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CLINICAL INVESTIGATIONS

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Factors associated with hospital admission and severe outcomes for older patients with COVID-19

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Abstract

Background: Morbidity and death due to coronavirus disease 2019 (COVID-19) experienced by older adults in nursing homes have been well described, but COVID-19's impact on community-living older adults is less studied. Similarly, the previous ambulatory care experience of such patients has rarely been considered in studies of COVID-19 risks and outcomes.

Methods: To investigate the relationship of advanced age (65+), on risk factors associated with COVID-19 outcomes in community-living elders, we identified an electronic health records cohort of older patients aged 65+ with laboratory-confirmed COVID-19 with and without an ambulatory care visit in the past 24 months ($n = 47{,}219$) in the New York City (NYC) academic medical institutions and the NYC public hospital system from January 2020 to February 2021. The main outcomes are COVID-19 hospitalization; severe outcomes/Intensive care unit (ICU), intubation, dialysis, stroke, in-hospital death), and in-hospital death. The exposures include demographic characteristics, and those with ambulatory records, comorbidities, frailty, and laboratory results.

Results: The 31,770 patients with an ambulatory history had a median age of 74 years; were 47.4% male, 24.3% non-Hispanic white, 23.3% non-Hispanic black, and 18.4% Hispanic. With increasing age, the odds ratios and attributable fractions of sex, race–ethnicity, comorbidities, and biomarkers decreased except for dementia and frailty (Hospital Frailty Risk Score). Patients without ambulatory care histories, compared to those with, had significantly higher adjusted rates of COVID-19 hospitalization and severe outcomes, with strongest effect in the oldest group.

Conclusions: In this cohort of community-dwelling older adults, we provided evidence of age-specific risk factors for COVID-19 hospitalization and severe outcomes. Future research should explore the impact of frailty and dementia in severe COVID-19 outcomes in community-living older adults, and the role of engagement in ambulatory care in mitigating severe disease.

KEYWORDS

age-specific risk factors, ambulatory care, community-living older adults, COVID-19

INTRODUCTION

As of September 2021, more than 234 million infections and over 4 million deaths from coronavirus disease 2019 (COVID-19) have been documented globally.[1] New York City (NYC) was an early epicenter with approximately 203,000 confirmed cases reported during the first 3 months of the pandemic.[2] Studies from China, Europe, and the United States have described characteristics of COVID-19 confirmed cases, and identified risk factors for severe outcomes. Consistently identified risk factors are older age, male sex, and diagnoses of hypertension, cardiovascular disease, and diabetes.[3–9]

Multiple studies demonstrate that age is one of the strongest risk factors for severe illness; the mortality of COVID-19 in older adults has been striking.[10] The Centers for Disease Control and Prevention reported that although individuals older than age 65 comprise 17% of the total population of the United States, they account for 31% of COVID-19 infections, 45% of hospitalizations, 53% of intensive care unit admissions, and 80% of deaths.[11] Similarly, studies from Europe and China have identified risk factors for mortality in patients aged 65 years or older, including increasing age, male sex, chronic kidney disease (CKD), stroke history, respiratory symptoms, poor functional status, frailty, lymphocytopenia, and increased D-dimer.[12–16] In the United States, research on the impact of COVID-19 in older adults has often focused on nursing home residents and found that age, male sex, impaired cognitive and physical function were independently associated with mortality.[17,18]

In general, studies of COVID-19 risks and outcomes begin with a hospitalized or nursing home cohort and do not focus on community-living older adults, or access information about their previous ambulatory care experience. To address this need, we leveraged electronic health record (EHR) data from the exceptionally large and racially–ethnically diverse NYC patient population, including ambulatory care data previous to COVID-19 diagnosis, to evaluate how key prognostic factors, including increasing age, comorbidities, and laboratory histories, are associated with COVID-19 outcomes.

Key points

- For patients aged 85+, the five risk factors with the highest attributable fractions of COVID-19 severe outcomes were frailty, chronic kidney disease, male sex heart failure, and dementia.
- Only dementia increased in importance for COVID-19 outcomes with increasing age, while most comorbidities and biomarkers showed decreased effect with age.
- Patients of COVID-19, especially older patients, without ambulatory care histories had significantly higher rates of hospitalization and severe outcomes.

Why does this paper matter?

This study of 47,219 COVID-19 positive, community-living older adults in New York City suggests that risk factors for COVID-19 outcomes change with increasing age.

METHODS

Setting and study cohort

We identified all patients aged 65 or older tested for Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) between March 1, 2020, and February 15, 2021, in the INSIGHT Network of NYC's major academic medical institutions, and in the public NYC Health + Hospitals (H+H) system. The INSIGHT network includes all inpatient and outpatient administrative and clinical data, using a common standard, from the five major academic medical institutions: NY-Presbyterian/Columbia University Irving Medical Center, NY-Presbyterian/Weill Cornell Medical Center, the Mount Sinai Health System, Montefiore Medical Center, and NYC Langone Health.[19] NYC H+H is the largest public healthcare system in the United States and provides essential inpatient, outpatient, and home-based services to more than 1 million patients each year at more than 70 locations across the city's five boroughs. In March 2019, all H+H patient care sites finished transitioning to a unified Epic EHR system.

Confirmed COVID-19 was defined as a positive lab result of nasopharyngeal or oropharyngeal swab specimens, queried by a series of SARS-CoV-2 testing codes. We categorized the eligible patients into two cohort: the ambulatory care cohort of patients with at least one ambulatory visit in the 24 months preceding a COVID-19 diagnosis in their EHRs in INSIGHT or H+H, and the no-ambulatory care cohort of patients with no prior ambulatory EHR records. Within INSIGHT or H+H, patient records could be identified if the ambulatory care was in the same or in a different healthcare system than the hospitalization.

