

ORIGINAL RESEARCH

Infectious Disease

Clinical characteristics of COVID-19 patients evaluated in the emergency department: A retrospective cohort study of 801 cases

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Abstract

Background: Coronavirus disease 2019 (COVID-19), the disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has exacted devastating tolls. Despite its pervasiveness, robust information on disease characteristics in the emergency department (ED) and how that information predicts clinical course remain limited.

Methods: We conducted a retrospective cohort study of the first ED visit from SARS-CoV-2-positive patients in our health system, from February 21, 2020 to April 5, 2020. We reviewed each patient's ED visit(s) and included the first visit with symptoms consistent with COVID-19. We collected demographic, clinical, and treatment variables

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from electronic health records and structured manual chart review. We used multivariable logistic regression to examine the association between patient characteristics and 2 primary outcomes: a critical outcome and hospitalization from index visit. Our critical outcome was defined as death or advanced respiratory support (high flow nasal cannula or greater) within 21 days.

Results: Of the first 1030 encounters, 801 met our inclusion criteria: 15% were over age 75 years, 47% were female, and 24% were non-Hispanic white. We found 161 (20%) had a critical outcome and 393 (49%) were hospitalized. Independent predictors of a critical outcome included a history of hypertension, abnormal chest x-ray, elevated neutrophil to lymphocyte ratio, elevated blood urea nitrogen (BUN), measured fever, and abnormal respiratory vital signs (respiratory rate, oxygen saturation). Independent predictors of hospitalization included abnormal pulmonary auscultation, elevated BUN, measured fever, and abnormal respiratory vital signs.

Conclusions: In this large, diverse study of ED patients with COVID-19, we have identified numerous clinical characteristics that have independent associations with critical illness and hospitalization.

KEYWORDS

COVID-19, critical characteristics, emergency, hospitalization

1 | INTRODUCTION

1.1 | Background

Coronavirus disease 2019 (COVID-19), the disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has extracted incalculable tolls in healthcare settings and society at large. By the end of 2020, over a third of a million Americans had COVID-19 confirmed deaths and more than 100,000 excess deaths had been associated with the pandemic, not including the anticipated mortality impacts of lost educational and economic attainment.¹⁻³ Despite significant scientific inquiry in response to this disease burden, no therapies have emerged as curative and the modest benefits seen in the best studied therapies are marginal.^{4,5} For these reasons, supportive care remains the mainstay of therapy, and decision-making around use of these supportive care resources (ie, admission to hospital) is the keystone in the provision of COVID-19 care.

1.2 | Importance

Although significant COVID-19 disease is a condition primarily seen in emergency department (ED) and hospital settings, little has been published on characteristics of the disease in the ED. Most studies involving ED patients include them indirectly, by observing patients who have already been hospitalized.⁶⁻¹² When ED patients have been directly studied, the study population also included non-ED patients or included in the analysis a majority of patients not confirmed to have COVID-19.¹³⁻¹⁵ Many models have examined population-level

associations, or included variables driven primarily by data-collection convenience, emphasizing comorbidities or numerous laboratory values over the patient-level clinical features, examination findings, and diagnostic data typically available in the ED.^{16,17} These approaches are understandable given the urgent need to address COVID-19, but it is anticipated that use of more granular ED data will offer stronger associations between patient characteristics and clinically important outcomes.

1.3 | Goals of this investigation

Despite COVID-19's pervasiveness, robust information on ED clinical evaluation and how that information predicts clinical course remain limited. Therefore, we undertook a retrospective cohort study of a diverse group of ED patients diagnosed with COVID-19 in a multi-center, non-surge, community setting. Additionally, we used multivariable logistic regression to assess predictors of 2 clinically meaningful outcomes from index ED visit: hospitalization and a critical outcome of death or high flow nasal cannula (HFNC) or greater respiratory support within 21 days.

2 | METHODS

2.1 | Study design and setting

We conducted a retrospective cohort study of the first 1030 ED patient-visits with an in-system laboratory test positive for

SARS-CoV-2 and an ED visit within 21 days before or after the test. The study took place in the 21 community EDs of Kaiser Permanente Northern California (KPNC), an integrated health care system that provides comprehensive medical care for greater than 4 million members with approximately 1.2 million annual ED visits. KPNC members represent approximately one-third of the population in areas served and are highly representative of the ethnic and socioeconomic diversity of the surrounding population.¹⁸ KPNC is a learning healthcare system with an applied research agenda and is supported by a comprehensive integrated electronic health record (Epic, Verona, WI), which includes inpatient, outpatient, emergency, pharmacy, laboratory, and imaging data. The Research Determination Committee for the KPNC region determined the project did not meet the regulatory definition of research involving human subjects per 45 CFR 46.102(d). The study was conducted in accordance with the principles of the Declaration of Helsinki.

2.2 | Selection of participants

A goal of 1000 patients was selected for convenience at the study outset based on data availability for COVID-19 patients in our system at that time. We examined a consecutive series of the first 1030 positive SARS-CoV-2 tests with an ED visit within 21 days before or after test order time. A 21-day time window was used in either direction of test order time because a patient may have been tested after requiring significant respiratory support and have several weeks of preceding symptoms (and ED visits) or could have been tested very early on in illness and have several weeks before meeting 1 of our outcomes. The SARS-CoV-2 tests were reverse transcriptase polymerase chain reaction-based tests. We reviewed all ED visits meeting these criteria and the first ED visit for symptoms consistent with COVID-19 was included and designated as the index visit (Figure S1).

