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Epidemiology and Outcomes of Hospitalized Adults with SARS-CoV-2 Community-Acquired Pneumonia in Louisville, Kentucky

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Abstract

Background: During the ongoing pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), SARS-CoV-2 community-acquired pneumonia (CAP) has been the primary cause of hospitalization. The objective of this study was to evaluate the clinical characteristics and outcomes of 1,013 patients hospitalized with SARS-CoV-2 CAP from September 2020 through March 2021 in Louisville, Kentucky.

Methods: This was a retrospective observational study of 1,013 patients hospitalized with SARS-CoV-2 CAP at eight of the adult hospitals in the city of Louisville from September 2020 through March 2021. Patients with 1) a positive reverse transcriptase-polymerase chain reaction (RT-PCR) for SARS-CoV-2, 2) fever, cough, or shortness of breath, and 3) an infiltrate on chest imaging were defined as having SARS-CoV-2 CAP. Data were abstracted from each hospital's electronic health record. Descriptive statistics were performed on clinical and epidemiological characteristics of hospitalized patients with SARS-CoV-2 CAP. Demographic characteristics of the study population were compared with census data from the city of Louisville. Data were analyzed by descriptive and inferential statistics using R version 3.4.0.

Results: Of the 1,013 patients hospitalized with SARS-CoV-2 CAP, the median age was 65 years, 53% were males, 24% reported their race as African American or Black, and 6% identified as Hispanic. The most frequent comorbidities were hypertension (73%), obesity (56%), and diabetes (43%). At the time of admission, 60% required supplemental oxygen. The mortality rate was 19% for the total population and 45% for the 359 patients admitted to the intensive care unit (ICU). For each comorbidity, the proportion of hospitalized patients with SARS-CoV-2 CAP was significantly different from the Louisville population ($P<0.001$). No significant differences were noted in race or ethnicity compared to the city of Louisville.

Conclusions: The elderly, males, and patients with a history of coronary artery disease, cerebrovascular disease, chronic obstructive pulmonary disease, hypertension, diabetes, renal disease, or obesity are overrepresented among hospitalized patients with SARS-CoV-2 CAP compared to the Louisville population. These patients are also more likely to require ICU care and experience worse clinical outcomes, with death occurring in approximately one in every five hospitalizations.

Introduction

Before the COVID-19 pandemic, viral community-acquired pneumonia (CAP) was diagnosed in approximately 30% of adults hospitalized with CAP.[1] The most commonly identified viruses were influenza, rhinovirus, and respiratory syncytial virus (RSV).[2] Currently, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the primary respiratory viral pathogen causing CAP. As the current pandemic progresses, the burden of SARS-CoV-2 CAP is changing, and the clinical characteristics and outcomes of hospitalized adults with SARS-CoV-2 CAP will continue to evolve, especially as new variants emerge, such as the Delta variant. An up-to-date understanding of the type of patients hospitalized with SARS-CoV-2 CAP will be necessary for investigators to develop optimal interventions to combat this infection. To better understand the current epidemiology of SARS-CoV-2 CAP, we evaluated the clinical characteristics and outcomes of 1,013

consecutive patients recently hospitalized with SARS-CoV-2 CAP from September 2020 through March 2021 in the city of Louisville, Kentucky.

Methods

Study design, subjects, and setting

This was a retrospective observational study of 1,013 consecutive patients with a diagnosis of SARS-CoV-2 CAP hospitalized at eight of the nine adult acute care hospitals in the city of Louisville, Kentucky. Hospitalizations between September 2020 and March 2021 were included in this analysis. Patients were followed until hospital discharge or in-hospital death.

Human subjects protection

The study was approved by the Institutional Review Board (IRB) at the University of Louisville Human Subjects Research Protection Program Office (IRB number 20.0257) and by the research offices at each participating hospital. The study was exempt from informed consent.

Study coordinating center

The Center of Excellence for Research in Infectious Diseases (CERID), located at the University of Louisville Division of Infectious Diseases, directed all study operations (CERIDlouisville.org). Members of CERID 1) developed the study data collection form and the study database, 2) collected data from hospital electronic medical records, 3) recorded data into the study database, and 4) performed quality control of collected data by initiating and resolving queries. Data were collected and managed using Research Electronic Data Capture (REDCap®) tools hosted at the University of Louisville Division of Infectious Diseases. REDCap® is a secure, web-based software platform designed to support data capture for research studies, providing an intuitive interface for validated data capture.[3] After all data queries were resolved, the study database was locked for data analysis.

Data collection

Patient data were abstracted from hospital electronic medical records. Collected data included patient age, sex, race/ethnicity, body mass index, type of residence, medical and social history, physical examination findings, laboratory findings, chest radiographs and chest computer tomography (CT) findings, medications, intensive care unit (ICU) admission, and need for invasive mechanical ventilation (IMV). The self-reported race variable was categorized as African American/Black, Caucasian/White, and Other. The Other self-reported race category included Asian, American Indian or Alaskan Native, Native Hawaiian or Pacific Islander, and unknown or unspecified; these were grouped together because of small sample sizes. Ethnicity was categorized as Hispanic or non-Hispanic.

Study definitions

SARS-CoV-2 CAP: A patient hospitalized with 1) a positive SARS-CoV-2 reverse transcriptase-polymerase chain reaction (RT-PCR) from a nasopharyngeal swab or other respiratory sample(s), 2) fever, cough, or shortness of breath, and 3) evidence of pulmonary infiltrates on chest radiograph or chest CT scan.

SARS-CoV-2 CAP with ARDS: Presence of acute respiratory distress syndrome (ARDS) was defined as bilateral opacities on a chest radiograph or CT scan not fully explained by cardiac failure or fluid overload with PaO_2/FiO_2 ≤300 on ventilator settings that included positive end-expiratory pressure (PEEP) ≥5 cm H_2O.[4]

In-hospital mortality: All-cause mortality during hospitalization. Patients transferred to end-of-life palliative care were considered to have expired during hospitalization, and the date of transfer was used as the date of death.