Main outcomes

We assessed three primary outcomes: inpatient hospital admission; severe outcome, defined as a composite of

care in the intensive care unit, use of mechanical ventilation, dialysis, stroke, or in-hospital death; and in-hospital death. Dialysis and stroke are both restricted to patients who did not have dialysis or stroke before their COVID-19 diagnosis. To increase confidence that the outcomes are COVID-19 related, we defined inpatient hospital admissions within 30 days of COVID-19 diagnosis, and the severe outcome or in-hospital death outcomes within 30 days of diagnosis or 14 days post discharge.

Variables

We obtained variables from the EHRs, including age at time of COVID-19 testing, sex, race–ethnicity reported by the patient (non-Hispanic white [NHW], non-Hispanic black [NHB], Asian, Hispanic, other–multiracial, and unknown). Age was categorized into three groups: 65–74, 75–84, and 85+. For the ambulatory care cohort, we obtained variables from patients' ambulatory care histories of vitals, chronic diseases, and lab tests. Vitals include blood pressure and body mass index (BMI) (defined by average of patients' BMI in the 24-month medical history, categorized as <18, 18–29.9, 30–39.9, and 40+). Chronic disease was defined as history of hypertension, heart failure, myocardial infarction (MI), CKD, lung disease (defined by chronic obstructive pulmonary disease or asthma), diabetes, dementia, and cancer. Laboratory tests included albumin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), calcium, hemoglobin, lymphocyte, total protein, bilirubin, chloride, hemoglobin A1c, and white blood cell count (WBC). Average results over the past 24 months were used. We defined the Hospital Frailty Risk Score (HFRS) based on multiple co-occurring International Classification of Diseases (ICD)-10 codes from patients' diagnosis history and classified patients as low, intermediate, and high frailty as developed by Gilbert et al.[20]

Statistical methodology

We used descriptive statistics to characterize patients by age groups. We used mixed-effects multivariable logistic regressions to estimate the adjusted odds ratios (aORs) of each risk factor for each age group in the ambulatory care cohort. For the age interaction of each risk factor of interest, a separate model was run. These models included as explanatory variables, the indicator variables of age groups, the interaction of the age group and the risk factor of interest, and the remaining covariates, including demographic characteristics (age, sex, race–ethnicity, and BMI), month of diagnosis, comorbidities (diabetes, hypertension, heart failure, MI, CKD, lung disease, and dementia), frequencies of ambulatory visits in the past 2 years, hospital system (H+H or INSIGHT), and hospitals (as random effects). HFRS was included in separate models from comorbidities to avoid double counting. The aORs of the risk factor for each group and its 95% confidence intervals were estimated. The p-values of the interaction terms tested the hypothesis of whether the risk factor has age-specific associations with the outcome. Only race–ethnicity and BMI had missing data, which were coded as "unknown" and included in the models. No missing data were imputed. Biomarker models have different sample sizes because each biomarker was measured on a different subset of patients. We also estimated the adjusted attributable fraction (AF, %) for each covariate.[21] AF quantifies the impact of an exposure on an outcome, which takes account of both the aORs and the prevalence of the risk factor.[21] When assessing the association between ambulatory care history and COVID-19 outcomes, we combined the ambulatory care cohort and the no-ambulatory care cohort. The aORs of the ambulatory care history (no vs. yes) were estimated by adjusting patients' age, sex, race–ethnicity, month of diagnosis, hospital system, and hospitals (as random effects). All statistical analyses were conducted with R version 3.6.3. All analyses used two-sided statistical tests and a p-value less than 0.05 was statistically significant.

RESULTS

Ambulatory care cohort characteristics by age groups

During the study period, we identified 47,219 COVID-19-positive patients age 65 or older (22,388 in INSIGHT, 24,831 in H+H). Among these patients, the ambulatory care cohort contained 31,770 (67.3%) COVID-19 positive older patients (median age 73.5 years; 47.4% men). Figure 1 shows the cohort selection process and outcome prevalence. Table 1 summarizes the characteristics of the ambulatory care cohort by age groups. There were 17,890 (56%), 9500 (30%), and 4380 (14%) in the 65–74, 75–84, and 85+ age groups, respectively. The entire cohort was racially diverse; 24.3% NHW, 23.3% NHB, 18.4% Hispanics, and 5.4% Asian. COVID-19 patients in the older age group were more likely to be female and NHW, had lower BMI, and were more likely to have comorbidities. Table S1 provides the lab results in the past 24 months for the ambulatory care cohort by age groups. Patients in the 75–84 and 85+ age groups had lower albumin, ALT, calcium, hemoglobin, lymphocyte, and total protein; and higher AST, bilirubin, chloride, hemoglobin A1c, and WBC 24 months prior to

their COVID-19 diagnosis. In the ambulatory care cohort, 12,225 (38.5%) patients were hospitalized within 30 days post COVID-19 diagnosis, 6500 (20.5) patients experienced severe outcomes, and 4706 (14.8%) died. Patients in the older age group were more likely to be admitted and have severe outcomes. Of the patients aged 85+, 51.5% were hospitalized, 34.3% experienced severe outcomes, and 29.9% died in hospitals.

