 from suicide) compared to three patients (0.02%) in the placebo arm.<sup>15</sup>

Based on the total number of patients who presented to the ED, we observed a higher mortality rate among non-vaccinated patients (2.6%) when compared to vaccinated patients (2.2%) who presented during the same period and followed up for the same duration.

In conclusion, to our knowledge, this is the first observational study to describe causes of ED visits, hospital admissions, and death events in patients within 10 days of COVID-19 vaccination. However, larger studies are needed to determine the AEs associated with COVID-19 vaccines across all age groups. Providing this type of information to health workers is crucial because they not only have a responsibility

to detect AEs after immunization but also to reassure the general population over the safety of the vaccines used, especially in the context of vaccination hesitancy that we are facing. In addition, physicians should stress the importance of complete vaccination given its benefits and prioritize equal access to immunization among different races/ethnicities to reduce and prevent racial health disparity.

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## CONFLICTS OF INTEREST

The authors declare that they have no conflict of interest.

## AUTHOR CONTRIBUTIONS

TK and MF contributed equally to this article. TK, MF, MAW, and KM contributed to the literature review. TK, MF, KM, MAW, MA, RB, and FA contributed to the study design and conceptualization. TK, MF, RB, JC, HP, and FA contributed to data collection and curation. TK, MF, RB, KM, MA, JC, HP, and FA contributed to data analysis and interpretation. TK, MF, KM, MA, and FA wrote the initial draft. All authors contributed to reviewing and editing the final draft and verified the underlying data.

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## SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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