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Research Article

Patient Factors and Hospital Outcomes Associated With Atypical Presentation in Hospitalized Older Adults With COVID-19 During the First Surge of the Pandemic

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Abstract

Background: Literature indicates an atypical presentation of COVID-19 among older adults (OAs). Our purpose is to identify the frequency of atypical presentation and compare demographic and clinical factors, and short-term outcomes, between typical versus atypical presentations in OAs hospitalized with COVID-19 during the first surge of the pandemic.

Methods: Data from the inpatient electronic health record were extracted for patients aged 65 and older, admitted to our health systems' hospitals with COVID-19 between March 1 and April 20, 2020. Presentation as reported by the OA or his/her representative is documented by the admitting professional and includes both symptoms and signs. Natural language processing was used to code the presence/absence of each symptom or sign. Typical presentation was defined as words indicating fever, cough, or shortness of breath; atypical presentation was defined as words indicating functional decline or altered mental status.

Results: Of 4 961 unique OAs, atypical presentation characterized by functional decline or altered mental status was present in 24.9% and 11.3%, respectively. Atypical presentation was associated with older age, female gender, Black race, non-Hispanic ethnicity, higher comorbidity index, and the presence of dementia and diabetes mellitus. Those who presented typically were 1.39 times more likely than those who presented atypically to receive intensive care unit–level care. Hospital outcomes of mortality, length of stay, and 30-day readmission were similar between OAs with typical versus atypical presentations.

Conclusion: Although atypical presentation in OAs is not associated with the same need for acute intervention as respiratory distress, it must not be dismissed.

Keywords: Complaints, COVID-19, Pandemic, Signs, Symptoms

Older adults (OAs; 65 years and older) account for nearly 15% of all COVID-19 infections and 81% of COVID-19-related deaths (1). Although a myriad of symptoms and signs continue to be recognized as indicative of COVID-19, the typical presentation has been characterized by fever, cough, and shortness of breath. However, an emerging literature points to an atypical presentation in the OA population, characterized by functional decline and altered mental status. A series of case reports and observational studies (2–8) found that OAs with COVID-19 presented to the hospital with altered mental status, generalized weakness, delirium, increased agitation, falls, lethargy, loss of appetite, and confusion, which occurred both with and without typical COVID-19 symptoms.

The mere identification of this atypical presentation in OAs, characterized by functional decline and altered mental status, has largely been the focus of studies published to date. Less attention has been paid to the demographic and clinical characteristics of OA COVID-19 patients who present fully or partially atypically, and how this patient profile differs from those with a typical COVID-19 presentation. Existing data suggest that older age (9,10) and arrival to the hospital from a facility (rather than from home (11)) are related to atypical presentation, but other demographic and clinical factors' relationship to presentation has yet to be explored.

Short-term outcomes of patients presenting atypically versus typically have been minimally examined, with hospital mortality receiving the most attention. Most existing studies (6,12) indicate that hospital mortality is related to atypical presentation, although one study (13) found that there was no significant difference between typical and atypical presentations in mortality or hospital length of stay (LOS). Other outcomes such as receipt of intensive care unit (ICU)-level care or hospital readmission status across typical versus atypical presentations have not been examined.

Although the prior literature is critically important (14), there are several gaps. Existing studies have relatively small sample sizes, some rely on clinicians' retrospective memory of subjective reporting of patients' presentations, and many are focused on the oldest-old patients aged 80 and older. Only some of these studies were conducted on hospitalized patients, which represent the most acutely ill subgroup of OAs. Furthermore, the data comparing demographic and clinical variables across type of presentation (atypical or typical) are minimal and explore few variables, such as age and residence prior to arrival at the hospital. In regard to short-term outcomes associated with different presentations, there are inconsistent data on hospital mortality and minimal data on hospital LOS, ICU-level care, and hospital readmission.

To fill these gaps, the purpose of the present study is to (i) identify the frequency of atypical presentation, defined as it is in the literature as functional decline and altered mental status; (ii) compare demographic (age, gender, race, ethnicity, and residence prior to hospital) and relevant clinical (severity of illness on presentation, comorbidity index, presence of dementia, diabetes, or hypertension) variables between OAs with typical versus atypical presentations; and (iii) compare short-term hospital outcomes (ICU-level care, hospital mortality, hospital LOS, and 30-day hospital readmission), between OAs with typical versus atypical presentations, in a large cohort of COVID-19, hospitalized OAs admitted to a multihospital system serving a major metropolitan area of the United States.

Method

Study Sample and Procedures

The Northwell COVID-19 Research Consortium and institutional review board approved the study. All data were extracted from the inpatient electronic health record (EHR) (Sunrise Clinical Manager) of OAs meeting the following eligibility criteria: age greater than or equal to 65; admitted to 1 of 11 health system hospitals between March 1, 2020 and April 20, 2020 (this timeframe was selected because it covers the beginning and height of the first surge of the pandemic in the area, New York, where this health system is located (15)) and confirmed diagnosis of COVID-19 infection by positive polymerase chain reaction result of a nasopharyngeal sample. Clinical course and outcomes were monitored until June 10, 2020. Transfers from one in-system hospital to another were merged and considered as a single visit. For OAs with multiple admissions during the study period, only the first admission was included.

All data elements underwent a vigorous process of data harmonization, ensuring that the data fields represent clinically relevant information. An iterative process was undertaken that consisted of a recurring loop of query, refinement, data validation by manually reviewing randomly selected charts, and inter-rater agreement, followed by further query refinement, until variable accuracy was achieved. In addition, the team hand-searched a random selection of charts to ensure data quality and integrity. Clinical members of the research team led quality control and data validation of clinical variables.

Study Measures and Coding

Data included demographic, clinical, hospital course, and hospital outcome factors, as well as presentation on arrival to the hospital (both patient reported and objectively collected).