Risk factors for hospitalization by age group

Figure 2A presents the aORs of demographic and comorbidity risk factors for hospitalization by age group. Male sex, minority race–ethnicity, underweight (BMI < 18), histories of diabetes, hypertension, heart failure, MI, CKD, lung disease, dementia, and HFRS are all significantly associated with higher risks of admission in the age group 50–64. However, most risk factors, while still significant, showed decreasing associations with advancing age, including male sex, NHB, diabetes, hypertension, CKD, lung disease, and HFRS (all interaction *p*-values <0.05). The impact of racial–ethnic minority was stronger in the younger age group, except for Asian. In contrast to the patients aged 65–74, NHB, Hispanic, and other race group patients aged 75+ had insignificant aORs compared to NHW patients. Asian patients had consistently higher adjusted admission prevalence in all age groups. Underweight, overweight, or extreme obesity is insignificantly associated with admission in the 75–84 and 85+ age groups, compared to the reference group of BMI (18–29.9). Figure 2B presents the aORs of hospitalization for biomarkers measured from ambulatory histories by age group. Lower albumin, calcium, chloride, total protein, lymphocyte, and higher ALT, AST, bilirubin, ferritin, A1c, and WBC were all significantly associated with higher risks of admission in the age group 65–74. Almost all biomarkers showed decreasing associations as age increased. For the patients aged 85+, no biomarker remained significantly associated with hospitalization. The adjusted associations of the risk factors (demographics, comorbidities, biomarkers) by age groups for severe outcomes and in-hospital death were consistent with those for admission (Figures S1 and S2**)**.

AF of risks for COVID-19 outcomes by age group

Figure 3 gives the AF for comorbidity exposure for COVID-19 hospitalization by age groups. For patients aged 65–74, HFRS (24% and 18% for intermediate and high HFRS, respectively), hypertension (24%), CKD (17%), male sex (6%), and lung disease (6%) had the highest AFs for hospitalization. As age group increased, the AFs of most comorbidities decreased, while the AFs of heart failure, dementia, and high HFRS increased. For

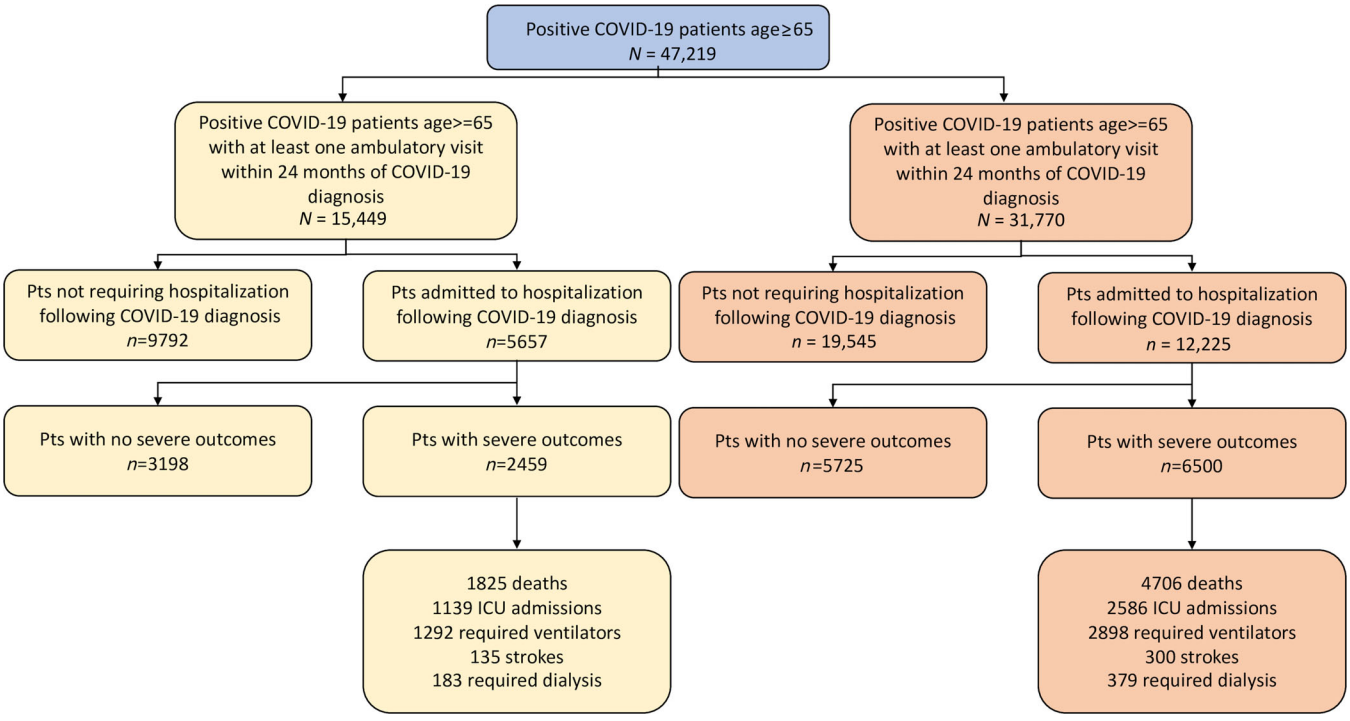

FIGURE 1 Study flow chart and outcomes for NYC COVID-19 patients aged 65+

TABLE 1 Baseline characteristics and outcomes of NYC COVID-19 ambulatory care cohort, by age groups