Clinical success: Hospitalized patients who were discharged alive and returned to the residence from which they were admitted.

Clinical presentation

Adapted from the National Institutes of Health guidelines for COVID-19, the clinical presentation of hospitalized patients with SARS-CoV-2 CAP was classified in the following 5 stages:[5]

Stage 1: Hospitalized patients with SARS-CoV-2 CAP but no need for supplemental oxygen.

Stage 2: Hospitalized patients with SARS-CoV-2 CAP and need for low-flow supplemental oxygen (*e.g.*, low-flow nasal cannula).

Stage 3: Hospitalized patients with SARS-CoV-2 CAP and need for high-flow supplemental oxygen or non-invasive ventilation.

Stage 4: Hospitalized patients with SARS-CoV-2 CAP and need for invasive mechanical ventilation, but without the presence of ARDS.

Stage 5: Hospitalized patients with SARS-CoV-2 CAP, need for invasive mechanical ventilation, and ARDS, defined as having a PaO_2/FiO_2 of 201–299 (mild ARDS), 101–199 (moderate ARDS), or ≤100 (severe ARDS).

Severity of disease, comorbid burden, and rates of in-hospital mortality

Severity of SARS-CoV-2 CAP at the time of hospitalization was evaluated using two well-established CAP scores, the pneumonia severity index (PSI) score and the CURB-65 score.[6, 7] The Charlson comorbidity index was used to measure the comorbidity burden.[8] Bar charts were used to describe the distribution of scores, as well as the percentage of patients in each category who died.

Geospatial epidemiology

The geomasked location of the home address of each patient with SARS-CoV-2 CAP enrolled in the study was obtained through the US Census Bureau website.[9] A kernel density heatmap was created using each patient's address at the time of SARS-CoV-2 CAP hospitalization. Areas of elevated relative risk of contracting SARS-CoV-2 CAP based on underlying population density were identified using Kuldorff's spatial scan statistic.

Cardiac and cardiovascular events

The following cardiac or cardiovascular events that were present at the time of admission or developed during hospitalization were collected: heart failure, cardiac arrest, cardiogenic shock, acute myocardial infarction, pulmonary edema, new arrhythmia, acute worsening of a chronic arrhythmia, cerebrovascular accident, pulmonary embolism, myocarditis, and deep vein thrombosis.

Coinfections

A patient with a microorganism isolated from blood, respiratory, or urine samples in addition to SARS-CoV-2 infection was defined as having a coinfection. Community-acquired coinfections were defined as microorganisms identified during the first 72 hours of hospitalization. Hospital-acquired coinfections were defined as microorganisms identified more than 72 hours after hospital admission.

Clinical outcomes

Binary outcomes evaluated included hospital discharge, need for invasive mechanical ventilation, admission to the ICU, septic shock, ARDS, and death. For those experiencing any of the previously listed events, time-to-event endpoints evaluated included time to hospital discharge alive (length of hospital stay), time to removal of IMV, time to discharge from the ICU, time to first cardiovascular event, time to septic shock, time to development of ARDS, and time to death. Time-to-event data were right-truncated at 30 days.

Statistical analysis

Continuous patient characteristics were summarized as medians and interquartile ranges (IQR), while categorical patient characteristics were summarized as frequencies and percentages. Comparisons of age, race and ethnicity, and comorbidities between the study population and Louisville's population demographics were performed using one-sample z-tests of proportions, with null values equal to the Louisville proportion. Louisville population data were taken from the 2017 Behavioral Risk Factor Surveillance System (BRFSS) Smart Data database and the 2019 American Community Survey 5-year estimates.[10, 11] In geospatial analysis, the associated likelihood ratio test using Monte Carlo hypothesis testing was performed for Kuldorff's spatial scan statistic. Time-to-event outcomes were compared using log-rank tests, with Kaplan–Meier curves produced. Median survival times and 95% confidence limits were reported. Analyses were performed using R version 3.4.0 (R Foundation for Statistical Computing, Vienna, Austria). P-values were two-sided, with statistical significance set at $P<0.05$.

Results

Study population and clinical presentation

A total of 1,013 patients were hospitalized with SARS-CoV-2 CAP. Demographics and comorbidities for hospitalized patients with SARS-CoV-2 CAP are depicted in **Table 1**.

COVID-19 vaccination coverage

Among the 1,013 patients hospitalized with SARS-CoV-2 CAP, 30 (3%) were vaccinated for COVID-19 prior to hospitalization. All 30 patients were vaccinated with the BNT162b2 (Pfizer–BioNTech) vaccine; seven (23%) received two doses, and 14 (47%) received one dose. The remaining nine patients did not specify their vaccine dose. This study preceded booster vaccine doses. Median time since the last COVID-19 vaccination dose received prior to hospitalization was 11 days (IQR 5, 13), with a range of 2–76 days.

Comparisons of SARS-CoV-2 CAP patients' race and ethnicity with the Louisville population are shown in **Figure 1**. There were no statistically significant differences in race and ethnicity between our cohort and the Louisville population.

Comparisons of SARS-CoV-2 CAP patients' comorbidities with the Louisville population are shown in **Figure 2**. Every comorbidity was significantly different from the Louisville population.