Demographic Factors

Demographic factors included age (3-level categorical variable: 65–74, 75–84, and 85 years and older), gender (male or female), race (Black, Asian, White, other, and not available), ethnicity (Hispanic/Latino, Non-Hispanic/non-Latino, or missing), body mass index (underweight [below 18.5], normal [18.5–24.9], overweight [25–29.9], obese [30 or above], and missing), and residence prior to hospital arrival (home, facility, or missing).

Clinical Factors

Clinical factors included Modified Early Warning Score (MEWS; 2-level categorical variable in which scores 1–4 indicate not severely ill and 5–13 indicate severely ill), comorbidity index (calculated based on the Charlson Comorbidity Index [CCI], excluding the age component) (16), and the presence/absence of specific comorbidities (diabetes mellitus, hypertension, atrial fibrillation, chronic obstructive pulmonary disease, asthma, cancer, coronary artery disease, chronic kidney disease, or end-stage renal disease, and dementia). Clinical factors relevant in the COVID-19 literature (MEWS, comorbidity index, presence/absence of diabetes mellitus, hypertension, and dementia) were compared across presentations, whereas the remaining clinical factors were used for descriptive purposes only.

Hospital Course Factors

Hospital course factors included Do Not Resuscitate (DNR) order (defined as no DNR, early DNR [within 24 hours of hospital admission], and late DNR [greater than 24 hours after hospital admission] (17)) and first documented form of oxygen (4-level variable categorized as (i) none; (ii) nasal cannula, ventimask; (iii) nonrebreather, high-flow, and noninvasive ventilation; and (iv) intubation).

Hospital Outcome Factors

Hospital outcome factors included ICU-level care (defined as intubation or administration of pressors: vasopressin, norepinephrine, phenylephrine, epinephrine, esmolol, or dobutamine), hospital mortality (expired vs discharged alive), hospital LOS in days, and hospital readmission within 30 days (yes or no).

Patient-Reported Presentation

Patient-reported hospital presentation was extracted from the Chief Complaint section of the EHR and included both symptoms and

signs. Presentation is self-reported by patients and/or their representatives and collected upon arrival to the hospital and entered into the EHR by the admitting professional. As these data are captured qualitatively using free text, we used a natural language processing (NLP) software (Clinical Regex (18–20)) to code the presence or absence of each symptom or sign for each OA. Briefly, using a predefined ontology, the software displays clinical notes that contain highlighted keywords. Human experts review the highlighted keywords to determine whether the context is relevant to the outcome of interest. Human experts then label notations using pre-specified codes (eg, using a "zero" to label notations where keywords appeared out of context for exclusion, or using a "one" to label notations for inclusion). This NLP approach allows for semiautomated chart review and reduces the complexity and time required to extract text-based information from EHRs. Using this tool allowed for the identification of variations in documentation of the same symptom or sign (ie, "shortness of breath" and "SOB" were both identified and combined into the same category). It also allowed differentiation of negative findings (ie, "no SOB"). We had a trained staff member verify accuracy.

COVID-19 symptoms and signs classified as typical were as follows: fever/chills (indicated by the words fever, chills, rigors), cough (indicated by the following words: cough, bloody sputum, hemoptysis, coughing up blood), or shortness of breath (indicated by the acronym SOB or words: difficulty breathing, hypoxia, low o2 sat, low oxygen saturation, respiratory distress, tachypnea, rapid respiratory rate, purse-lip breathing, cyanotic, low oxygen). Symptoms or signs classified as atypical were as follows: functional decline (indicated by the following words: falls, found on floor, head injury, fell, fall, trip, weakness, fatigue, tired, can't walk, difficulty ambulating/walking, can't get out of bed, cannot walk, feeling tired, general malaise, debility, failure to thrive, dehydration, weight loss, poor oral intake, decreased PO, loss of appetite, decreased appetite, not eating, poor appetite, anorexia, syncope, passed out, light headedness, light headed, spinning, vertigo, dizziness, presyncope), or altered mental status (indicated by the following words: altered mental status, confusion, agitated, forgetful, lethargy, lethargic, drowsy, or the acronym AMS). Other symptoms or signs (ie, gastrointestinal, cardiovascular, neurological, genitourinary, and other) were included in the descriptive characterization of the sample but are not considered part of the typical or atypical presentations, as they are defined in existing studies.

Although symptoms and signs are often added to the Centers for Disease Control and Prevention's list of indicative of COVID-19, we chose these definitions of "typical" and "atypical" presentations because (i) fever, cough, and shortness of breath remain the "hallmark" symptoms of COVID-19 despite that other symptoms or signs are considered common; (ii) our categorization is based on symptoms and signs considered typical or atypical at the time at which this manuscript was prepared; and (iii) we followed the categorization of what is considered typical and atypical in the existing COVID-19 literature (2–5,7,9,11).

The presentation grouping variable for the comparison analyses was created based on these data and is a 2-level variable: typical presentation compared with atypical presentation. The typical presentation level consisted of OAs with typical symptoms or signs only. Individuals in the typical group reported at least cough, fever, or shortness of breath, but did not need to have all of these to qualify for this group. The atypical presentation level consisted of OAs with either (i) atypical symptoms or signs only or (ii) both typical and atypical symptoms or signs. Although we could have grouped presentation in several different ways, we chose this grouping because our specific research question focused on whether the presence of atypical symptoms or signs (with or without typical symptoms or signs) is related to specific demographic and clinical patient-level factors and outcomes.

Objectively Collected Hospital Presentation Data

Fever on arrival based on thermometer reading (defined as ≥37.8°C); heart rate (categorized based on the systemic inflammatory response syndrome criteria as ≤90 or >90 bpm (21)); blood pressure (systolic < 90 or ≥ 90 mm Hg); and hypoxia (oxygen saturation ≤ 94). As the purpose of this article is related to patient-reported hospital presentation, this objectively captured data will only be used to describe the sample.