Age groups	Overall	65–74	75–84	85+	*p*
N	31,770	17,890	9500	4380	
Demographics					
Age (median [IQR])	73.5 [68.8, 80.6]	69.33 [67.0, 71.9]	79.34 [77.1, 81.9]	89.11 [86.8, 92.1]	<0.001
Male (%)	15,073 (47.4)	8834 (49.4)	4443 (46.8)	1796 (41.0)	<0.001
Race–ethnicity (%)					<0.001
NHW	7724 (24.3)	3683 (20.6)	2427 (25.5)	1614 (36.8)	
Asian	1728 (5.4)	1001 (5.6)	477 (5.0)	250 (5.7)	
Hispanic	5854 (18.4)	3151 (17.6)	1904 (20.0)	799 (18.2)	
NHB	7404 (23.3)	4342 (24.3)	2224 (23.4)	838 (19.1)	
Other	6431 (20.2)	4085 (22.8)	1757 (18.5)	589 (13.4)	
Unknown	2629 (8.3)	1628 (9.1)	711 (7.5)	290 (6.6)	
BMI (median [IQR])	27.4 [24.1, 31.3]	28.2 [25.0, 32.2]	27.0 [24.0, 31.0]	25.5 [22.1, 29.0]	<0.001
BMI categories (%)					<0.001
18–29.9	14,234 (44.8)	7307 (40.8)	4580 (48.2)	2347 (53.6)	
<18	393 (1.2)	115 (0.6)	144 (1.5)	134 (3.1)	
30–39.9	6399 (20.1)	4013 (22.4)	1798 (18.9)	588 (13.4)	
40+	953 (3.0)	670 (3.7)	241 (2.5)	42 (1.0)	
Unknown	9791 (30.8)	5785 (32.3)	2737 (28.8)	1269 (29.0)	
Comorbidities					
Diabetes (%)	13,522 (42.6)	7664 (42.8)	4264 (44.9)	1594 (36.4)	<0.001
Heart failure (%)	9244 (29.1)	4201 (23.5)	3207 (33.8)	1836 (41.9)	<0.001
Hypertension (%)	21,668 (68.2)	11,597 (64.8)	6912 (72.8)	3159 (72.1)	<0.001
CKD (%)	11,693 (36.8)	5684 (31.8)	3998 (42.1)	2011 (45.9)	<0.001
Lung disease (%)	7169 (22.6)	3766 (21.1)	2374 (25.0)	1029 (23.5)	<0.001
MI (%)	3200 (10.1)	1544 (8.6)	1045 (11.0)	611 (13.9)	<0.001
Dementia (%)	6247 (19.7)	2444 (13.7)	2176 (22.9)	1627 (37.1)	<0.001
Cancer (%)	4519 (14.2)	2563 (14.3)	1469 (15.5)	487 (11.1)	<0.001
HFRS (median [IQR])	5.10 [0.9, 12.3]	3.50 [0.0, 9.7]	6.80 [1.7, 14.1]	9.70 [3.3, 17.8]	<0.001
HFRScat (%)					<0.001
Low	15,165 (49.5)	9964 (57.4)	3861 (42.3)	1340 (32.4)	
Intermediate	9632 (31.4)	5040 (29.0)	3167 (34.7)	1425 (34.4)	
High	5839 (19.1)	2358 (13.6)	2104 (23.0)	1377 (33.2)	
No of Amb visits (per year, median [IQR])	8.1 [2.7, 19.6]	8.0[2.5, 19.1]	8.4 [2.8, 20.2]	7.8 [2.8, 20.7]	0.007
Outcomes (*n* and % of age group)					
Hospitalization (%)	12,225 (38.5)	5851 (32.7)	4117 (43.3)	2257 (51.5)	<0.001
Ventilator (%)	2898 (9.1)	1532 (8.6)	970 (10.2)	396 (9.0)	<0.001
ICU (%)	2586 (8.1)	1395 (7.8)	861 (9.1)	330 (7.5)	<0.001
Dialysis (%)	379 (1.2)	238 (1.3)	124 (1.3)	17 (0.4)	<0.001
Stroke (%)	300 (0.9)	134 (0.7)	110 (1.2)	56 (1.3)	<0.001
Severe[a] (%)	6500 (20.5)	2703 (15.1)	2293 (24.1)	1504 (34.3)	<0.001
Death (%)	4706 (14.8)	1668 (9.3)	1729 (18.2)	1309 (29.9)	<0.001
Days of hospital stay (median [IQR])	5.0 [2.0, 11.0]	4.0 [1.0, 11.0]	6.0 [2.0, 12.0]	6.0 [3.0, 12.0]	<0.001
Days from COVID dx to death (median [IQR])	8.0 [4.0, 15.0]	10.0 [5.0, 20.0]	8.0 [4.0, 14.0]	6.0 [3.0, 11.0]	<0.001

Abbreviations: ALT, alanine aminotransferase; AMB, ambulatory; AST, aspartate aminotransferase; CKD, chronic kidney disease; dx, diagnosis; HFRS, Hospital Frailty Risk Score; MI, myocardial infarction; NHB, non-Hispanic black; NHW, non-Hispanic white.

[a]Severe outcome is defined as a composite of care in the intensive care unit, use of mechanical ventilation, dialysis, stroke, or in-hospital death.