2.3 | Manual chart review process

Twelve practicing emergency medicine clinicians served as abstractors. All received standardized training on data collection methods and use of the data collection tool, which was modified to its final form after an iterative process.¹⁹ The principal investigator answered and arbitrated all coding questions and monitored data collection by regularly assessing abstractor performance and providing targeted feedback. We asked abstractors to report if the possibility of COVID-19 was recognized by the treating ED clinician during the ED visit, either explicitly (ie, documented as such in the note or the discharge instructions) or implicitly (ie, ordered a SARS-CoV-2 test or ordered isolation precautions specific to COVID-19 practices). All encounters in which the initial abstractor reported that COVID-19 was “unrecognized” by the treating clinician were abstracted by a second abstractor and adjudicated by a third if the first 2 interpretations were incongruent. We also asked abstractors to determine if the ED visit was for symptoms poten-

The Bottom Line

In 801 patients who visited the emergency department with COVID-19, 20% had a critical outcome, defined as death or receipt of high flow nasal cannula, noninvasive ventilation, or invasive mechanical ventilation. Factors associated with a critical outcome included a history of hypertension, abnormal chest x-ray, elevated neutrophil to lymphocyte ratio, elevated BUN, fever, abnormal respiratory rate, or low oxygen saturation.

tially consistent with COVID-19 (see Table 3 for a list of symptoms we considered to be consistent with COVID-19). All encounters deemed incompatible with COVID-19 disease symptoms (eg, ankle pain after ankle trauma) were reviewed by a second abstractor and agreed on by consensus after discussion. To assess inter-rater agreement, 100 cases were randomly selected and independently reviewed by 2 abstractors; we calculated a kappa on abstractor identification of the presence of shortness of breath as a symptom. We used accepted kappa ranges to assess the quality of our agreement.²⁰

2.4 | Study variables from chart review

We abstracted the following patient-level variables during manual chart review: COVID-19 risk factors including sick contacts, travel history, and occupational risk; reported symptoms, timeline of illness, pregnancy state, and impression of immune suppression. Patient symptoms were grouped into clinically relevant categories, for example lower respiratory (eg, cough, chest pain, shortness of breath), and gastrointestinal (nausea, vomiting, diarrhea, and abdominal pain). We similarly grouped chief complaints into categories with commonly recognized synonyms (eg, fever and chills, and weakness and fatigue).

We also reviewed ED clinician pulmonary auscultation findings and assigned a primary descriptor: clear, coarse, crackles/rales, diminished/decreased, rhonchi, wheezing, not examined, and other. Additionally, we abstracted radiology interpretations of chest x-ray (CXR) reports, use of bedside ultrasound, and use of computed tomography (CT) scans that involve at least part of the lung field (chest or abdomen studies). CXR imaging was abstracted by a single abstractor from the final radiologist read of the first available CXR after ED start time. We categorized each CXR based on the number and distribution of opacity-like findings, as these categories may predict hospitalization and disease severity.^{21,22}

2.5 | Study variables from automated data collection

A comprehensive list of data was collected from automated data sources including patient age, gender, body mass index (BMI), race,

smoking history, KP health plan membership status, select comorbidities, and select chronic medication use. Chronic medication use was assessed by observing system-filled prescriptions in a 100-day window from 121 days prior to index visit to 21 days prior to index visit, and included bronchodilators, steroids, immunosuppressants, angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARB), and other anti-hypertensives. Medications that may have been prescribed to treat a COVID-19 like illness were assessed by observing system-filled prescriptions in a 21-day window immediately prior to the index ED visit. These included medications at the time purported to treat COVID-19 (hydroxychloroquine, lopinavir), bronchodilators (beta agonists, inhaled steroids), systemic corticosteroids, antivirals, and antibiotics. Additionally, we identified the administration of these same medications in the ED. We electronically identified diagnostic results including index SARS-CoV-2 test order timing and ED laboratory values as well as ED vital signs. We also describe the highest level of respiratory support (HLRS) achieved during the index hospitalization, the time to achieve the HLRS, hospitalization length of stay, 30-day all-cause mortality rates, and hospitalization within 21 days for those not initially hospitalized.

2.6 | Outcomes

We assessed 2 primary outcomes: a critical outcome within 21 days of index ED visit and hospital admission from index ED visits. A critical outcome was defined as death from any cause or use of advanced respiratory support (HFNC, non-invasive ventilation including continuous or biphasic positive airway pressure, or invasive ventilation). Our critical outcome measure is congruent with the World Health Organization ordinal scale for COVID-19 severity 5 through 8 (5 being non-invasive ventilation or HFNC, 8 being death).²³ To identify death occurring outside our healthcare system, we used a state mortality database that links to the California State Department of Vital Statistics.

2.7 | Data analyses

We reported baseline characteristics among patients that did and did not meet 1 of our 2 primary outcomes, allowing for calculation of an unadjusted odds ratio (OR). We conducted a multivariable logistic regression with facility level random effect to assess patient characteristics associated with each outcome and report ORs and 95% confidence intervals (CIs).²⁴

We initially included variables considered to be clinically meaningful that also had a statistically significant association ($P < 0.05$) with our outcomes on unadjusted analysis. We then narrowed our selections prioritizing variables associated with our critical outcome as well as laboratory tests that were more prevalent as an approach likely to maximize the clinical interpretability of our model. We then pruned our variable selection based on a variable to outcome ratio of 10:1 to pre-

vent over fitting. For simplicity and to aid in comparison, we used the same variables in both outcomes. We examined model fit and performance by examining the area under the receiver operator curve (ROC) curves and reporting the P -values of the Hosmer-Lemeshow goodness of fit test.

We performed an analysis in our multivariable model using heart rate in lieu of temperature, given a known association between the variables. We also performed another analysis using our critical outcome with a 7-day instead of the 21-day post ED visit window. All analyses were performed using SAS (Cary, NC) 9.4 and R Studio (Boston, MA) 3.14.

3 | RESULTS

3.1 | Demographics

Of the 1030 encounters examined, 801 met our inclusion criteria: the median age was 55 years (interquartile range [IQR] = 42–67); 47% were female, 24% were non-Hispanic white, and 70% were obese or overweight (Table 1). Common comorbidities included hypertension (40%), hyperlipidemia (35%), a history of smoking (27%), and diabetes mellitus (24%). We observed previously demonstrated patient-level factors associated with our critical outcome, including unadjusted associations with incrementally older age, male gender, and numerous comorbidities.^{25–27} Some of the strongest associations between comorbidities and our critical outcome were seen in congestive heart failure, peripheral vascular disease, chronic kidney disease, diabetes mellitus, hypertension, and hyperlipidemia. Not witnessed in our cohort were observations of unadjusted increased risk with higher BMI or specific ethnicities.