Statistical Analyses

Data were first summarized using descriptive statistics. Specifically, categorical variables were summarized using frequencies and percentages; continuous variables were summarized using mean and *SD*. To compare demographic and relevant clinical factors between typical and atypical presentations, categorical variables were examined using chi-square test, and continuous variables were examined using nonparametric Kruskal–Wallis test because the data were not normally distributed. We also compared short-term outcomes without controlling for any relevant variables and calculated unadjusted *p* values. To compare short-term hospital outcomes between typical and atypical presentations while controlling for relevant variables, logistic regression was performed for hospital mortality (death in hospital or alive at discharge), repeat admission within 30 days (yes or no), and ICU-level care (yes or no), and linear regression was performed for hospital LOS in days. The relevant variables controlled for in our regressions were as follows: age, gender, race, residence prior to hospital, comorbidity index, MEWs score, first documented oxygen, and DNR order. All analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC).

Results

Sample Description

In total, 4 961 OAs were included in the data set. The average age was 77.3 (*SD* = 8.4, range = 65–107), and just over half were male (56.0%), nearly half were White (46.8%), and a substantial proportion were Black (20.8%) and Hispanic or Latino (15.1%). The majority had Medicare (93.4%), spoke English (81.6%), and arrived at the hospital from home (79.0%). With regard to body mass index, 2.2% of the samples were underweight, 21.3% were normal weight, 26.0% were overweight, 20.9% were obese, and 30.0% were missing data on this variable.

The top 2 most common comorbidities were hypertension (61.1%) and diabetes mellitus (36.8%), followed by chronic kidney disease or end-stage renal disease (16.3%), atrial fibrillation (14.5%), cancer (8.8%), chronic obstructive pulmonary disease (8.5%), coronary artery disease (5.3%), and asthma (5.0%). The majority (62.9%) did not have a DNR, nearly a third (31.4%) had a late DNR, and 5.7% had an early DNR. Based on MEWS, the majority (59.8%) were not severely ill, 30.5% met criteria for severe illness, and 9.7% were missing this data. Regarding the first documented form of oxygen, 4.6% were intubated, 9.7% received 100% nonrebreather, high-flow, or noninvasive ventilation, and 65.4% received nasal cannula or ventimask. The remaining 20.3% did not

receive oxygen supplementation on arrival to the hospital. About one third of OAs (35.2%) died while in the hospital. The average hospital LOS was 10 days (*SD* = 10.0). Few (6.7%) were readmitted to the hospital within 30 days of discharge. Overall, 23.4% of the sample received ICU-level care.

Objectively collected data captured on hospital arrival indicate 27.5% were febrile (based on thermometer temperature > 37.8°C), 53.6% had a heart rate over 90 bpm, 3.8% had low blood pressure, and 50.2% were hypoxic. See Table 1 for full demographic and clinical details.

Table 1. Comparison of Patient Demographics, Clinical Factors, and Hospital Outcomes Between Typical and Atypical Presentations (Unadjusted)

Variable	Total Sample (*N* = 4 961)	Typical Presentation[a] (*n* = 2 835) *n* (%) or Mean (*SD*)	Atypical Presentation[a] (*n* = 1 645) *n* (%) or Mean (*SD*)	*p* Value
Age				<.0001
65–74 y	2 168 (43.7)	1 346 (69.2)	599 (30.8)	
75–84 y	1 728 (34.8)	952 (60.6)	620 (39.4)	
≥85 y	1 065 (21.5)	537 (55.8)	426 (44.2)	
Gender				.002
Male	2 777 (56.0)	1 648 (65.2)	879 (34.8)	
Female	2 184 (44.0)	1 187 (60.8)	766 (39.2)	
Race				.00001
Black	1 033 (20.8)	504 (54.0)	429 (46.0)	
Asian	398 (8.0)	255 (72.2)	98 (27.8)	
White	2 322 (46.8)	1 343 (63.7)	765 (36.3)	
Other	1 017 (20.5)	626 (68.2)	292 (31.8)	
Not Available	191 (3.9)	107 (63.7)	61 (36.3)	
Ethnicity[b]				<.0001
Hispanic/Latino	750 (15.1)	485 (71.0)	198 (29.0)	
Not Hispanic/Latino	3 935 (79.3)	2 192 (61.8)	1 358 (38.3)	
Residence prior to hospital[c]				.20
Home	3 918 (79.0)	2 240 (62.9)	1 324 (37.2)	
Facility	1 030 (20.8)	589 (65.2)	315 (34.9)	
MEWS[d]				.80
Not severely ill	2 966 (59.8)	1 700 (63.6)	975 (36.4)	
Severely ill	1 512 (30.5)	884 (64.0)	498 (35.8)	
Comorbidity Index	3.4 (2.8)	3.2 (2.8)	3.6 (2.8)	<.0001
Dementia				<.0001
Yes	647 (13.0)	310 (54.3)	261 (45.7)	
No	4 314 (87.0)	2 525 (64.6)	1 384 (35.4)	
Diabetes mellitus				.002
Yes	1 827 (36.8)	1 000 (60.4)	656 (39.6)	
No	3 134 (63.2)	1 835 (65.0)	989 (35.0)	
Hypertension				.24
Yes	3 031 (61.1)	1 737 (62.6)	1 037 (37.4)	
No	1 930 (38.9)	1 098 (64.4)	608 (35.6)	
Hospital mortality[e]				<.0001[f]
Died in hospital	1 747 (35.2)	1 064 (67.3)	518 (32.7)	
Discharged alive	3 053 (61.5)	1 676 (60.9)	1 076 (39.1)	
Length of stay (d)	10.0 (10.0)	10.4 (10.6)	9.4 (9.4)	.2574[f]
Repeat admission (within 30 d)				.0479[f]
Yes	331 (6.7)	169 (57.9)	123 (42.1)	
No	4 630 (93.3)	2 666 (63.7)	1 522 (36.3)	
ICU-level care				<.0001[f]
Yes	1 159 (23.4)	764 (71.7)	301 (28.3)	
No	3 802 (76.6)	2 071 (60.6)	1 344 (39.4)	

Notes: ICU = intensive care unit.