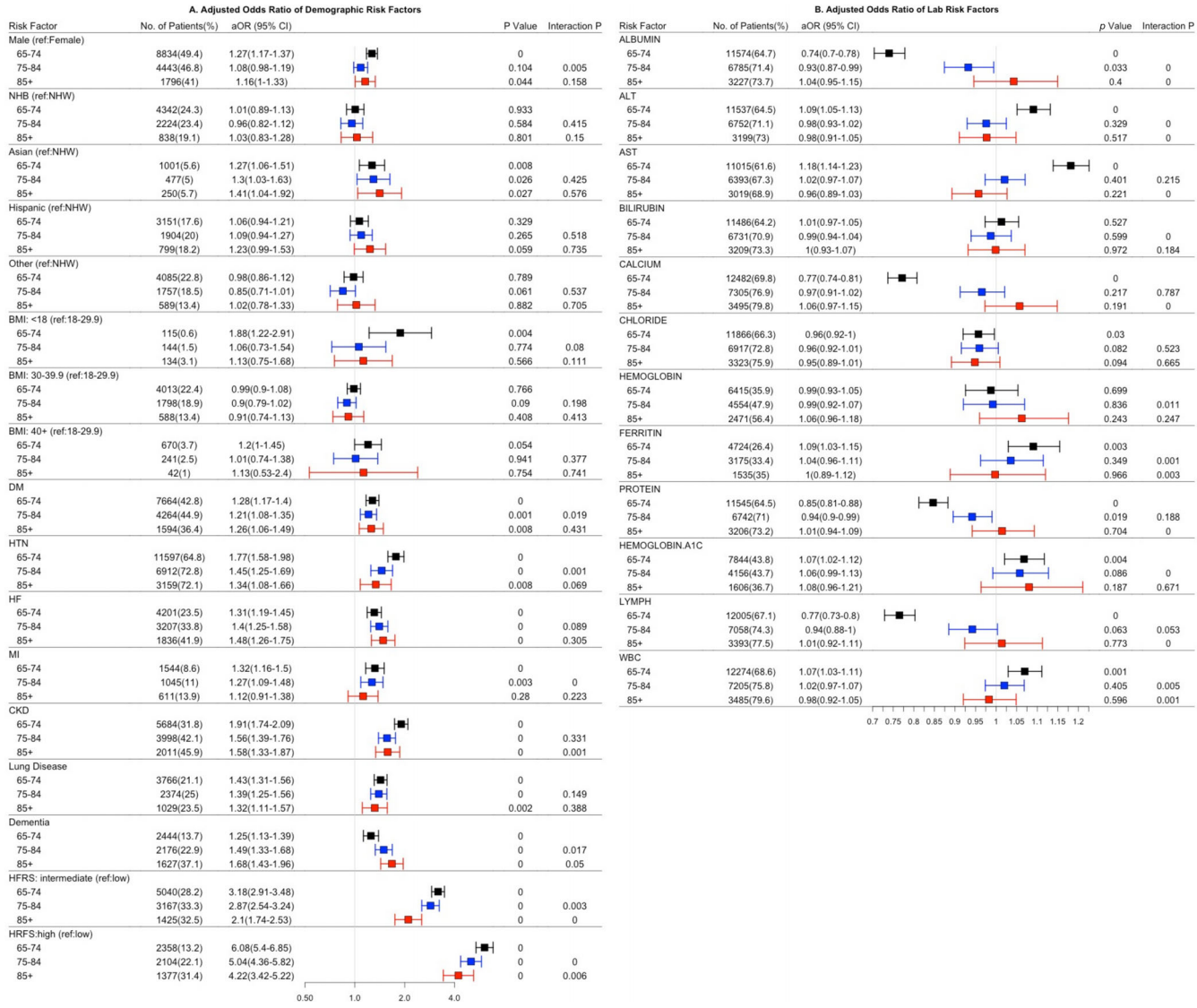

FIGURE 2 Adjusted odds ratios of demographic and comorbidity risk factors (A), and biomarkers (B) of COVID-19 hospital admission by age groups (ambulatory cohort). Adjustment factors include age group, interaction term with age group, sex, race–ethnicity, BMI, diabetes, hypertension, heart failure, MI, CKD, lung disease dementia, ambulatory visit frequency, and month of diagnosis and system (INSIGHT vs. H+H). Individual hospital indicators were included as random effects on the intercept level for all models. N(%) for demographic risk factors (A) is presented as the number of patients in the corresponding level (percent of the total number of patients in the ambulatory cohort). N(%) for the continuous lab test (B) is presented as the number of patients with nonmissing lab measurements (percent of the total number of patients in the ambulatory cohort). The p-value column presents the p-values testing the corresponding aOR to the null hypothesis (aOR = 1). The interaction p-value column presents the *p*-value comparing the corresponding aOR to the aOR of the reference age group 65–74 (the interaction term). ALT, alanine aminotransferase; AST, aspartate aminotransferase; CKD, chronic kidney disease; DM, diabetes; HFRS, Hospital Frailty Risk Score; HTN, hypertension; LYMPH, lymphocyte; MI, myocardial infarction; NHB, non-Hispanic black; NHW, non-Hispanic white; WBC, white blood cell

patients aged 75–84, HFRS (22% and 22% for intermediate and high scores), hypertension (16%), CKD (13%), heart failure (7%), and dementia (6%) had the highest AFs. For patients aged 85+, HFRS (15% and 26% for intermediate and high scores), hypertension (12%), CKD (11%), dementia (10%), and heart failure (7%) had the highest AFs. For severe outcomes and in-hospital mortality, the patterns were similar. Dementia was the only risk factor for all outcomes with increasing AF with increasing age groups (Figures S3 and S4**)**.

Variation in COVID-19 outcomes by ambulatory care histories

Among the 47,219 patients, 15,449 (32.7%) had no-ambulatory care records in the 24 months prior to COVID-19 diagnosis (no-ambulatory care cohort, Table S2). There are 9137 (59%), 4286 (28%), and 2026 (13%) in the 65–74, 75–84, and 85+ age groups, respectively, in the no-ambulatory cohort. Fewer older patients had no-ambulatory history (34%, 31%, and 31% for age