3.2 | Triage characteristics

We found 22% of patients arrived at the ED by ambulance, including a large minority (46%) of those who met our critical outcome (Table 2). The most common chief complaints were shortness of breath (41%), cough (37%), and fever (32%). Less common were gastrointestinal chief complaints (10%) or systemic chief complaints like weakness (5%). We found 15% were known to have COVID-19 at the time of triage or initial clinical assessment. In triage, 59% patients were identified as having a fever by history, 10% as having an upper respiratory symptom, and 35% as having a symptom of systemic illness. Being transported via ambulance and registering with chief complaints of weakness or shortness of breath was all more likely in patients with a critical outcome.

3.3 | Clinical characteristics

The most commonly endorsed type of complaint was a lower respiratory symptom (90% of patients), the most common being cough (82%)

TABLE 1 Patient demographics and comorbidities: hospitalization and critical outcomes

Characteristic	Total cohort (N = 801)	Hospitalization from ED		Critical outcome	
		Discharged (N = 408)	Hospitalized (N = 393)	Not Critical (N = 640)	Critical (N = 161)
Age in years, median (IQR)	55 (42–67)	47.5 (37–59)	62 (50–74)	52 (40–63)	66 (54–79)
18–44, no. (%)	238 (29.7)	173 (42.4)	65 (16.5)	225 (35.2)	13 (8.1)
45–54, no. (%)	161 (20.1)	91 (22.3)	70 (17.8)	129 (20.2)	32 (19.9)
55–64, no. (%)	176 (22.0)	82 (20.1)	94 (23.9)	145 (22.7)	31 (19.3)
65–74, no. (%)	110 (13.7)	39 (9.6)	71 (18.1)	77 (12.0)	33 (20.5)
75+, no. (%)	116 (14.5)	23 (5.6)	93 (23.7)	64 (10.0)	52 (32.3)
Sex					
Male, no. (%)	424 (52.9)	208 (51.0)	216 (55.0)	324 (50.6)	100 (62.1)
Race, no. (%)					
White	193 (24.1)	84 (20.6)	109 (27.7)	146 (22.8)	47 (29.2)
African American	83 (10.4)	42 (10.3)	41 (10.4)	68 (10.6)	15 (9.3)
Asian	183 (22.8)	83 (20.3)	100 (25.4)	138 (21.6)	45 (28.0)
Hispanic	266 (33.2)	156 (38.2)	110 (28.0)	224 (35.0)	42 (26.1)
Other	76 (9.5)	43 (10.5)	33 (8.4)	64 (10.0)	12 (7.5)
Ever smoker, no. (%)	212 (26.5)	78 (19.1)	134 (34.1)	150 (23.4)	62 (38.5)
Health plan member, no. (%)	681 (85.0)	331 (81.1)	350 (89.1)	534 (83.4)	147 (91.3)
Currently pregnant, no. (%)	6 (0.7)	4 (1.0)	2 (0.5)	6 (0.9)	0 (0.0)
Comorbid conditions, no. (%)					
Congestive heart failure	56 (7.0)	14 (3.4)	42 (10.7)	29 (4.5)	27 (16.8)
Coronary heart disease	33 (4.1)	11 (2.7)	22 (5.6)	20 (3.1)	13 (8.1)
Hypertension	323 (40.3)	112 (27.5)	211 (53.7)	213 (33.3)	110 (68.3)
Hyperlipidemia	278 (34.7)	94 (23.0)	184 (46.8)	186 (29.1)	92 (57.1)
Peripheral vascular disease	142 (17.7)	35 (8.6)	107 (27.2)	89 (13.9)	53 (32.9)
Chronic obstructive pulmonary disease	108 (13.5)	47 (11.5)	61 (15.5)	78 (12.2)	30 (18.6)
Sleep apnea	118 (14.7)	39 (9.6)	79 (20.1)	80 (12.5)	38 (23.6)
Asthma	140 (17.5)	70 (17.2)	70 (17.8)	112 (17.5)	28 (17.4)
Diabetes mellitus	189 (23.6)	68 (16.7)	121 (30.8)	127 (19.8)	62 (28.5)
Rheumatologic disease	17 (2.1)	5 (1.2)	12 (3.1)	11 (1.7)	6 (3.7)
Liver disease	11 (1.4)	1 (0.2)	10 (2.5)	6 (0.9)	5 (3.1)
Renal disease	67 (8.4)	15 (3.7)	52 (13.2)	40 (6.3)	27 (16.8)
Cancer	74 (9.2)	26 (6.4)	48 (12.2)	52 (8.1)	22 (13.7)
Immune suppression	33 (4.1)	12 (2.9)	21 (5.3)	23 (3.6)	10 (6.2)
BMI category ^a					
12–24.9	163 (20.4)	72 (17.7)	91 (23.2)	125 (19.5)	38 (23.6)
25–29.9	239 (29.8)	120 (29.4)	119 (30.3)	189 (29.5)	50 (31.1)
30–34.9	160 (20.0)	75 (18.4)	85 (21.6)	124 (19.4)	36 (22.4)
35+	161 (20.1)	72 (17.7)	89 (22.7)	125 (19.5)	36 (22.4)

Abbreviations: ED, emergency department; OR, odds ratio; IQR, interquartile range; BMI, body mass index.

^aSeventy-eight patients had BMI data unavailable.