[a]9.7% of the total sample (*n* = 481) did not qualify for the typical or atypical presentation groups and were not included in comparison analyses.

[b]5.6% of the total sample (*n* = 276) and 5.5% of the sample used for the typical and atypical comparison (*n* = 247) were missing ethnicity data.

[c]0.3% of the total sample (*n* = 13) and 0.3% of the sample used for the typical and atypical comparison (*n* = 12) were missing residence prior to hospital arrival data.

[d]9.74% (*n* = 483) of the total sample and 9.4% (*n* = 423) of the presentation sample were missing MEWS data.

[e]3.2% (*n* = 161) of the total sample and 3.3.% (*n* = 146) of the presentation sample are missing hospital mortality data.

[f]Unadjusted *p* values presented for outcomes.

Frequency of Symptom Presentations

The most commonly endorsed presentations were typical: shortness of breath (50.3%), fever and chills (37.7%), and cough (26.5%), followed closely by atypical presentations: functional decline (24.9%) and altered mental status (11.3%). Other presentations were as follows: gastrointestinal (8.9%), cardiovascular (3.5%), neurological (3.3%), genitourinary (0.6%), and other (ie, abnormal lab result, laceration, pacemaker malfunction, etc.; 6.5%).

Comparison Between Presentations on Demographic and Relevant Clinical Factors

The population was divided into 2 types of presentation: typical presentation (OAs with typical presentation only, n = 2 835 or approximately 57.0%) versus atypical presentation (OAs with atypical presentation only or a combination of typical and atypical presentations, n = 1 645 or approximately 33.0%). Of those with atypical presentation, nearly half (49%) had atypical symptoms and signs alone, and 51% had both atypical and typical symptoms and signs. Nearly 10% (n = 481) of OAs presented with only symptoms or signs that were considered neither typical nor atypical based on the literature (eg, chest pain was the only presenting complaint) and were excluded from subsequent analysis.

Comparing between presentations on demographic and clinical factors, OAs with atypical presentations were statistically significantly more likely to be older, female, Black, non-Hispanic, have a higher comorbidity index, have dementia, and/or have diabetes. There were no statistically significant differences between typical and atypical presentations in residence prior to hospitalization (community vs facility), in severity of illness, or in the presence of hypertension. Comparing our short-term outcomes between typical and atypical presentations without controlling for relevant variables, only hospital mortality repeat admission and receipt of ICU-level care were significant. See Table 1 for additional details on unadjusted comparisons of demographic, relevant clinical, and outcome variables between these 2 presentations.

Comparison Between Presentations on Short-Term Hospital Outcomes

Multivariate logistic (binary outcomes) and linear regression (continuous outcome) analyses were conducted to examine differences in hospital outcomes between OAs with typical versus atypical presentations, while controlling for variables known to contribute to mortality in the COVID-19 literature: age (22–24), gender (23,25), race (26), residence prior to hospital arrival (27), comorbidity index (25), MEWS (28), first documented oxygen (24,29), and DNR order (24). There were no statistically significant differences in hospital mortality, hospital LOS, or hospital readmission between typical and atypical presentations. However, those who presented typically were 1.39 times more likely than those who presented atypically to receive ICU-level care (p = .0007). See Tables 2–5 for details comparing hospital outcomes between presentations.

Table 2. Multivariable Logistic Regression. Patient Factors Associated With ICU-Level Care (Yes vs No)

Patient Characteristics	OR (95% CI)
Typical symptom vs atypical symptom	1.39 (1.15, 1.67)**
Age	0.92 (0.90, 0.93)*
Gender (male vs female)	1.46 (1.22, 1.75)*
Race	
Black vs White	0.76 (0.60, 0.96)***
Asian vs White	1.11 (0.82, 1.52)
Other vs White	1.09 (0.87, 1.36)
Unknown vs White	0.69 (0.42, 1.13)
Comorbidity Index	1.02 (0.98, 1.05)
Admission from (facility vs home)	0.47 (0.36, 0.60)*
MEWS (scores >4, severely ill, vs scores 1–4)	3.87 (3.18, 4.71)*
First documented oxygen delivery	
Nasal cannula vs none	4.02 (2.90, 5.57)*
Nonrebreather vs none	6.19 (4.22, 9.09)*
Mechanical ventilation vs none	999.99 (0.00, 999.99)
DNR	
No DNR at all vs late DNR	0.49 (0.40, 0.60)*
Early DNR vs late DNR	0.35 (0.21, 0.58)*

Notes: CI = confidence interval; Comorbidity Index = Charlson Comorbidity Index (without age component); DNR = Do-Not-Resuscitate; ICU = intensive care unit; MEWS = Modified Early Warning Score; OR = odds ratio.
*p < .0001; **p < .001; ***p < .05.

Discussion

In this large cohort of OAs aged 65 and older hospitalized with COVID-19 during the first surge of the pandemic, over a third presented with atypical symptomatology, characterized by functional decline and altered mental status. We also found that those with atypical presentation were older, more likely to be female, Black, non-Hispanic, have a higher comorbidity index, have dementia, and/or have diabetes. There were no significant differences in hospital mortality, hospital LOS, or 30-day hospital readmission when comparing typical and atypical presentations; however, those who presented typically were 1.3 times more likely than those who presented atypically to receive ICU-level care.

Our findings that a substantial group of OAs with COVID-19 present atypically is consistent with the existing literature. In a smaller and older sample (73 hospitalized OAs, aged 80 and older) in New York State (8), atypical presentations included altered mental status (36%), generalized weakness (38%), and falls (14%). One hundred and eleven residents of long-term care facilities in the United States presented most commonly with loss of appetite (61.3%), lethargy (42.3%), and increased agitation (38.7%) (6). In a study (7) of 817 OA patients presenting to the emergency department in the United States with COVID-19, delirium was the sixth most common of all presenting symptoms (28% of the sample), and 16% had delirium as their primary symptom. Furthermore, 37% had no typical COVID-19 symptoms or signs.