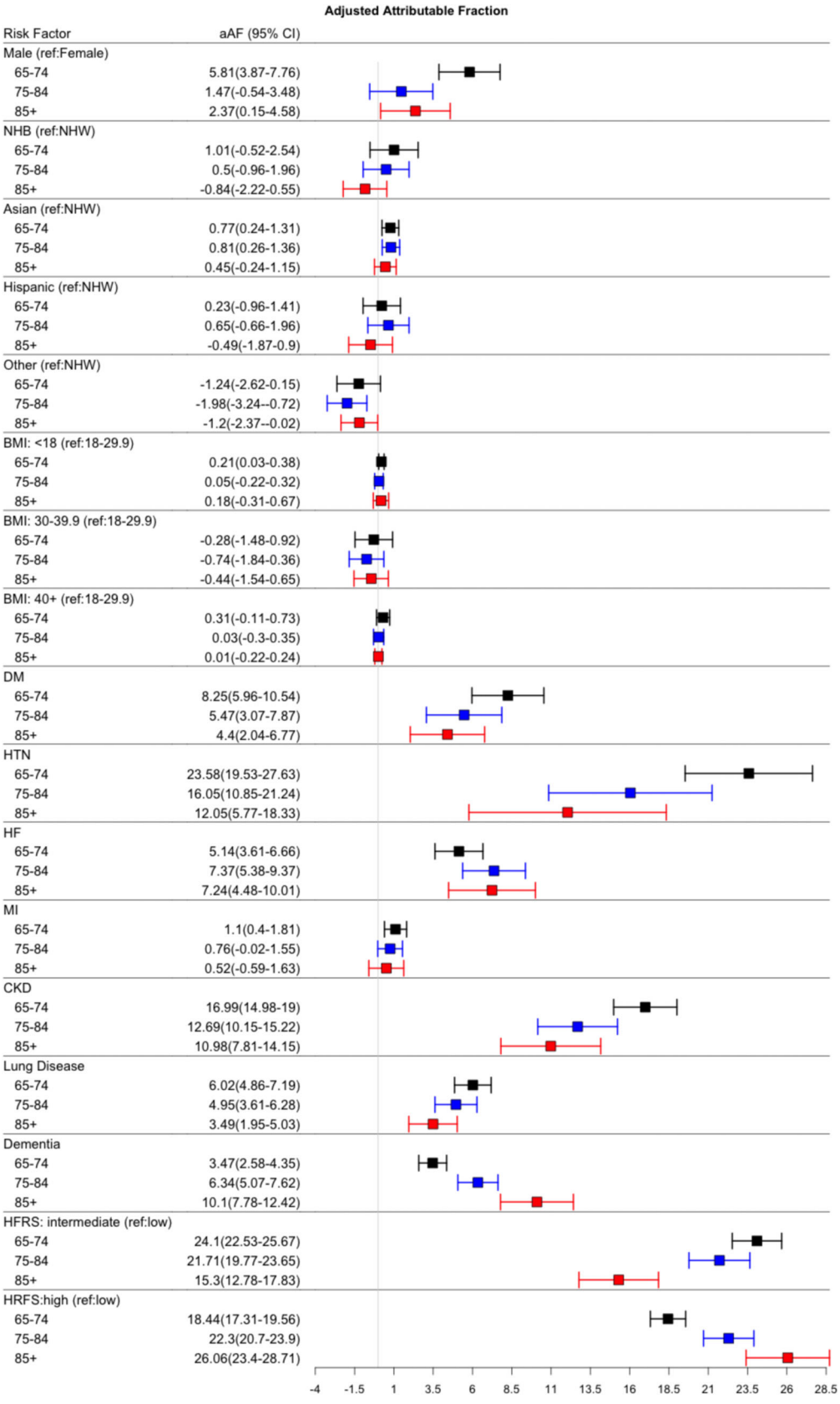

FIGURE 3 Adjusted attributable fraction of demographic and comorbidity risk factors of COVID-19 hospital admission by age groups (ambulatory cohort). Adjustment factors include age group, interaction term with age group, sex, race–ethnicity, BMI, diabetes, hypertension, heart failure, MI, CKD, lung disease dementia, ambulatory visit frequency, and month of diagnosis and system (INSIGHT vs. H+H). Individual hospital indicators were included as random effects on the intercept level for all models. CKD, chronic kidney disease; DM, diabetes; HFRS, Hospital Frailty Risk Score; HTN, hypertension; NHB, non-Hispanic black; NHW, non-Hispanic white; MI, myocardial infarction

group 65–74, 75–84, and 85+, respectively). Asian, other, and unknown race–ethnicity patients had higher proportions of no-ambulatory history (38%, 41%, 36%, and 57% for NHW, Asian, other, and unknown, respectively). Adjusting for age, sex, and race, no-ambulatory care patients, compared to those with ambulatory care