TABLE 2 Patient triage assessment: hospitalization and critical outcomes

Characteristic	Total cohort (N = 801)	Hospitalization from ED		Critical outcome	
		Discharged (N = 408)	Hospitalized (N = 393)	Not critical (N = 640)	Critical (N = 161)
ED means of arrival, no. (%)					
Ambulance	179 (22.3)	42 (10.3)	137 (34.9)	105 (16.4)	74 (46.0)
Other	622 (77.7)	366 (89.7)	256 (65.1)	535 (83.6)	87 (54.0)
Chief complaint group ^a , no. (%)					
Fever	257 (32.1)	132 (32.4)	125 (31.8)	208 (32.5)	49 (30.4)
Influenza-like	46 (5.7)	28 (6.9)	18 (4.6)	39 (6.1)	7 (4.3)
Weakness	41 (5.1)	14 (3.4)	27 (6.9)	24 (3.8)	17 (10.6)
Neurological	56 (7.0)	40 (9.8)	16 (4.1)	49 (7.7)	7 (4.3)
Mental	7 (0.9)	3 (0.7)	4 (1.0)	4 (0.6)	3 (1.9)
Sore throat	17 (2.1)	13 (3.2)	4 (1.0)	17 (2.7)	0 (0.0)
Cough	292 (36.5)	164 (40.2)	128 (32.6)	245 (38.3)	47 (29.2)
Short of breath	326 (40.7)	125 (30.6)	201 (51.1)	233 (36.4)	93 (57.8)
Chest discomfort	40 (5.0)	22 (5.4)	18 (4.6)	35 (5.5)	5 (3.1)
Gastrointestinal	76 (9.5)	40 (9.8)	36 (9.2)	59 (9.2)	17 (10.6)
Known COVID-19 ^b	123 (15.4)	52 (12.7)	71 (18.1)	99 (15.5)	24 (14.9)
Symptom group by triage assessment ^c , no. (%)					
Fever	470 (58.7)	254 (62.3)	216 (55.0)	383 (59.8)	87 (54.0)
Upper respiratory	76 (9.5)	52 (12.7)	24 (6.1)	70 (10.9)	6 (3.7)
Lower respiratory	617 (77.0)	304 (74.5)	313 (79.6)	487 (76.1)	130 (80.7)
Systemic	283 (35.3)	160 (39.2)	123 (31.3)	228 (35.6)	55 (34.2)

Abbreviation: ED, emergency department.

^aGrouped by commonly recognized synonyms (eg, fevers and chills, weakness and fatigue).

^bRecognized by triage or clinician evaluation to already be positive for SARS-CoV-2.

^cGrouped by clinically relevant categories, for example lower respiratory (eg, cough, chest pain, shortness of breath).

(Table 3). About one-third of patients (32%) endorsed a gastrointestinal symptom, and only 4% of patients had neither fever nor respiratory symptoms. The only symptoms that had statistically significant associations with our critical outcome were shortness of breath (OR = 2.4 [1.7–3.5]) and confusion (OR = 4.6 [2.2–9.5]). As a whole, the median duration of symptoms at the time of ED visit was 7 days (IQR = 3–9). Documentation supporting that the clinician recognized the potential for COVID-19 was absent in 15% of cases. Clinicians documented perceived COVID-19 risk factors (such as travel) 17% of the time, and patient-identified sick contacts 24% of the time (Table S1).

In our cohort, vital sign abnormalities were common (Table 4). We found 42% had a documented temperature over 100.3°F, 47% had a heart rate over 100 beats/minutes, 48% had a respiratory rate over 22 breaths/minutes, and 33% had a pulse oximetry reading below 88%. Interestingly, 150 of the 161 patients (93%) with our critical outcome had oxygen saturations less than 93% in their index ED visit; another interpretation of this observation is that only 11 of the 468 patients (2%) with ED oxygen saturation over 93% experienced a critical outcome. Abnormal vital signs were universally associated with both our primary outcomes.

The majority of patients overall had a clear pulmonary examination (63%); of patients with a critical outcome, 45% had abnormal lung auscultation, with the most common abnormal finding being crackles/rales (22%). Most abnormal lung sounds were more common in our critical outcome with the exception of wheezing, which had similar prevalence across outcomes.

3.4 | Diagnostics

Laboratory testing was common in patients: 78% of patients had bloodwork analyzed, including the majority (57%) of patients discharged home from index visit (Tables 5 and S2). The majority of laboratory test results for all test types were normal in patients who met either of our primary outcomes. The only exceptions were lymphocyte count and the neutrophil to lymphocyte ratio (NLR), where 62% of patients with a critical outcome had abnormally increased values. Many tests had associations with our critical outcome, some of the strongest being elevated white blood cell (WBC) count, absolute neutrophil count, lymphocyte count, NLR, troponin, and lactic acid. Interestingly,