This finding of an atypical presentation occurring in substantial numbers of OAs is supported by the global research community. Approximately half of OA patients in studies in France (9) (52.7%) and Spain (30) (50%) presented with deterioration in their physical condition. Studies from the United Kingdom (11,13) show 27.6%–36%, 36%, and 22%–41% of OAs presented with falls, reduced mobility or generalized weakness, and delirium, respectively. Atypical presentation characterized by confusion, difficulty walking, and falls was present in 29%, 13% and 8%, respectively, of 102 hospitalized COVID-19 patients aged 80 and older in Denmark (12). Additional studies (10,31–34) further corroborate these findings.

Our findings provide evidence for guidelines by a number of organizations (French Society of Geriatrics and Gerontology (9), British Geriatrics Society, European Delirium Association, Faculty of Old Age Psychiatry at the Royal College of Psychiatrists (35)): that screening OAs based on typical symptoms or signs of COVID (fever, cough, shortness of breath) alone is insufficient. Fever, considered

Table 3. Multivariable Logistic Regression. Patient Factors Associated With Hospital Mortality (vs Discharged Alive)

Patient Characteristics	OR (95% CI)
Typical symptom vs atypical symptom	1.19 (1.00, 1.43)
Age	0.97 (0.96, 0.98)*
Gender (male vs female)	1.44 (1.21, 1.72)*
Race	
Black vs White	1.23 (0.97, 1.56)
Asian vs White	1.79 (1.30, 2.45)**
Other vs White	1.25 (0.99, 1.57)
Unknown vs White	0.92 (0.56, 1.50)
Comorbidity Index	1.07 (1.04, 1.10)*
Admission from (facility vs home)	1.05 (0.84, 1.30)
MEWS (scores > 4, severely ill, vs scores 1–4)	5.42 (4.51, 6.51)*
First documented oxygen delivery	
Nasal cannula vs none	2.50 (1.95, 3.21)*
Nonrebreather vs none	4.63 (3.29, 6.51)*
Mechanical ventilation vs none	13.21 (8.17, 21.35)*
DNR	
No DNR at all vs late DNR	0.09 (0.07, 0.11)*
Early DNR vs late DNR	0.91 (0.65, 1.29)

Notes: CI = confidence interval; Comorbidity Index = Charlson Comorbidity Index (without age component); DNR = Do-Not-Resuscitate; MEWS = Modified Early Warning Score; OR = odds ratio.
*$p < .0001$; **$p < .001$.

Table 4. Multivariable Linear Regression. Patient Factors Associated With Hospital Length of Stay

Patient Characteristics	OR (95% CI)
Typical symptom vs atypical symptom	1.01 (0.93, 1.09)
Age	0.98 (0.97, 0.99)*
Gender (male vs female)	0.93 (0.86, 1.00)
Race	
Black vs White	0.99 (0.89, 1.10)
Asian vs White	1.11 (0.96, 1.28)
Other vs White	1.05 (0.95, 1.17)
Unknown vs White	0.80 (0.99, 1.22)
Comorbidity Index	1.01 (0.99, 1.02)
Admission from (facility vs home)	0.69 (0.62, 0.76)*
MEWS (scores > 4, severely ill, vs scores 1–4)	0.87 (0.95, 1.04)
First documented oxygen delivery	
Nasal cannula vs none	1.47 (1.33, 1.63)*
Nonrebreather vs none	1.65 (1.92, 2.23)*
Mechanical ventilation vs none	1.99 (1.62, 2.45)*
DNR	
No DNR at all vs late DNR	0.75 (0.68, 0.82)*
Early DNR vs late DNR	0.32 (0.27, 0.38)*

Notes: CI = confidence interval; Comorbidity Index = Charlson Comorbidity Index (without age component); DNR = Do-Not-Resuscitate; MEWS = Modified Early Warning Score; OR = odds ratio.
*$p < .0001$.

Table 5. Multivariable Logistic Regression. Patient Factors Associated With 30-d Readmission (Yes vs No)

Patient Characteristics	OR (95% CI)
Typical symptom vs atypical symptom	0.95 (0.67, 1.35)
Age	1.04 (1.01, 1.06)***
Gender (male vs female)	1.34 (0.94, 1.91)
Race	
Black vs White	0.92 (0.59, 1.45)
Asian vs White	0.83 (0.40, 1.69)
Other vs White	1.09 (0.69, 1.72)
Unknown vs White	1.24 (0.52, 2.95)
Comorbidity Index	1.09 (1.03, 1.15)***
Admission from (facility vs home)	1.48 (0.96, 2.29)
MEWS (scores > 4, severely ill, vs scores 1–4)	0.55 (0.36, 0.86)***
First-documented oxygen delivery	
Nasal cannula vs none	1.11 (0.72, 1.72)
Nonrebreather vs none	0.96 (0.46, 1.97)
Mechanical ventilation vs none	0.88 (0.30, 2.60)
DNR	
No DNR at all vs late DNR	3.91 (2.35, 6.49)*
Early DNR vs late DNR	0.69 (0.20, 2.35)

Notes: CI = confidence interval; Comorbidity Index = Charlson Comorbidity Index (without age component); DNR = Do-Not-Resuscitate; MEWS = Modified Early Warning Score; OR = odds ratio.
*$p < .0001$; ***$p < .05$.

to be part of the hallmark of COVID-19, occurred in, at most, only 37.7% of our sample; this is consistent with reports of blunted typical inflammatory febrile responses in many OAs, due to changes in thermoregulation and decline of innate immunity (36).