Stages of clinical presentation at the time of hospital admission are depicted in **Figure 3**. While the clinical
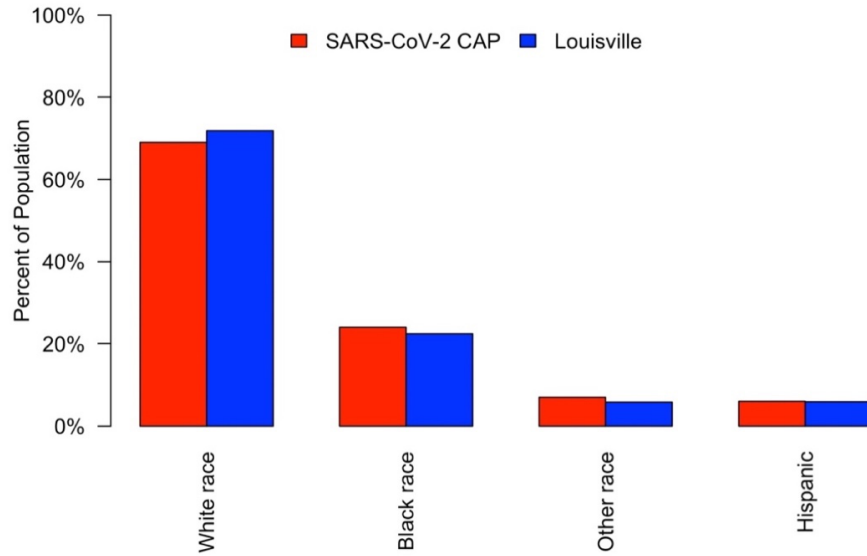
Figure 1. Comparisons race and ethnicity of hospitalized SARS-CoV-2 CAP patients with the Louisville population with associated *P*-values from hypothesis testing. All data are reported as a percentage of the population for that demographic.
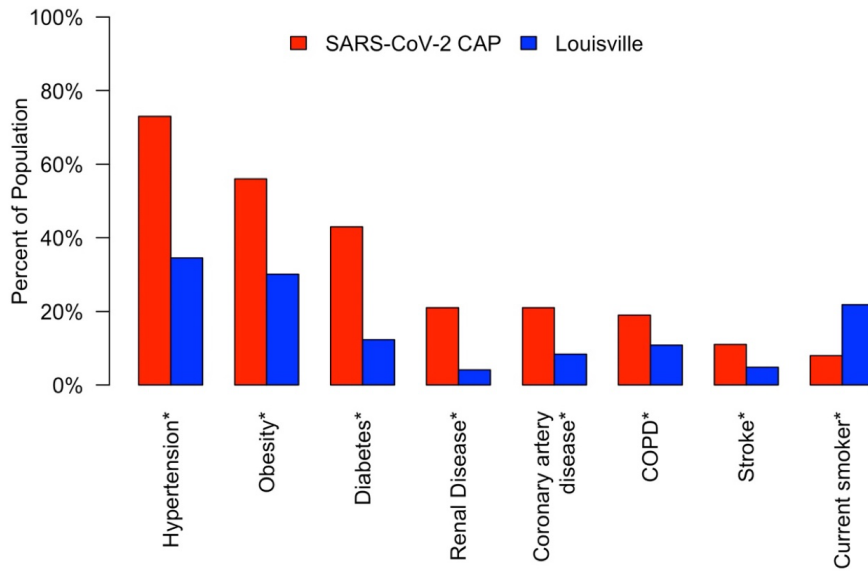

Figure 2. Comparison of rates of comorbidities of hospitalized SARS-CoV-2 CAP patients with rates in the Louisville population with associated *P*-values from hypothesis testing. *P*>0.001 for all comparisons. All data are reported as a percentage of the population for that comorbidity.

Table 1. Patient demographics and medical history of 1,013 patients hospitalized with SARS-CoV-2 community-acquired pneumonia.

	n (%)
Total n	1,013
Age, years (median [IQR])	65 [55, 75]
Male sex	532 (53)
Race	
African American	244 (24)
White	704 (69)
Other	66 (7)
Hispanic	58 (6)
Smoking history	
Never	533 (53)
Former	396 (39)
Current	84 (8)
Hypertension	740 (73)
Obesity	571 (56)
Diabetes	434 (43)
Coronary artery disease	216 (21)
Renal disease	210 (21)
Chronic obstructive pulmonary disease	192 (19)
Obstructive sleep apnea	192 (19)
Congestive heart failure	148 (15)
Asthma	124 (12)
Cerebrovascular disease	110 (11)
Neoplastic disease (active or within the last year)	101 (10)
Other immunocompromising conditions or therapies	76 (8)
Liver disease (non-cirrhotic)	30 (3)
Cirrhosis	15 (1)
Prior myocardial infarction	98 (10)
Peripheral vascular disease	34 (3)
Dementia	46 (5)
Connective tissue disorder	14 (1)
Peptic ulcer disease	19 (2)
Hemiplegia	16 (2)
Solid tumor	
Localized	72 (7)
Metastatic	25 (2)
Leukemia	12 (1)
Lymphoma	8 (1)
Acquired immunodeficiency syndrome	1 (0)
Charlson comorbidity index (median [IQR])	3 [2, 5]

Abbreviations: IQR, interquartile range.

presentation of SARS-CoV-2 CAP with no supplemental oxygen requirement (stage 1) was present in 40% of patients at the time of admission, 60% of the patients required some form of supplemental oxygen at hospital admission.

Geospatial epidemiology

The kernel density heatmap of each patient's home address at the time of hospitalization due to SARS-CoV-2 CAP is depicted in **Figure 4**.

The age distribution of adults hospitalized with SARS-CoV-2 CAP is depicted in **Figure 5**. A comparison of the percentage distribution of age groups between adults hospitalized with SARS-CoV-2 CAP and the adult population of Louisville is shown in **Figure 6.**

Signs and symptoms in patients with SARS-CoV-2 CAP are depicted in **Table 2.** The most common symptoms reported at admission were dyspnea and cough.