TABLE 3 Clinician characteristics: Hospitalization and critical outcomes

Characteristic	Total cohort (N = 801)	Hospitalization from ED		Critical outcome	
		Discharged (N = 408)	Hospitalized (N = 393)	Not critical (N = 640)	Critical (N = 161)
Symptom group ^a , no. (%)					
Fever	634 (79.2)	321 (78.7)	313 (79.6)	505 (78.9)	129 (80.1)
Upper respiratory	223 (27.8)	150 (36.8)	73 (18.6)	195 (30.5)	28 (17.4)
Lower respiratory	719 (89.8)	361 (88.5)	358 (91.1)	573 (89.5)	146 (90.7)
Gastrointestinal	255 (31.8)	110 (27.0)	145 (36.9)	212 (33.1)	43 (26.7)
Systemic	528 (65.9)	278 (68.1)	250 (63.6)	427 (66.7)	101 (62.7)
Atypical	35 (4.4)	17 (4.2)	18 (4.6)	28 (4.4)	7 (4.3)
Specific symptom, no. (%)					
Fever	599 (74.8)	295 (72.3)	304 (77.4)	475 (74.2)	124 (77.0)
Flu like	75 (9.4)	49 (12.0)	26 (6.6)	64 (10.0)	11 (6.8)
Chills	255 (31.8)	139 (34.1)	116 (29.5)	213 (33.3)	42 (26.1)
Weakness	312 (39.0)	138 (33.8)	174 (44.3)	245 (38.3)	67 (41.6)
Myalgia	270 (33.7)	174 (42.6)	96 (24.4)	244 (38.1)	26 (16.1)
Headache	135 (16.9)	83 (20.3)	52 (13.2)	118 (18.4)	17 (10.6)
Dizzy	49 (6.1)	22 (5.4)	27 (6.9)	37 (5.8)	12 (7.5)
Syncope	38 (4.7)	18 (4.4)	20 (5.1)	28 (4.4)	10 (6.2)
Confusion	31 (3.9)	2 (0.5)	29 (7.4)	15 (2.3)	16 (9.9)
Rash	7 (0.9)	3 (0.7)	4 (1.0)	6 (0.9)	1 (0.6)
Upper respiratory, no. (%)					
Nasal	154 (19.2)	107 (26.2)	47 (12.0)	132 (20.6)	22 (13.7)
Sore throat	115 (14.4)	80 (19.6)	35 (8.9)	105 (16.4)	10 (6.2)
Lower respiratory, no. (%)					
Cough	653 (81.5)	328 (80.4)	325 (82.7)	520 (81.3)	133 (82.6)
Sputum	86 (10.7)	42 (10.3)	44 (11.2)	72 (11.3)	14 (8.7)
Hemoptysis	11 (1.4)	4 (1.0)	7 (1.8)	8 (1.3)	3 (1.9)
Short of breath	452 (56.4)	182 (44.6)	270 (68.7)	335 (52.3)	117 (72.7)
Dyspnea on exertion	77 (9.6)	30 (7.4)	47 (12.0)	59 (9.2)	18 (11.2)
Chest pain	146 (18.2)	72 (17.6)	74 (18.8)	126 (19.7)	20 (12.4)
Gastrointestinal, no. (%)					
Nausea	139 (17.4)	63 (15.4)	76 (19.3)	112 (17.5)	27 (16.8)
Vomiting	79 (9.9)	39 (9.6)	40 (10.2)	67 (10.5)	12 (7.5)
Diarrhea	146 (18.2)	64 (15.7)	82 (20.9)	122 (19.1)	24 (14.9)
Abdominal pain	62 (7.7)	29 (7.1)	33 (8.4)	52 (8.1)	10 (6.2)
Median symptom duration in days (IQR)	7 (3–9)	5 (3–8)	7 (4–10)	6 (3–9)	7 (5–10)
Median infectious symptom duration in days (IQR)	7 (3–9)	5 (3–8)	7 (3–10)	6 (3–8)	7 (3–10)
Recognized as potentially COVID-19, no. (%)	123 (15.4)	52 (12.8)	71 (18.1)	99 (15.5)	24 (14.9)

Abbreviation: ED, emergency department.

^aGrouped by clinically relevant categories, for example lower respiratory (eg, cough, chest pain, shortness of breath).

TABLE 4 Vital signs and physical exam features: hospitalization and critical outcomes

Characteristic	Total cohort (N = 801)	Hospitalization from ED		Critical outcome	
		Discharged (N = 408)	Hospitalized (N = 393)	Not critical (N = 640)	Critical (N = 161)
Temperature, °F; no. (%)					
<98	22 (2.7)	19 (4.7)	3 (0.8)	20 (3.1)	2 (1.2)
98–100.3	444 (55.4)	286 (70.1)	158 (40.2)	392 (61.3)	52 (32.3)
100.4–102.9	283 (35.3)	92 (22.5)	191 (48.6)	194 (30.3)	89 (55.3)
103+	52 (6.5)	11 (2.7)	41 (10.4)	34 (5.3)	18 (11.2)
Systolic blood pressure ^a , mm Hg; no. (%)					
<90	67 (8.4)	6 (1.5)	61 (15.5)	18 (2.8)	49 (30.4)
90–119	414 (51.7)	150 (36.8)	264 (67.2)	327 (51.1)	87 (54.0)
120–139	216 (27.0)	155 (38.0)	61 (15.5)	192 (30.0)	24 (14.9)
140+	97 (12.1)	90 (22.1)	7 (1.8)	96 (15.0)	1 (0.6)
Heart rate, BPM ^b ; no. (%)					
<100	424 (52.9)	254 (62.3)	170 (43.3)	370 (57.8)	54 (33.5)
101–120	287 (35.8)	135 (33.1)	170 (43.3)	218 (34.1)	69 (42.9)
121+	90 (11.2)	19 (4.7)	152 (38.7)	52 (8.1)	38 (23.6)
Respiratory rate ^a , BPM ^c ; no. (%)					
≤22	411 (51.3)	313 (76.7)	98 (25.0)	394 (61.6)	17 (10.6)
23–28	185 (23.1)	63 (15.4)	122 (31.0)	143 (22.3)	42 (26.1)
29+	202 (25.2)	29 (7.1)	173 (44.0)	100 (15.6)	102 (63.4)
SpO ₂ , %; no. (%)					
≤88	243 (30.3)	5 (1.2)	238 (60.6)	100 (15.6)	143 (88.8)
89–92	90 (11.2)	21 (5.1)	69 (17.6)	83 (13.0)	7 (4.3)
93+	468 (58.4)	382 (93.6)	86 (21.9)	457 (71.4)	11 (6.8)
Pulmonary auscultation; no. (%)					
Clear	508 (63.4)	310 (76.0)	198 (50.4)	435 (68.0)	73 (45.3)
Coarse	19 (2.4)	3 (0.7)	16 (4.1)	12 (1.9)	7 (4.3)
Crackles/rales	88 (11.0)	22 (5.4)	66 (16.8)	53 (8.3)	35 (21.7)
Diminished/decreased	35 (4.4)	8 (2.0)	27 (6.9)	21 (3.3)	14 (8.7)
Not examined	74 (9.2)	40 (9.8)	34 (8.7)	59 (9.2)	15 (9.3)
Rhonchi	18 (2.2)	3 (0.7)	15 (3.8)	12 (1.9)	6 (3.7)
Wheezing	42 (5.2)	17 (4.2)	25 (6.4)	34 (5.3)	8 (5.0)
Other	17 (2.1)	5 (1.2)	12 (3.1)	14 (2.2)	3 (1.9)

Abbreviations: ED, emergency department; F, Fahrenheit.