Our results show that atypical presentation becomes more common with increasing age, which is consistent with the existing literature. Data (9) comparing 70- to 80-year-old adults with those 80 and older indicate that the latter group more often reported falls and sudden deterioration of general condition, but less often reported fever, implicating an association between increasing age and atypical presentation. This finding was further supported by a study conducted in Spain (10) of adults aged 65 and older, demonstrating that symptoms typically associated with COVID-19 (fever, cough, difficulty breathing) decreased with increasing age. This was coupled with an increase in atypical symptoms (confusion, presyncope, syncope). Advancing age is more often associated with sensory or cognitive impairments, which affect the ability to perceive or accurately report symptoms, leading to vague and nonspecific presentation of acute illness. Those with baseline functional and cognitive impairments may be unable to accurately identify and communicate their symptoms, a problem exacerbated by the need for protective personal equipment such as masks (37).

The other demographic and clinical factors significantly associated with atypical presentation—female gender, Black race, non-Hispanic ethnicity, greater number of comorbidities, and presence of diabetes—have been largely unexplored in this context until now and therefore represent important additions to the literature. The finding that atypical presentation was more common in females fits with the literature on other illnesses, such as acute coronary syndrome, where more women report additional symptoms other than the classic symptoms/signs of chest pain (38). Hispanic OAs often experience barriers to accessing healthcare (39), which could have prevented them from coming to the hospital in the absence of severe symptoms of high fever or shortness of breath. Non-Hispanic OAs are less likely to encounter these barriers and more likely to access the healthcare system. Although Hispanics were less likely to have an atypical presentation, Black race was associated with an atypical presentation. Additional studies are needed to investigate these differences in presentation among disparity populations. Although the difference in the number of comorbidities between the

typical and atypical presentations was statistically significant, it may not be clinically significant (ie, unclear clinical difference between comorbidity index scores of 3.21 and 3.55). Still, for OAs with more comorbidities (including diabetes), given their fragility, they may be more vulnerable to infections which necessitates hospitalization.

We did not find a statistically significant difference between atypical versus typical presentations in residence prior to arriving at the hospital, indicating that, regardless of where patients are coming from (home or facility), there was no difference in presentation. This is consistent with findings from a study in the United Kingdom (11), in which researchers found only a trend toward significance, such that facility residents more often presented with solely atypical symptoms than OAs presenting from home, 18.8% versus 8.6%. Though the difference was not statistically significant in our study, this finding provides clinically meaningful information for emergency department staff, that patients who are more functional and independent coming from home may present atypically just as often as more dependent patients arriving to the hospital from a facility.

In the reported cohort, short-term hospital outcomes of hospital mortality, hospital LOS, and hospital readmission were similar between OAs presenting typically versus atypically. This adds another piece of evidence to the literature, which currently presents an inconsistent picture where most (6,12), but not all (13), studies show that atypical presentation is related to hospital mortality. On the other hand, patients with typical presentation were more likely than patients with atypical presentation to receive ICU-level care, probably because of the respiratory concerns associated with typical presentations.

Clinical Implications

Our findings have important and immediate clinical implications in nonhospital settings, where clinicians are often faced with the challenge of deciding which of their OA patients should be screened for COVID-19 based on symptoms and signs, and what may necessitate a higher level of care. In addition, as the second surge of the pandemic subsides, the strict protocols for COVID-19 testing of all patients who arrive at the emergency room may lapse, thereby leaving the responsibility of who to test resting on hospital staff. As the pandemic wanes, awareness of an atypical presentation may translate to earlier COVID diagnosis, which is critically important to preventing transmission of the disease among OAs, as well as broader hospital populations, health care workers, and family members. While increasing clinicians' awareness is important, so too is increasing lay awareness, so that OAs and their caregivers do not delay seeking treatment.

The findings regarding outcome are clinically meaningful, as they highlight the importance of an atypical presentation. Although we found that atypical presentation in OAs does not necessitate the same need for ICU-level care as typical presentation (often characterized by respiratory distress), it must not be dismissed, as those presenting atypically have just as poor short-term outcomes of hospital LOS, 30-day readmission, and hospital mortality as those OAs presenting typically. Given that the difference between the atypical and typical presentations on hospital mortality, in particular approached statistical significance (p = .0547), future studies addressing this topic are needed.

Novelty of Study Findings

To the best of our knowledge, our study evaluating typical versus atypical presentation in hospitalized OAs with COVID-19 is the first to (i) demonstrate a relationship between atypical presentation and female gender, Black race, non-Hispanic ethnicity, as well as greater number of comorbidities and the presence of dementia or diabetes; (ii) demonstrate that a statistically significant relationship does exist between atypical presentation and ICU-level care; and (iii) demonstrate that a statistically significant relationship does not exist between atypical presentation and hospital outcomes (eg, LOS and readmission). Furthermore, for research questions that have already been posed in the COVID-19 presentation literature (ie, relationship between presentation and age, residence prior to hospital arrival, etc.), our study findings add to this literature, particularly given that our findings are based on a unique data set and novel analysis plan. The data set is unique because it includes reliable clinical information from over 4 000 patients across the full spectrum of older adulthood (starting at age 65) and contains clinically rich variables that underwent a vigorous process of data harmonization. Our analysis plan is novel because we extracted qualitative presentation data from the EHR and analyzed it using an innovative NLP tool.

Limitations

This study has several limitations. First, as is the case in other studies (11), it was limited to the data elements available in the EHR. This resulted in the inability to distinguish between OAs arriving from a facility for long-term care versus subacute rehabilitation versus assisted living. Key differences may exist between those coming from different types of facilities. Second, it is unclear whether presentations that are neither typical nor atypical (ie, genitourinary, cardiovascular) are indicative of COVID-19 in OAs or whether these symptoms and signs brought the patients to the hospital, but they were unrelated to an asymptomatic COVID-19 infection, which was found incidentally. Third, our data only report on patients who were admitted during the beginning or height of the first surge of the pandemic. As such, these data may not be generalizable to OAs diagnosed or treated during subsequent surges of COVID-19, as there have been many improvements in management for these patients over the course of the pandemic (ie, changes in standard of care, improvements in equipment availability, etc.). These limitations aside, our findings substantially add to the literature on presentation in COVID-19 among OAs.