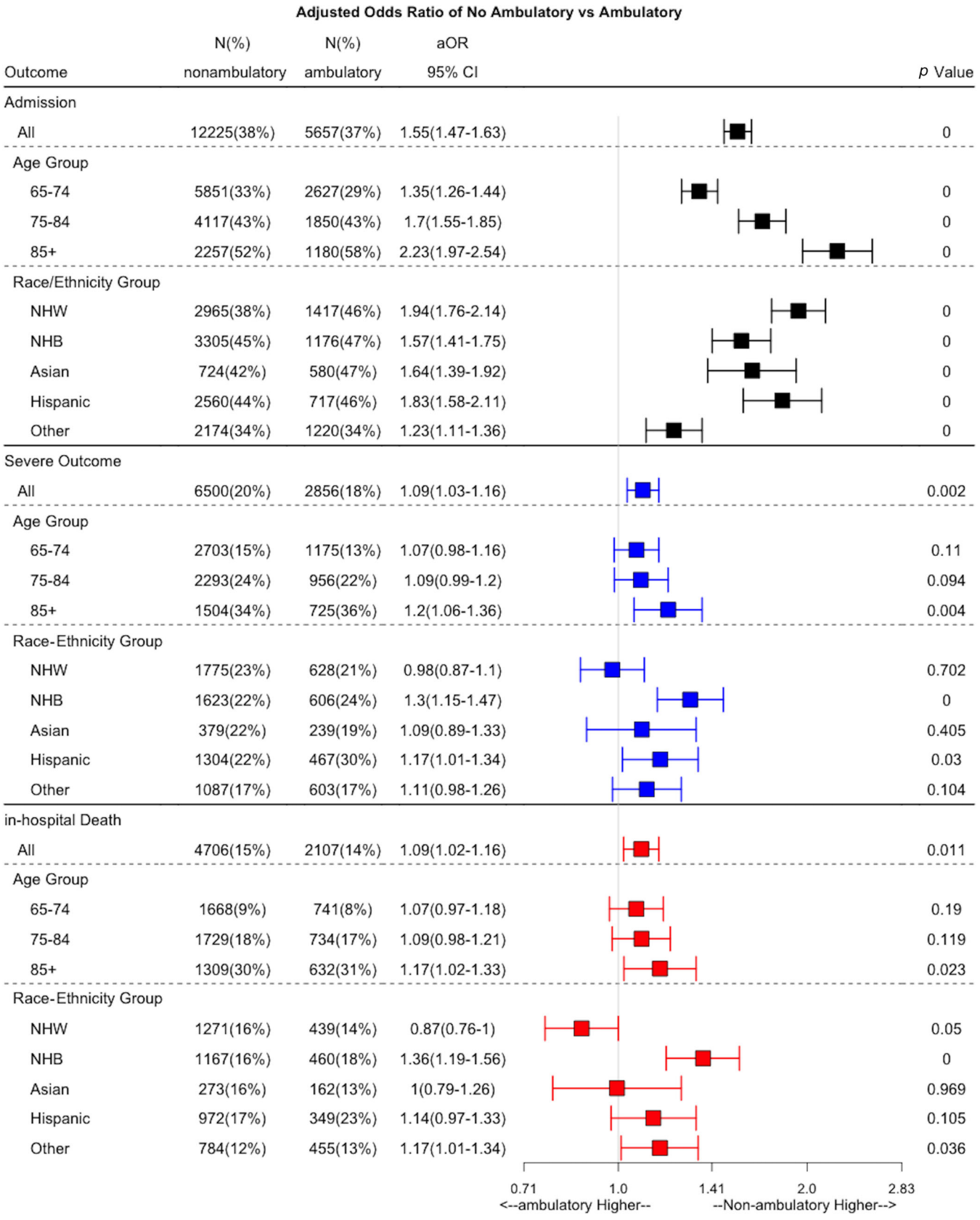

FIGURE 4 Adjusted odds ratios of ambulatory history (yes vs. no) for hospital admission, severe outcomes, and in-hospital death, overall and by age and race–ethnicity groups. Adjustment factors include age, sex, and race–ethnicity, month of diagnosis and hospital system (H+H vs. INSIGHT). Individual hospital indicators were included as random effects on the intercept level. *N* (%) no-ambulatory is presented as the number of patients with the corresponding outcome (percent of the total number of patients in the no-ambulatory cohort). *N* (%) ambulatory is presented as the number of patients with the corresponding outcome (percent of the total number of patients in the ambulatory cohort). The p-value column presents the p-values testing the corresponding aOR to the null hypothesis (aOR = 1). NHB, non-Hispanic black; NHW, non-Hispanic white

histories, were significantly more likely to be hospitalized (aOR = 1.55 [1.47–1.63]), experience severe outcomes (aOR = 1.09 [1.03–1.16]) and die in-hospital (aOR = 1.09 [1.02–1.16]). Furthermore, outcomes differences between patients with and without ambulatory care histories were greater in older age groups (aORs of hospitalization = 1.35 [1.26–1.44], 1.7[1.55–1.85], and 2.23 [1.97–2.54] in age groups 65–74, 75–84, and 85+ respectively, Figure 4).

DISCUSSION

Benefit of our study

COVID-19, prior to vaccine availability, was devastating for older adults, particularly frail elders in nursing homes. However, few studies have investigated the COVID-19 experience of community-dwelling older adults. Similarly, few studies have investigated COVID-19 outcomes in the oldest group (usually people 65 and older are considered together), or investigated the contribution of frailty to poor outcomes. Using data on COVID-19 patients aged 65 and older from the large and diverse EHR networks of NYC's public and private hospitals, where we could also study ambulatory care history of COVID-19 patients, this study provides evidence, a differential impact of risk factors for COVID-19 outcomes as age increases to 85 and older. For patients aged 65–74, hypertension, CKD, male sex, lung disease, and frailty, as measured by the HFRS, were the top five risk factors for hospitalization with the highest attributable risk fractions. With increasing age, the attributable risk fractions decreased for sex, race–ethnicity, and most comorbidities, while increased for dementia, heart failure, and frailty. Patients without ambulatory care histories, when compared to those with ambulatory care histories, had significantly higher adjusted rates of severe COVID-19 outcomes, especially in older patients. We additionally conducted a sensitivity analysis with only patients diagnosed before initiation of vaccination (March 2020-Dec 15, 2020). The results were consistent with our current results (Figures S5–S7**)**.

Our research utilizes several novel methods. First, we included patients who receive care at NYC academic medical institutions and the nation's largest public health system, providing an exceptionally diverse cohort in terms of race–ethnicity and socioeconomic status. Second, we focus on older adults (age 65 and up), who live in the community and not in nursing homes, a less-studied population severely impacted by COVID-19. Third, we investigate a majority–minority cohort, providing continuing insight into the differences in health status and outcomes illuminated by COVID-19. Finally, a broad spectrum of demographic and comorbidity covariates are estimated from the past 2-year ambulatory history before COVID-19 diagnosis, providing a different view of risk factor impact and facilitating comparisons with people without a history of ambulatory care.

Our findings are consistent with previous studies of frequencies of risk factors for COVID-19 outcomes. We found in-hospital mortality consistent with previous studies in older patients (27%–32%).[12,13] Similarly, our data showed older age, male sex, obesity, frailty (HFRS) and histories of hypertension, impaired renal function, cardiovascular disease, and diabetes were important risk factors.[7] Our data, which feature biomarkers done in the ambulatory setting previous to COVD-19 diagnosis, are also consistent with previous reports of the impact of biomarker risk factors on COVID-19 outcomes, including abnormal levels of C-reactive protein, lymphocytes, total bilirubin, and albumin.[22–25] In general, we found the effect of all risk factors, whether demographic, comorbidities, or biomarkers, decreased as age group increased, except for dementia. This is consistent with the general observation that strength of associations of risk factors decreases with increasing age for other common disease outcomes.[26] It is also notable in our majority–minority study cohort; the impact of being "not white" was much stronger in the younger age group.