Vital signs and laboratory values for patients hospitalized with SARS-CoV-2 CAP at admission are depicted in **Table 3.**

Relevant inflammatory markers at the time of hospitalization or first available value are depicted in **Table 4.**

Medications for in-hospital treatment of adults hospitalized with SARS-CoV-2 CAP are shown in **Table 5.**
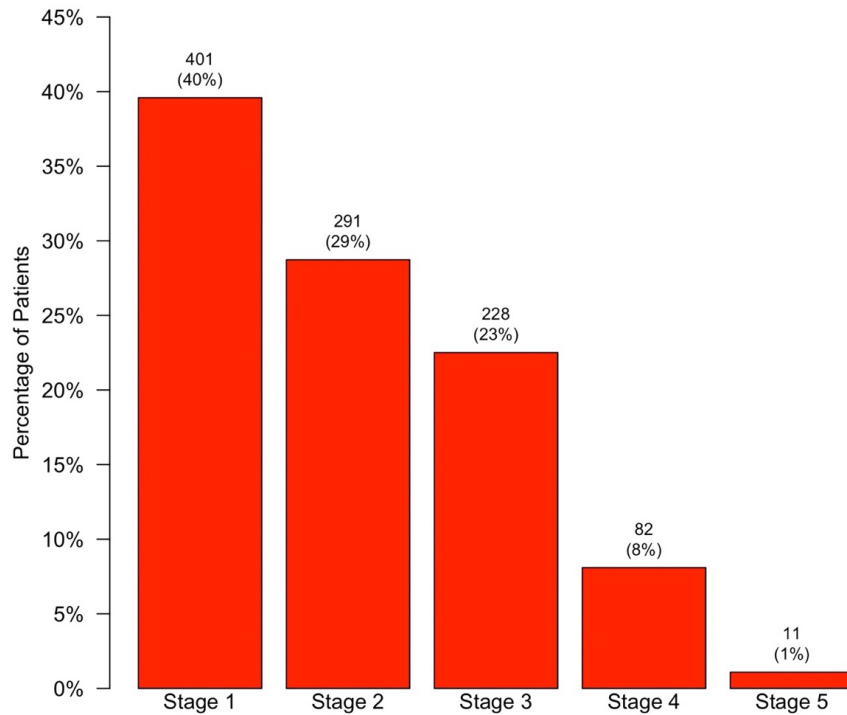
Stage 1: SARS-CoV-2 CAP with no supplemental oxygen
Stage 2: SARS-CoV-2 CAP with low-flow supplemental oxygen
Stage 3: SARS-CoV-2 CAP with high-flow supplemental oxygen or non-invasive ventilation
Stage 4: SARS-CoV-2 CAP with invasive mechanical ventilation
Stage 5: SARS-CoV-2 CAP with ARDS

Figure 3. Frequency and percentage of hospitalized patients with SARS-CoV-2 CAP in each of the 5 stages of clinical presentation at the time of hospital admission.

Coinfections

A total of 237 patients had a coinfection with SARS-CoV-2 CAP. The list of patients with community-acquired (*n*=110) and hospital-acquired (*n*=127) coinfections is summarized in **Table 6**. For each type of coinfection, the culture sites were characterized.

Severity of disease, comorbid burden, and associated rates of in-hospital mortality

The severity of SARS-CoV-2 CAP at the time of hospitalization—according to Pneumonia Severity Index and CURB-65 score—and comorbidity burden according to the Charlson Comorbidity Index are depicted in **Figures 7A–C**; associated rates of death or hospice care per class or score are depicted in **Figures 7D–F**.

Cardiac and cardiovascular events

The prevalence of cardiac and cardiovascular events in our cohort is depicted in **Table 7**. The most common event was a new arrhythmia, which was observed in

70 (7%) patients.

Clinical outcomes

Out of 1,013 patients hospitalized with SARS-CoV-2 CAP, 822 (81%) patients were discharged alive, and 191 (19%) patients died or went to hospice care. The median length of hospital stay was 7 days. Time to hospital discharge and time to in-hospital death are depicted in **Figures 8A** and **8B**, respectively. A total of 359 (35%) patients were admitted to the ICU, with 209 ICU admissions occurring on the first day of hospitalization. A total of 223 (22%) patients required invasive mechanical ventilation during their hospitalization. Time to ICU discharge and time to extubation are depicted in **Figures 8C** and **8D**, respectively. Time to the first cardiac or cardiovascular event for the 180 patients who experienced an event is depicted in **Figure 8E**. During hospitalization, a total of 99 (10%) patients experienced septic shock, and a total of 44 (4%) patients experienced ARDS. Time to septic shock and time to ARDS are depicted in **Figures 8F** and **8G**, respectively.