^aSeven patients had unavailable systolic blood pressure data and 3 had unavailable respiratory rate data.

^bBPM, beats/minute.

^cBPM, breaths/minute.

165 patients (21%) were tested for influenza, all of whom were negative.

We found that 80% of patients had a CXR completed in the ED, and 75% of those had abnormal findings (Table 6). Compared to patients without a critical outcome, patients with a critical outcome were less likely to have a normal CXR (9% vs 39% normal), and frequently had bilateral findings (73% vs 30%). Increasing number and distribution of opacity-like findings were associated with both outcomes in a progressive fashion.

3.5 | Medications

Of patients with chronic use of select medications, the most commonly used were antihypertensives: 8% used an ACE inhibitor, 3% used an ARB, and 30% used another anti-hypertensive (Table S3). In the 21 days before the index visit, we found that use of medications to potentially treat COVID-19 symptoms was uncommon. In the ED, patients were commonly given antibiotics (at least 50% of patients) and bronchodilators (35%), and to a lesser degree, corticosteroids (10%) and

TABLE 5 Laboratory diagnostics: hospitalization and critical outcomes

Characteristic	Total cohort (N = 801)	Hospitalization from ED		Critical outcome	
		Discharged (N = 408)	Hospitalized (N = 393)	Not critical (N = 640)	Critical (N = 161)
No. abnormal (%)					
WBC count	48 (6.0)	6 (1.5)	42 (10.7)	16 (2.5)	32 (19.9)
ANC	73 (9.1)	11 (2.7)	62 (15.8)	31 (4.8)	42 (26.1)
Lymphocyte count	225 (28.1)	39 (9.6)	186 (47.3)	125 (19.5)	100 (62.1)
NLR	217 (27.1)	35 (8.6)	182 (46.3)	117 (18.3)	100 (62.1)
Platelet count	97 (12.1)	35 (8.6)	62 (15.8)	65 (10.2)	32 (19.9)
BUN	100 (12.5)	17 (4.2)	83 (21.1)	52 (8.1)	48 (29.8)
Bicarbonate	140 (17.5)	41 (10.0)	99 (25.2)	90 (14.1)	50 (31.1)
Creatinine	103 (12.9)	24 (5.9)	79 (20.1)	58 (9.1)	45 (28.0)
Glucose	132 (16.5)	43 (10.5)	89 (22.6)	82 (12.8)	50 (31.1)
Potassium	101 (12.6)	37 (9.1)	64 (16.3)	68 (10.6)	33 (20.5)
ALT	124 (15.5)	29 (7.1)	95 (24.2)	86 (13.4)	38 (23.6)
AST	186 (23.2)	27 (6.6)	159 (40.5)	109 (17.0)	77 (47.8)
Troponin	36 (4.5)	1 (0.2)	35 (8.9)	9 (1.4)	27 (16.8)
BNP	67 (8.4)	14 (3.4)	53 (13.5)	32 (5.0)	35 (21.7)
CRP	96 (12.0)	9 (2.2)	87 (22.1)	52 (8.1)	44 (27.3)
D-dimer	72 (9.0)	10 (2.5)	62 (15.8)	42 (6.6)	30 (18.6)
Lactic acid	89 (11.1)	16 (3.9)	73 (18.6)	39 (6.1)	50 (31.1)
SARS-CoV-2 test timing					
Before index visit	124 (15.5)	52 (12.7)	72 (18.3)	97 (15.2)	27 (16.8)
During index visit	514 (64.2)	253 (62.0)	261 (66.4)	410 (64.1)	104 (64.6)
After index visit	163 (20.3)	103 (25.2)	60 (15.3)	133 (20.8)	30 (18.6)

Abbreviations: ALT, alanine aminotransferase; ANC, absolute neutrophil count; AST, aspartate aminotransferase; BNP, b natriuretic peptide; BUN, blood urea nitrogen; CRP, C-reactive protein; NLR, neutrophil to lymphocyte ratio; WBC, white blood cell.

TABLE 6 Radiology diagnostics: hospitalization and critical outcomes

Characteristic	Total cohort (N = 801)	Hospitalization from ED		Critical outcome	
		Discharged (N = 408)	Hospitalized (N = 393)	Not critical (N = 640)	Critical (N = 161)
Chest X-ray, no. (%)					
Normal	201 (25.1)	137 (33.6)	64 (16.3)	187 (29.2)	14 (8.7)
Single opacity	92 (11.5)	45 (11.0)	47 (12.0)	79 (12.3)	13 (8.1)
Unilateral opacities	30 (3.7)	8 (2.0)	22 (5.6)	20 (3.1)	10 (6.2)
Bilateral opacities	311 (38.8)	71 (17.4)	240 (61.1)	194 (30.3)	117 (72.7)
Other (ie, nodule)	4 (0.5)	2 (0.5)	2 (0.5)	4 (0.6)	0 (0.0)
Not done	163 (20.3)	145 (35.5)	18 (4.6)	156 (24.4)	7 (4.3)
CT, no. (%)	27 (3.4)	8 (2.0)	19 (4.8)	16 (2.5)	11 (6.8)
Point-of-care US, no. (%)	4 (0.5)	1 (0.3)	3 (0.8)	2 (0.3)	2 (1.2)

Abbreviations: CT, computed tomography; ED, emergency department; US, ultrasound.