The impact of dementia in community-living older adults has not previously been emphasized. The impact of dementia as a risk factor for poor COVID-19 outcomes in nursing home patients is widely assumed, but there are many older adults with dementia who live in the community. In general, dementia patients are well known to have been severely impacted by the isolation from their families and decreased caregiving support that was widespread during COVID-19 prior to vaccinations, whether they lived in the community or in nursing homes. International studies of risk factors for poor outcomes of COVID-19 in older adults consistently show frailty as an important risk factor.[12,13,16,17] Our data allowed us to specify the variable used in European studies, HFRS, and we found that frailty was a major risk factor for severe COVID-19 outcomes with the strongest odds ratios and attributable risk fractions. Further studies of the association between frailty, cognitive function, and COVID-19 will be important to understand its true impact on older adults, whether in nursing homes or the community.

With the current data, we were not able to explain why patients with no established ambulatory care histories had worse outcomes. Our data have a reasonable representation of the ambulatory experience of COVID-19 patients because we were able to access ambulatory care data from a healthcare system that may be different from the hospital where the person was admitted (i.e.,

ambulatory care at one H+H center, hospitalization at another). Studies have reported that suboptimal access to health care can cause people to delay evaluations, so people without ambulatory care history may have presented when sicker.[27] This nonambulatory care group was younger and more diverse. It is possible that middle-aged people do not feel the need to access ambulatory care, even if they have health conditions. In addition, individuals from vulnerable populations, including those with low socioeconomic status and immigrants, are more likely to have no primary physicians, visit multiple institutions to receive care, and may have insufficient information in EHRs to assess ambulatory history.[28] The data also demonstrate that older age groups, particularly 85+, were most affected. Future research is needed to confirm our findings and investigate hypotheses about the role of ambulatory care on COVID-19 outcomes and other outcomes. Finally, based on our results, we suggest vaccinations and interventions should be more aggressively targeted to older adults with frailty and cognitive impairments, especially those without ambulatory care histories. More resources, including routine testing, contact tracings, implementations of COVID-safe measures for caregivers, should be spent on protecting the older vulnerable adults in nursing homes and in communities.

Limitations

Our study has several limitations. First, some patients may be misclassified as to their ambulatory care experience. Some H+H hospitals (with about 14% of patients) transited to Epic later than 2018 so the actual queried periods are less than 24 months for patients in those hospitals. We used presence of ambulatory history to define a person as community-dwelling, so there could be misclassification because some people could have had a nursing home stay during the look-back period. Second, although INSIGHT uses the common data model and all H+H EHRs are unified in one Epic system, there may be heterogeneous missing proportions among hospitals. About 20% and 8% of patients have "other" and "unknown" race–ethnicity, and 31% of patients have missing BMI. We believe our large sample size and racial diversity should mitigate missingness. We found less impact of BMI than some other researchers, but we are focusing on an older age group were other characteristics appear to have more impact. Finally, we estimated frailty using the HFRS, which is an ICD10-based index developed in a British population and externally validated in a Canadian population. We have not compared its concordance with commonly used frailty scales in the U.S. population.

CONCLUSIONS

Despite these limitations, we have provided some new insights into the impact of COVID-19 on community-dwelling older adults, finding differential impacts of risk factors with rising age, emphasizing the roles of dementia and frailty as risks for severe outcomes, and investigating these issues in a majority–minority population. In addition, the somewhat protective role of ambulatory care experience is surprising and should be further investigated. The combined INSIGHT and H+H EHR datasets can be used together and are powerful tools for understanding the impact of risk factors and disease in large, diverse populations.

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This article has not been previously published and is not being considered for publication elsewhere, in whole or in part.

CONFLICT OF INTEREST

Authors report no relevant disclosures.

AUTHOR CONTRIBUTIONS

All authors have read and approved the manuscript. Jiyu Kim, Caroline Blaum, and Judy Zhong designed the study. Rosie Ferris, Mauricio Arcila-Mesa, Claudia Pulgarin, Johanna Dolle, Roopa Kalyanaraman Marcello, and Judy Zhong contributed to the acquisition of data. Jiyu Kim, Hyungrok Do, and Judy Zhong contributed to the data analysis, and interpretation of data. Jiyu Kim, Caroline Blaum, and Judy Zhong drafted the manuscript. All authors contributed to critical revisions of the manuscript.

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SUPPORTING INFORMATION

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

Table S1. Baseline demographic characteristics and outcomes of NYC COVID-19 patients, overall and by presence of ambulatory history.

Table S2. Lab results of NYC COVID-19 ambulatory care cohort by age groups.

Figure S1. Adjusted odds ratios of demographic and comorbidity risk factors and biomarkers of COVID-19 severe outcomes by age groups.

Figure S2. Adjusted odds ratios of demographic and comorbidity risk factors and biomarker of covid-19 in-hospital mortality by age groups.

Figure S3. Adjusted attributable fraction of demographic and comorbidity risk factors of COVID-19 severe outcomes by age groups.

Figure S4. Adjusted attributable fraction of demographic and comorbidity risk factors of COVID-19 in-hospital mortality by age groups.

Figure S5. Adjusted odds ratios of demographic and comorbidity risk factors and biomarkers of COVID-19 hospital admission by age groups for patients diagnosed before December.

Figure S6. Adjusted odds ratios of demographic and comorbidity risk factors and biomarkers of COVID-19 severe outcomes by age groups for patients diagnosed before December.

Figure S7. Adjusted odds ratios of demographic and comorbidity risk factors and biomarkers of COVID-19 mortality by age groups for patients diagnosed before December.

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