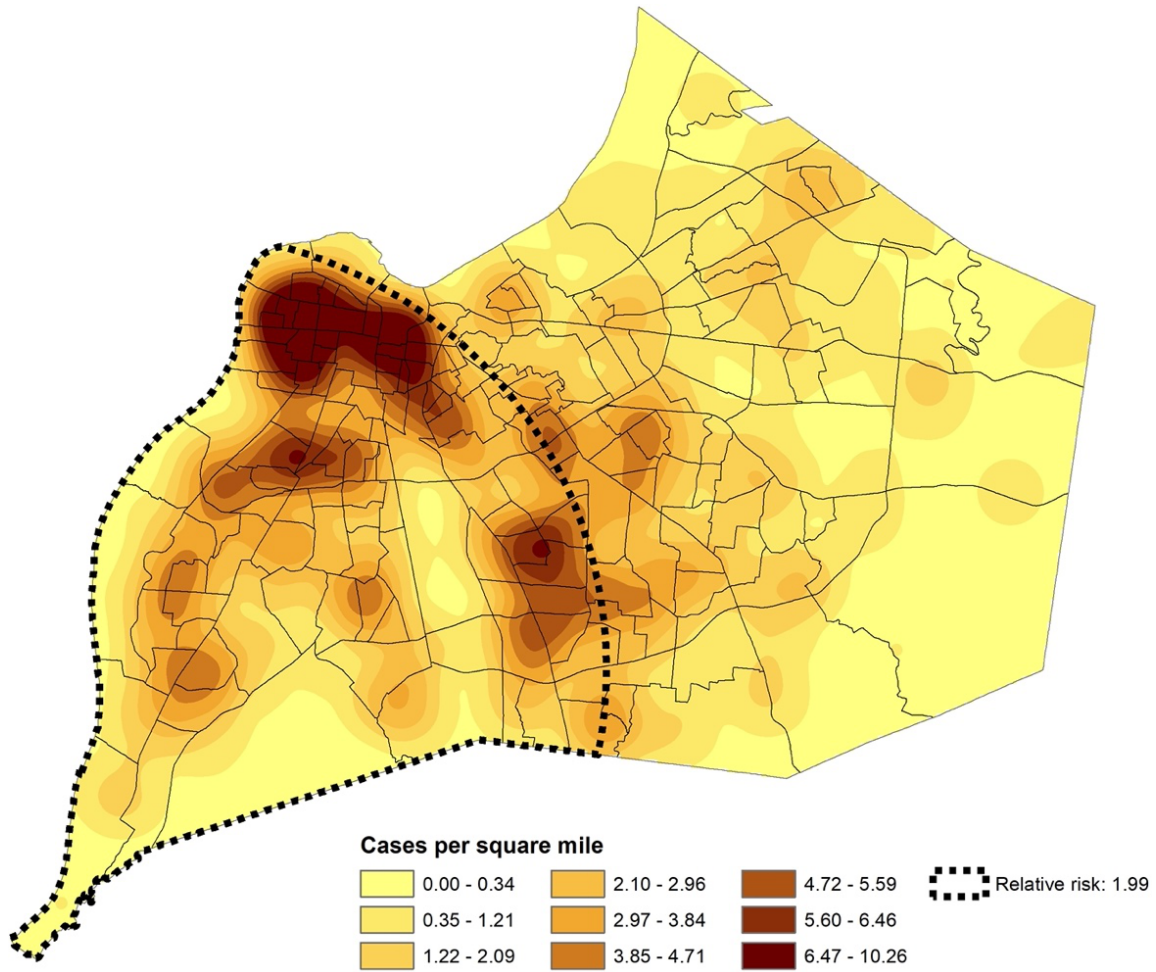In-hospital mortality stratified by ICU admission, de-

Figure 4. Kernel density heatmap of residential addresses of patients hospitalized with SARS-CoV-2 CAP. Dotted lines indicate areas with an elevated risk of hospitalization due to SARS-CoV-2 CAP.

mographics, and comorbidities is depicted in **Figure 9**. Death was observed in 45% of patients who were admitted to the ICU.

Discussion

Findings

The primary findings of our study show that from September 2020 through March 2021, the distribution of race of hospitalized patients with SARS-CoV-2 CAP matches the distribution of race in the city of Louisville, as opposed to what we previously demonstrated in July 2020.[12] In the present study, we observed an increased risk of hospitalization due to SARS-CoV-2 CAP among patients in the western half of the city, which has a higher prevalence of minority populations and has been associated with a lower socioeconomic position.[13]

This population of hospitalized SARS-CoV-2 CAP patients was older, with a median age of 65 years compared to 63 years as reported in March through July 2020.[12] Hypertension remained the most prevalent comorbidity among hospitalized patients with SARS-CoV-2 CAP, which is consistent with findings from a large multicenter study conducted in the United States and recent COVID-19 data published by the Centers for Disease Control and Prevention (CDC).[14, 15] In addition to hypertension, obesity, diabetes, renal disease, coronary artery disease, chronic obstructive pulmonary disease (COPD), and cerebrovascular disease were also shown to have higher prevalence rates among hospitalized patients with SARS-CoV-2 CAP compared to the general Louisville population. Given the comorbid status of hospitalized patients, the median Charlson comorbidity index score was 3 (IQR 2, 5) with an estimated 10-year survival rate of 77%.[7]
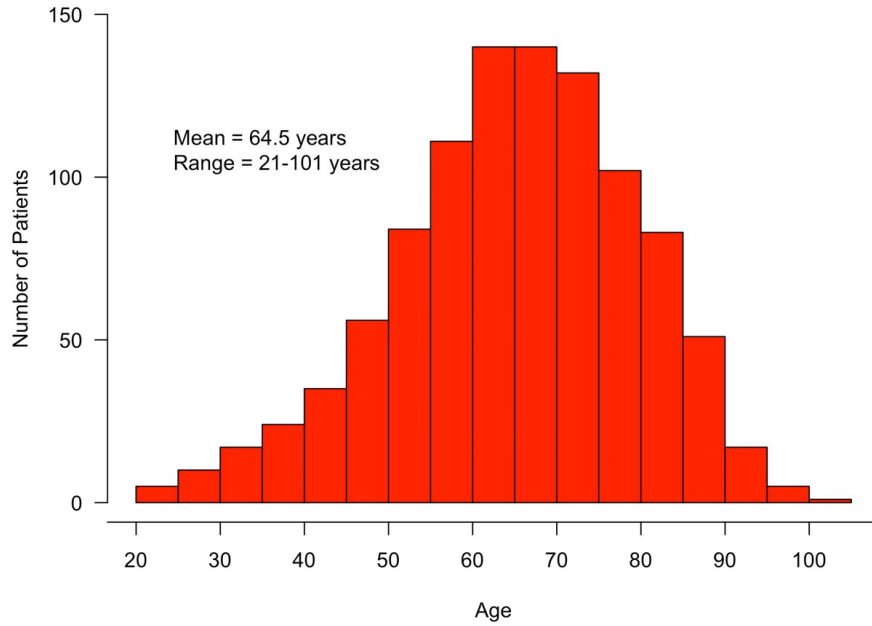
During the study period from September 2020 through