TABLE 7 Adjusted association between patient characteristics and hospitalization and critical outcomes

Characteristic	Hospitalization adjusted OR (95% CI)	Critical outcome: adjusted OR (95% CI)
Demographics and comorbidities		
Age 65+ years	1.3 (0.7–2.5)	1.4 (0.8–2.4)
Gender: female	1.3 (0.8–2.0)	0.7 (0.4–1.1)
Ever smoker	1.3 (0.8–2.2)	1.0 (0.6–1.7)
Hypertension	1 (0.6–1.7)	1.7 (1.0–3.1)
Hyperlipidemia	1.6 (0.9–2.8)	1.3 (0.7–2.3)
Diabetes mellitus	0.8 (0.4–1.6)	0.9 (0.5–1.6)
BMI \geq 30	1.4 (0.9–2.3)	1.5 (0.9–2.4)
Physical exam		
Temperature >100.3°F	2.4 (1.5–3.8)	2.2 (1.3–3.7)
Respiratory rate >23 BPM	3.4 (2.1–5.6)	3.8 (2.0–7.1)
SpO ₂ <93%	20.8 (12.1–35.9)	8.7 (4.4–17.4)
Abnormal pulmonary auscultation	1.7 (1.1–2.8)	1.1 (0.7–1.8)
Labs and imaging		
NLR: high	1.6 (0.9–3.1)	1.7 (1.1–2.7)
BUN: high	10.1 (2.4–42.8)	3.6 (1.8–7.2)
Glucose: high	0.5 (0.3–1.0)	1.3 (0.7–2.3)
Chest X-ray: abnormal	1.7 (0.9–3.0)	2.5 (1.2–5.1)
Chest X-ray: not done	0.7 (0.3–1.3)	2.1 (0.8–5.6)

Abbreviations: CI, confidence interval; BMI, body mass index; BPM, breaths per minute; BUN, blood urea nitrogen; F, Fahrenheit; NLR, neutrophil to lymphocyte ratio; OR, odds ratio.

hydroxychloroquine (19%). For patients discharged home these same medications were uncommonly prescribed.

3.6 | Clinical trajectory

Of 408 patients discharged home from the ED after index visit, 116 (28%) returned to the ED within 21 days (Table S4). Sixty-five of those 116 who returned (56%) were hospitalized; only 4 had a critical outcome. For those with a critical outcome, the median time to HLRS was 34 hours (IQR = 11–77) and hospitalization duration was 12 days (IQR = 7–23). Overall, 73 patients (9%) died within 30 days of the index visit. Among all patients hospitalized from index ED visit, the mean time to HLRS was 6 hours (IQR = 1–37), and the median hospital length of stay was 6 days (IQR = 3–12).

3.7 | Multivariable model

Our final multivariable models included 16 variables (Table 7). Independent predictors of a critical outcome included a history of hyperten-

sion (OR = 1.7 [1.0–3.1]), abnormal CXR (OR = 2.5 [1.2–5.1]), elevated NLR (OR = 1.7 [1.1–2.7]), elevated blood urea nitrogen (BUN) (OR = 3.6 [1.8–7.2]), measured fever (OR = 2.2 [1.3–3.7]), and abnormal respiratory vital signs (respiratory rate OR = 3.8 [2.0–7.1], oxygen saturation OR = 8.7 [4.4–17.4]). Independent predictors of hospitalization from index ED visit included abnormal pulmonary auscultation (OR = 1.7 [1.1–2.8]), elevated BUN (OR = 10.1 [2.4–42.8]), measured fever (OR = 2.4, [1.5–3.8]), and abnormal respiratory vital signs (oxygen saturation OR = 20.8 [12.1–35.9], respiratory rate OR = 3.4 [2.1–5.6]). The area under the ROC curve for our outcomes was 91% and 94% for our critical outcome and hospitalization, respectively. The *P*-values for the Hosmer-Lemeshow goodness of fit test were 0.19 and 0.81, respectively.

3.8 | Other analyses

We performed an analysis looking at our critical outcome at 7 days instead of 21 days; we found minimal change in our modelling results. Additionally, our assessment of interrater agreement between 2 reviewers on 109 charts for the identification of shortness of breath as a symptom demonstrated substantial agreement, $\kappa = 0.74$ (95% CI 0.61–0.87) and 87% agreement.

3.9 | Limitations

One limitation of our study is that it disproportionately includes critical COVID-19 illness, because these patients are more likely to be identified due to a need for acute medical care. Additionally, early testing recommendations favored patients being or already hospitalized, making it more likely to capture critical cases. Despite this limitation, a meaningful fraction of our cohort was not admitted and did not meet our critical outcome (ie, had mild or moderate disease), which offers important characteristic data to report associations.

Examining an outcome of hospitalization has many limitations. Although we feel this is an appropriate and vital perspective to capture, taken on its own it is an unreliable measure due to variability from numerous influences. Despite this, hospitalization captures an otherwise unobservable summation of factors that includes clinical gestalt. This complex but meaningful contribution has unique value, especially when taken in the context of other data.

Another limitation of our study is the possibility that some of our study patients followed up in other facilities. Despite this possibility, the vast majority of patients were KP health plan members (85%), and we were able to capture deaths occurring outside of the KPNC system using state mortality databases, mitigating this limitation.

The retrospective nature of our study is another limitation that may impact our ability to reliably capture information. Despite the limitations of a retrospective approach, we did employ manual chart review techniques, which improved our granular data extraction compared to studies that relied entirely on automated data collection. Additionally, our study was conducted with typical methodology standards used for

clinical research, without suspended standards due to the pandemic.²⁸ Given the pitfalls of using exceptions for research standards in COVID-19, we feel our study's contribution is meaningful despite a retrospective limitation.^{28,29}

4 | DISCUSSION

We studied a large diverse population of patients with SARS-CoV-2 infection and an associated ED visit for COVID-19 symptoms in a non-surge setting in the first months of the COVID-19 pandemic. Of the 801 study patients, 161 (20%) had a critical outcome and 394 (49%) were hospitalized. Independent predictors of a critical outcome included a history of hypertension, abnormal CXR, elevated NLR, elevated BUN, measured fever, and abnormal respiratory vital signs. Independent predictors of hospitalization from index ED visit included abnormal pulmonary auscultation, elevated BUN, measured fever, and abnormal respiratory vital signs.