Future research in this area should focus on the duration of atypical versus typical presentations and differences in long-term outcomes, including recovery of functional abilities, between atypical and typical presentations. Long-term follow-up of OAs who survive hospitalization for COVID-19 will elucidate long-term outcomes associated with various disease presentations.

Conclusions

Atypical presentation of COVID-19, characterized by functional decline and altered mental status, was present in more than a third of this large cohort of hospitalized OAs aged 65 and older. Atypical presentation was significantly more common among older patients, females, Blacks, non-Hispanics, those having a higher comorbidity index, and those with the presence of dementia and diabetes. Hospital outcomes of hospital mortality, hospital LOS, and readmission were similar for atypical and typical presentations, but those who presented typically were 1.39 times more likely to receive ICU-level care than those who presented atypically. Future work should

further explore the different subtypes of atypical presentation, atypical COVID presentation in females, and in particular the long-term outcomes of OAs with atypical presentation.

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Conflict of Interest

None declared.

Author Contributions

A.M. contributed to study design, assisted with data management, statistical analysis, and interpretation, and led the manuscript writing. She had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. E.B. contributed to study design, clinical expertise, and statistical interpretation and reviewed and provided feedback on the manuscript. L.C. contributed to study design and coding of qualitative data and provided feedback on the manuscript. Y.L. assisted with preparation of data for analysis and provided feedback on the manuscript. Ale.M. contributed to study design, clinical expertise, statistical interpretation, and reviewed and provided feedback on the manuscript. M.Z. contributed to statistical analysis and interpretation and reviewed and provided feedback on the manuscript. M.C. contributed to study design and clinical expertise and reviewed and provided feedback on the manuscript. Y.D. contributed natural language processing tool expertise and reviewed and provided feedback on the manuscript. C.L. contributed natural language processing tool expertise and reviewed and provided feedback on the manuscript. M.Q. assisted with preparation of data for analysis and provided feedback on the manuscript. M.D. contributed to study design, and provided feedback on the manuscript. L.S. contributed to study design, assisted with data management and statistical interpretation, and facilitated the manuscript writing.

References

1. Centers for Disease Control and Prevention. Demographic Trends of COVID-19 Cases and Deaths in the US Reported to CDC. 2020. https://covid.cdc.gov/covid-data-tracker/#demographics. Accessed December 31, 2020.
2. Isaia G, Marinello R, Tibaldi V, Tamone C, Bo M. Atypical presentation of Covid-19 in an older adult with severe Alzheimer disease. *Am J Geriatr Psychiatry*. 2020;28:790–791. doi:10.1016/j.jagp.2020.04.018
3. Norman RE, Stall NM, Sinha SK. Typically atypical: COVID-19 presenting as a fall in an older adult. *J Am Geriatr Soc*. 2020;68:E36–E37. doi:10.1111/jgs.16526
4. Soysal P, Kara O. Delirium as the first clinical presentation of the coronavirus disease 2019 in an older adult. *Psychogeriatrics*. 2020;20:763–765. doi:10.1111/psyg.12587
5. Tee LY, Yap B, Sidhu GK, Goh KS, Rosario BH. Atypical presentation of COVID-19 in an older adult: lethargy and vomiting from severe hypovolemic hyponatremia. *Geriatr Gerontol Int*. 2020;20:839–840. doi:10.1111/ggi.13990
6. Atalla E, Zhang R, Shehadeh F, et al. Clinical presentation, course, and risk factors associated with mortality in a severe outbreak of COVID-19 in Rhode Island, USA, April–June 2020. *Pathogens (Basel, Switzerland)*. 2020;10:1–10. doi:10.3390/pathogens10010008
7. Kennedy M, Helfand BKI, Gou RY, et al. Delirium in older patients with COVID-19 presenting to the emergency department. *JAMA Netw Open*. 2020;3:e2029540–e2029540. doi:10.1001/jamanetworkopen.2020.29540
8. Nabors C, Sridhar A, Hooda U, et al. Characteristics and outcomes of patients 80 years and older hospitalized with coronavirus disease 2019 (COVID-19). *Cardiol Rev*. 2021;29:39–42. doi:10.1097/crd.0000000000000368
9. Annweiler C, Sacco G, Salles N, et al. National French survey of COVID-19 symptoms in people aged 70 and over. *Clin Infect Dis*. 2021;72:490–494. doi:10.1093/cid/ciaa792
10. Martín-Sánchez FJ, Del Toro E, Cardassay E, et al. Clinical presentation and outcome across age categories among patients with COVID-19 admitted to a Spanish emergency department. *Eur Geriatr Med*. 2020;11:829–841. doi:10.1007/s41999-020-00359-2
11. Rawle MJ, Bertfield DL, Brill SE. Atypical presentations of COVID-19 in care home residents presenting to secondary care: a UK single centre study. *Aging Med (Milton (NSW))*. 2020;3:237–244. doi:10.1002/agm2.12126
12. Karlsson LK, Jakobsen LH, Hollensberg L, et al. Clinical presentation and mortality in hospitalized patients aged 80+ years with COVID-19 – a retrospective cohort study. *Arch Gerontol Geriatr*. 2021;94:104335. doi:10.1016/j.archger.2020.104335
13. Gan JM, Kho J, Akhunbay-Fudge M, et al. Atypical presentation of COVID-19 in hospitalised older adults. *Irish J Med Sci*. 2020:1–6. doi:10.1007/s11845-020-02372-7 [Epub ahead of print]. PMID: 32959219 PMCID: PMC7505490.
14. Lithander FE, Neumann S, Tenison E, et al. COVID-19 in older people: a rapid clinical review. *Age Ageing*. 2020;49:501–515. doi:10.1093/ageing/afaa093
15. New York State Department of Health. *Daily Hospitalization Summary by Region*. 2021. https://forward.ny.gov/daily-hospitalization-summary-region. Cited May 18, 2021.
16. Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care*. 2005;43:1130–1139. doi:10.1097/01.mlr.0000182534.19832.83
17. Patel K, Sinvani L, Patel V, et al. Do-not-resuscitate orders in older adults during hospitalization: a propensity score-matched analysis. *J Am Geriatr Soc*. 2018;66:924–929. doi:10.1111/jgs.15347
18. Agaronnik N, Lindvall C, El-Jawahri A, He W, Iezzoni L. Use of natural language processing to assess frequency of functional status documentation for patients newly diagnosed with colorectal cancer. *JAMA Oncol*. 2020;6:1628–1630. doi:10.1001/jamaoncol.2020.2708
19. Lindvall C, Lilley EJ, Zupanc SN, et al. Natural language processing to assess end-of-life quality indicators in cancer patients receiving palliative surgery. *J Palliat Med*. 2019;22:183–187. doi:10.1089/jpm.2018.0326
20. Udelsman B, Chien I, Ouchi K, Brizzi K, Tulsky JA, Lindvall C. Needle in a haystack: natural language processing to identify serious illness. *J Palliat Med*. 2019;22:179–182. doi:10.1089/jpm.2018.0294
21. Rangel-Frausto MS, Pittet D, Costigan M, Hwang T, Davis CS, Wenzel RP. The natural history of the systemic inflammatory response syndrome (SIRS). A prospective study. *JAMA*. 1995;273:117–123.
22. Kang SJ, Jung SI. Age-related morbidity and mortality among patients with COVID-19. *Inf Chemother*. 2020;52:154–164. doi:10.3947/ic.2020.52.2.154
23. Li X, Xu S, Yu M, et al. Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan. *J Allergy Clin Immunol*. 2020;146:110–118. doi:10.1016/j.jaci.2020.04.006
24. Sapienza LG, Nasra K, Calsavara VF, Little TB, Narayana V, Abu-Isa E. Risk of in-hospital death associated with Covid-19 lung consolidations on chest computed tomography – a novel translational approach using a radiation oncology contour software. *Eur J Radiol Open*. 2021;8:100322. doi:10.1016/j.ejro.2021.100322
25. Jin JM, Bai P, He W, et al. Gender differences in patients with COVID-19: focus on severity and mortality. *Front Public Health*. 2020;8:152. doi:10.3389/fpubh.2020.00152
26. Golestaneh L, Neugarten J, Fisher M, et al. The association of race and COVID-19 mortality. *EClinicalMedicine*. 2020;25:100455. doi:10.1016/j.eclinm.2020.100455