Figure 5. Histogram depicting the distribution of age among patients hospitalized with SARS-CoV-2 CAP.
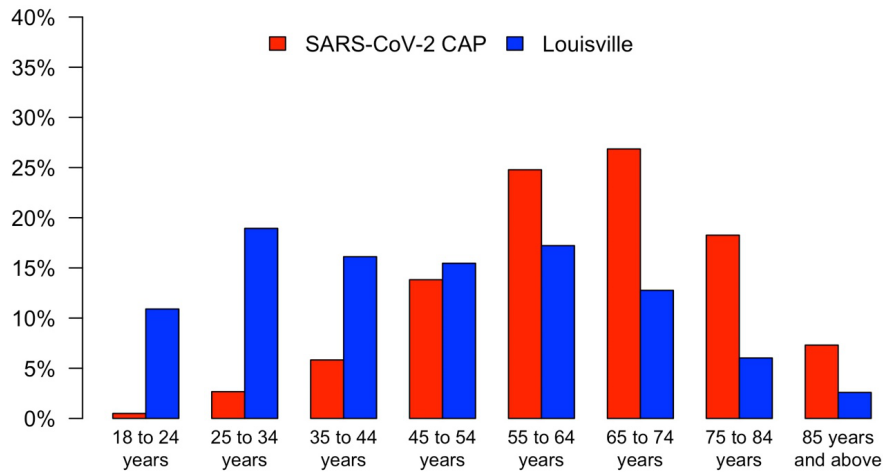

Figure 6. Comparison of SARS-CoV-2 CAP patients' age groups with age groups of the Louisville population. All data are reported as percentage of the population for that comorbidity. **Abbreviations:** PSI, pneumonia severity index, CCI, Charlson comorbidity index.

March 2021, 30 (3%) hospitalized patients were vaccinated for COVID-19 prior to hospitalization; seven (23%) received two doses, and 14 (47%) received one dose. This study preceded booster vaccine doses. A CDC Morbidity and Mortality Weekly Report study done in 13 jurisdictions found similar results, showing that from April 2021 through July 2021, fully vaccinated people accounted for 14% of COVID-19 hospitalizations.[16] While vaccination rates during the time of the present study were relatively low, there were still a few breakthrough cases that required hospitalization. However, it is difficult to draw conclusions as four of the seven fully vaccinated patients were hospitalized within 2 weeks of their second vaccine dose.