Our study findings provide more nuanced data to supplement the findings of other published studies. Petrilli et al evaluated 4103 patients with COVID-19 diagnosed in the ED or ambulatory setting during the first New York City COVID-19 surge. They examined with separate multivariable models characteristics associated with hospitalization or critical illness.³⁰ Similar to our modelling they found that hypoxia (oxygen saturation <88%) had the greatest association with critical illness and also identified inflammatory markers and comorbidities with value. Their critical illness outcome was limited to hospitalized patients, making that model less helpful in aiding a decision to hospitalize from the ED. Additionally, their hospitalization model did not involve vital signs or laboratory results because 78% of their patients were seen in ambulatory settings where they had neither performed. Examination findings such as pulmonary auscultation and diagnostic radiological evaluation such as CXR were also absent, likely for the same reasons that data on vital signs were not available. The absence of these data available in typical ED care obscures conclusions as to the independent associations of hospitalization.

Innovative tools were developed early on in the pandemic to identify ambulatory patients who may be at risk of critical illness or hospitalization after presenting with symptoms concerning for COVID-19. The CoVa and COVAS scores studied by Sun et al¹³ and Sharp et al,¹⁵ respectively, are 2 such tools. These tools included either ED visits and outpatient respiratory tent visits (CoVa) or ED visits (COVAS) in patients with symptoms concerning for COVID-19. Both tools use demographics, comorbidities, and vital signs, and the CoVa score incorporated CXR findings as well. Both performed admirably in their goal at predicting 7-day need for hospitalization or critical illness. Their models were particularly useful early on in a pandemic when testing availability was constrained, but the overall confirmed COVID-19 rate was low (1647/11586 [14%] in CoVa and 2059/26600 [8%] for COVAS), limiting the utility in understanding prognosticators among patients with confirmed COVID-19 disease. The tools also did not incorporate physical examination findings or laboratory diagnostics, the latter which has been well-described in hospitalized patients

to be associated with critical illness and the former that is not well studied.

Most COVID-19 studies that examine diagnostic data as predictors of critical illness include already hospitalized patients.^{9,30-34} Similar to our analysis, several of these studies have observed independent associations with abnormal CXR findings.^{33,35} Studies that examined diagnostic laboratory results have also found independent associations, including elevated NLR, BUN, glucose, C-reactive protein, D-Dimer, troponin, and others. These findings are supported by the results of our multivariable model (NLR, BUN, and glucose). Physical examination findings (specifically pulmonary auscultation) were not examined as predictors in these studies.³⁶ This is presumably because they were not reliably available using only electronic data capture. Another interesting consideration is the variation in body temperatures association with outcomes between studies. This could be due to different temperature obtainment practices, such as non-oral temperatures. In our non-surge setting, 96% of temperatures acquired were from an oral or core route, which would be expected to aid in accurate temperature representation and allow for observation of predictive value if present. In our multivariate model, an elevated temperature was associated with increased odds of a critical outcome. In a study by Garibaldi et al¹⁹ that had many of the same conditions as our study (eg, multi-center, non-surge), they also noted meaningful independent association with measured fever, although like most studies they do not describe their temperature acquisition method.

Our study shifts the focus from hospitalized to ED patients, providing valuable insight into the triage and self-declaration of patients early on in a pandemic that may be useful for better understanding COVID-19 as well as future pandemic responses. For example, our nurse triage data demonstrate that in a care-as-usual triage encounter, clinically important infectious symptoms were identified the vast majority of the time. The triage nurse identified a lower respiratory symptom in 617 patients out of 719 patients (86%) identified as having such symptoms by the clinician evaluation. Among those with a critical outcome, nurse triage data identified 130 patients of 146 (89%) with lower respiratory symptoms later confirmed by the treating clinician. A separate interesting and diagnostic testing observation is the 100% negative influenza testing rate (from 165 tests) for our cohort. The time lag between our dataset and the initial reported data out of Wuhan, China is only weeks to months, suggesting that confounding concomitant illness in a novel pandemic may rapidly approach negligible rates as risk mitigation behaviors are deployed in the public sphere.^{37,38}

Although previously described for other medical conditions but not well addressed in clinical decision-making surrounding COVID-19, there is a distinction between the population risk factors that describe who is at risk for severe disease prior to clinical assessment from those at risk of severe disease after clinical data are available. Although age and comorbidities have strong associations with severe COVID-19 disease and hospitalization, these population-level factors appear to not carry significant independent value when compared to granular clinical data such as vital signs, laboratory results, examination findings, and imaging results. For example, our model suggests that a clinician should be more concerned about a COVID-19-positive 35-year-old

female with hypertension, measured fever, and an elevated BUN (with otherwise normal evaluation) than a COVID-19-positive 65-year-old male former smoker with hyperlipidemia (and otherwise normal evaluation). After an ED assessment, the population level associates of critical illness such as age and certain comorbidities no longer carry the predictive value that they did prior to clinical evaluation. For patients without overt indication for admission to hospital, our data suggests characteristics of their ED evaluation that may influence a decision to hospitalize, help determine a level of outpatient monitoring, or inform clinician-patient conversations about risk of progression.

In summary, we identified patient-level clinical variables from ED encounters that carry independent associations with severe COVID-19 and hospitalization. Our study adds significantly to the understanding of the clinical trajectory of COVID-19 through inclusion of a diverse, community-based, multi-center cohort of patients.

AUTHOR CONTRIBUTIONS

DMC, DRV, DWB, DRS, MVK, and DGM conceived the study and its design. DMC, ASR, and MER obtained research funding. DMC, DRV, DWB, DRS, ERH, JSL, EJD, MVK, SDC, MG, JS, SCB, and IDM performed manual chart review. LL performed the programming and analysis. DMC, DRV, DWB, DRS, and MER interpreted the data. DMC and MER oversaw the study as a whole. DMC drafted the manuscript and all authors contributed substantively to its critical revision and its final approval. DMC takes responsibility for the paper as a whole.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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