27. Andrade JA, Muzykovsky K, Truong J. Risk factors for mortality in COVID-19 patients in a community teaching hospital. *J Med Virol*. 2021;23:3184–3193. doi:10.1002/jmv.26885
28. Wang L, Lv Q, Zhang X, et al. The utility of MEWS for predicting the mortality in the elderly adults with COVID-19: a retrospective cohort study with comparison to other predictive clinical scores. *PeerJ*. 2020;8:e10018. doi:10.7717/peerj.10018
29. Grasselli G, Greco M, Zanella A, et al. Risk factors associated with mortality among patients with COVID-19 in intensive care units in Lombardy, Italy. *JAMA Intern Med*. 2020;180:1345–1355. doi:10.1001/jamainternmed.2020.3539
30. Gutiérrez Rodríguez J, Montero Muñoz J, Jiménez Muela F, et al. Variables associated with mortality in a selected sample of patients older than 80 years and with some degree of functional dependence hospitalized for COVID-19 in a geriatrics service. *Rev Esp Geriatr Gerontol*. 2020;55:317–325. doi:10.1016/j.regg.2020.07.002
31. D'Adamo H, Yoshikawa T, Ouslander JG. Coronavirus disease 2019 in geriatrics and long-term care: the ABCDs of COVID-19. *J Am Geriatr Soc*. 2020;68:912–917. doi:10.1111/jgs.16445
32. Davis P, Gibson, R., Wright, E., et al. Atypical presentations in the hospitalised older adult testing positive for SARS-CoV-2: a retrospective observational study in Glasgow, Scotland. *Scott Med J*. 2020;0:1–9. doi:10.1177/0036933020962891
33. Li T, Lu L, Zhang W, et al. Clinical characteristics of 312 hospitalized older patients with COVID-19 in Wuhan, China. *Arch Gerontol Geriatr*. 2020;91:104185. doi:10.1016/j.archger.2020.104185
34. Livingston G, Rostamipour H, Gallagher P, et al. Prevalence, management, and outcomes of SARS-CoV-2 infections in older people and those with dementia in mental health wards in London, UK: a retrospective observational study. *Lancet Psychiatry*. 2020;7:1054–1063. doi:10.1016/S2215-0366(20)30434-X
35. British Geriatrics Society, EDA, Old Age Psychiatry Faculty. Coronavirus: Managing Delirium in Confirmed and Suspected Cases 2020. https://www.bgs.org.uk/resources/coronavirus-managing-delirium-in-confirmed-and-suspected-cases. Accessed February 27, 2021.
36. Shaw AC, Goldstein DR, Montgomery RR. Age-dependent dysregulation of innate immunity. *Nat Rev Immunol*. 2013;13:875–887. doi:10.1038/nri3547
37. Knollman-Porter K, Burshnic VL. Optimizing effective communication while wearing a mask during the COVID-19 pandemic. *J Gerontol Nurs*. 2020;46:7–11. doi:10.3928/00989134-20201012-02
38. Haider A, Bengs S, Luu J, et al. Sex and gender in cardiovascular medicine: presentation and outcomes of acute coronary syndrome. *Eur Heart J*. 2020;41:1328–1336. doi:10.1093/eurheartj/ehz898
39. Escarce J, Kapur, K. *Hispanics and the Future of America: Access to and Quality of Health Care*. Washington, DC: National Academies Press; 2006.