At the time of hospital admission, the majority of patients with SARS-CoV-2 CAP presented with shortness of breath, cough, and fever. Vital signs and laboratory findings during the first 24 hours of hospital admission were within normal ranges except for minor deviations in heart rate, systolic blood pressure, SpO_2/FiO_2, PaO_2/FiO_2, blood urea nitrogen, procalcitonin, D-dimer, C-reactive protein, and interleukin-6. Coinfections were identified in 23% of our SARS-CoV-2 CAP patients. Hospital-acquired and community-acquired coinfections included *Escherichia coli*, methicillin-resistant *Staphylococcus aureus* (MRSA), and other Staphylococcus species. Studies have shown a general decline in influenza and influenza-like ill-
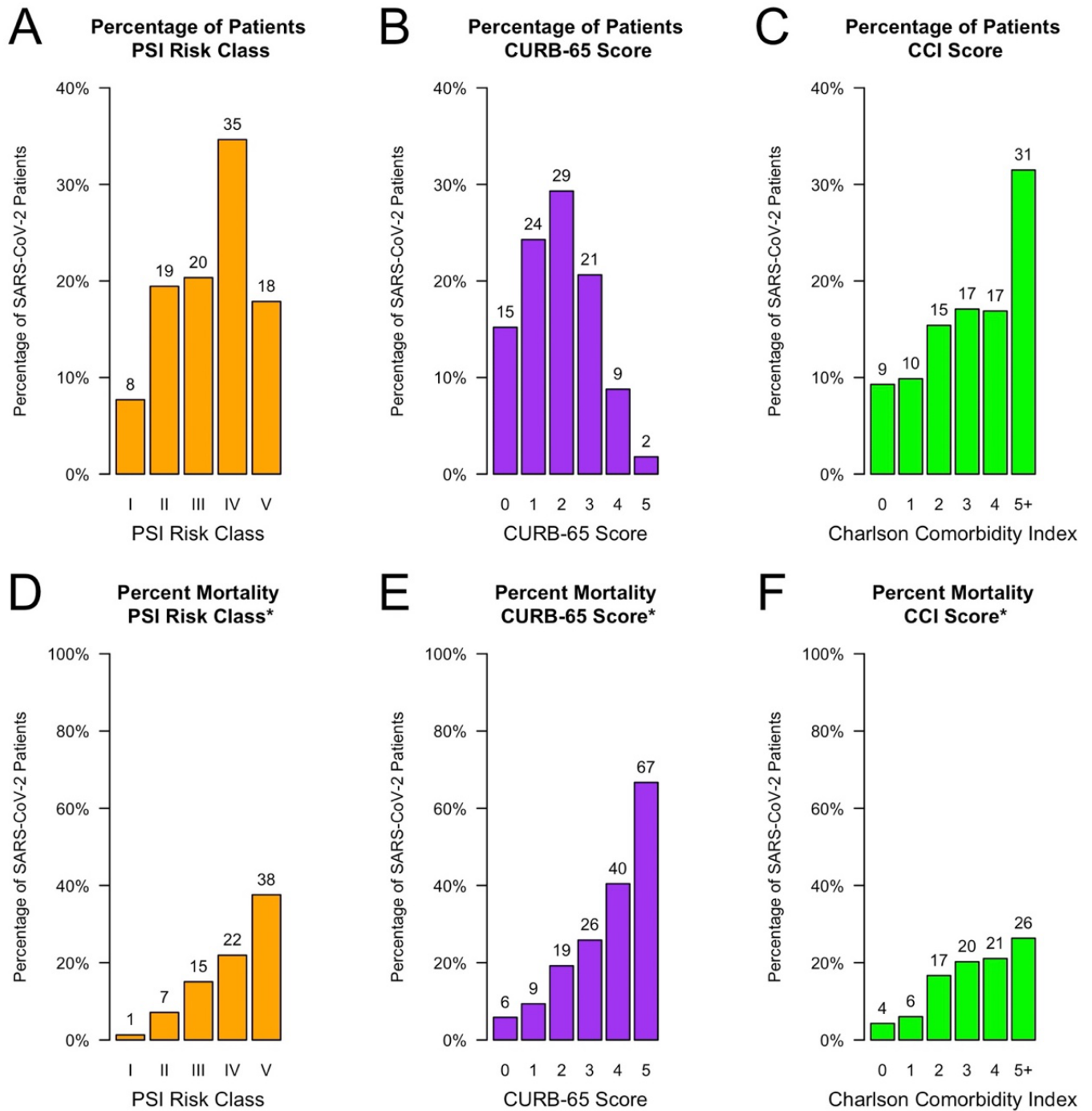
Figure 7. The distribution of patients hospitalized with SARS-CoV-2 CAP by PSI risk class (orange), CURB-65 score (purple), and Charlson comorbidity index (green) are shown in the top row of the figure. Rates of in-hospital mortality by PSI risk class, CURB-65 score, and Charlson comorbidity index are displayed in the bottom row. Asterisks represents a significant linear association with mortality.
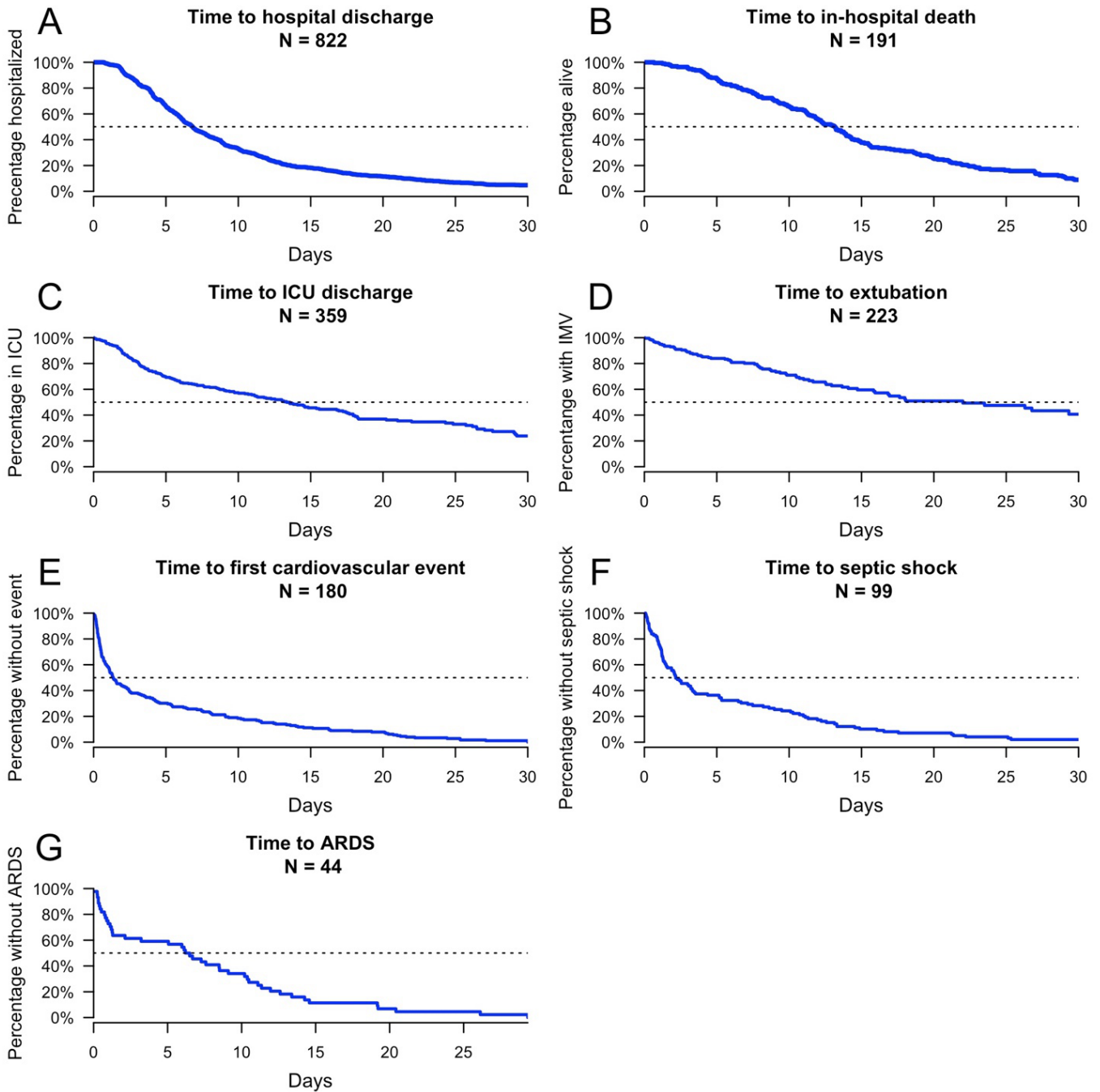
Figure 8. Time-to-event outcomes in days of patients hospitalized with SARS-CoV-2 CAP: A) time to hospital discharge, B) time to in-hospital death, C) time to intensive care unit discharge, D) time to extubation, E) time to first cardiovascular event, F) time to septic shock, G) time to ARDS.

Table 2. Signs and symptoms for patients hospitalized with SARS-CoV-2 CAP.

	n (%)
Total n	1,013
Dyspnea	757 (75)
Cough	683 (67)
Fever or subjective fever	518 (51)
Fatigue	450 (44)
Myalgia	233 (23)
Nausea	227 (22)
Diarrhea	195 (19)
Sputum	166 (16)
Chest pain	154 (15)
Vomit	128 (13)
Headache	125 (12)
Confusion	101 (10)
Ageusia	91 (9)
Anosmia	78 (8)
Dizziness	61 (6)
Congestion	54 (5)
Sore throat	30 (3)
Rhinorrhea	15 (1)
Hemoptysis	12 (1)
Constipation	9 (1)

Table 3. Vital signs and laboratory findings at the time of hospitalization. The third column shows the percentage of patients for whom data were unavailable.

	Median [IQR]	% Data missing
Total n	1,013	
Heart rate (beats/min)	100.0 [83.0, 111.5]	0.2
Respiratory rate (breaths/min)	23.0 [20.0, 28.0]	0.2
Systolic blood pressure (mmHg)	122.0 [106.0, 139.0]	0.2
Diastolic blood pressure (mmHg)	63.0 [53.0, 74.0]	0.2
Temperature (°C)	37.2 [36.8, 38.0]	0.2
SpO_2/FiO_2	332.1 [230.0, 438.1]	1.2
PaO_2/FiO_2	202.8 [101.5, 290.5]	60.6
White blood cell$\times$1,000 per uL	7.3 [4.8, 11.5]	0.7
Neutrophils$\times$1,000 per uL	5.8 [3.5, 9.6]	9.3
Lymphocytes$\times$1,000 per uL	0.8 [0.5, 1.1]	10.6
Neutrophil/lymphocyte	7.4 [4.1, 13.8]	10.6
Hematocrit (%)	37.9 [33.8, 41.8]	0.7
Glucose (mg/dL)	135.0 [113.0, 187.0]	0.7
Blood urea nitrogen (mg/dL)	21.0 [14.0, 34.0]	0.8
Creatinine (mg/dL)	1.1 [0.8, 1.6]	0.7

Abbreviations: IQR, interquartile range.

Table 4. Inflammatory markers at time of hospitalization or first available value. The third column shows the percentage of patients for whom data were unavailable.

	Median [IQR]	% Data missing
Total n	1,013	
Ferritin (ng/dL)	399.0 [190.8, 819.0]	28.9
Procalcitonin (ug/L)	0.2 [0.1, 0.6]	26.2
Lactate (mmol/L)	1.5 [1.1, 2.0]	45.2
D-Dimer (ng/mL)	773.0 [351.8, 1498.0]	28.5
Interleukin-6 (pg/mL)	22.1 [10.5, 56.6]	72.2
C-reactive protein (mg/L)	31.8 [8.2, 97.8]	24

Abbreviations: IQR, interquartile ragne.

Table 5. Medications for the in-hospital treatment of SARS-CoV-2 CAP.

Variable	n (%)
Total n	1,013
Steroids	891 (88)
Low molecular weight heparin	737 (73)
Hydroxychloroquine	2 (0.2)
Remdesivir	556 (55)
Azithromycin	486 (48)
Heparin	259 (26)
Convalescent plasma	191 (19)
Monoclonal antibodies	14 (1)

nesses during the SARS-CoV-2 pandemic, which has been attributed to non-pharmaceutical interventions, such as masking, social distancing, and improved hand hygiene.[17, 18] A large retrospective study published in 2020 showed that hospitalized COVID-19 patients with community- and hospital-acquired coinfections had worse clinical outcomes than patients with SARS-CoV-2 alone, which may be an important consideration in the use of antibiotic therapies.[19]

On the first day of hospital admission, 60% of the patients hospitalized with SARS-CoV-2 CAP required some form of oxygen. Approximately 21% of patients were admitted to the ICU on the first day of hospital admission. Other studies, including the data previously described from March through July 2020, show a high rate of ICU admission on the first day of hospitalization.[12, 20, 21] The severity of SARS-CoV-2 CAP cases

at hospital admission may suggest a delay by some patients in seeking medical care.

Some of the most frequently used medications in the treatment of hospitalized patients with SARS-CoV-2 CAP during September 2020 through March 2021 were steroids, remdesivir, and convalescent plasma. We observed an increase in the use of these medications compared to the data we previously described from March through July 2020.[12] There was also a dramatic decline in the use of hydroxychloroquine after the U.S. Food & Drug Administration revoked the emergency use authorization to use hydroxychloroquine and chloroquine to treat COVID-19 in certain hospitalized patients.

The severity of SARS-CoV-2 CAP estimated from the Pneumonia Severity Index, the CURB-65, and the

Table 6. Number of patients with coinfections, including micro-organisms and culture sites, in adults hospitalized with SARS-CoV-2 CAP.

Organism	Total n	Culture site (n)
Community-acquired coinfections	110	
Staphylococcus non-aureus	25	Blood culture (22), sputum (1), urine culture (2)
Escherichia coli	16	Urine culture (15), NP swab (1)
MRSA	12	Blood culture (5), sputum (4), NP swab (3)
MSSA	8	Blood culture (4), sputum (4)
Pseudomonas aeruginosa	6	Sputum (4), urine culture (2)
Other Streptococcus species	6	Blood culture (4), urine culture (2)
Klebsiella pneumoniae	4	Sputum (2), urine culture (2)
Influenza A Untyped	3	NP swab (3)
Morganella species	3	Blood culture (1), urine culture (2)
Proteus species	3	Blood culture (1), sputum (1), urine culture (1)
Streptococcus pneumoniae	3	Blood culture (1), BAL (1), urinary antigen (1)
Aspergillus species	2	Blood culture (1), BAL (1)
Enterobacter species	2	Urine culture (2)
Fusobacterium species	2	Blood culture (2)
Influenza B	2	NP swab (2)
Klebsiella aerogens	2	Blood culture (1), urine culture (1)
Lactobacillus	2	Urine culture (2)
Streptococcus pyogenes	2	Blood culture (1), OP swab (1)
Aerococcus urinae	1	Urine culture (1)
Group B *Streptococcus agalactiae*	1	Blood culture (1)
Moraxella osloensis	1	Blood culture (1)
Hospital-acquired coinfections	127	
MRSA	23	Blood culture (3), sputum (15), BAL (2), urine culture (2), NP swab (1)
Staphylococcus non-aureus	21	Blood culture (19), sputum (1), urine culture (1)
Escherichia coli	19	Blood culture (2), sputum (7), BAL (1), urine culture (9)
MSSA	13	Blood culture (2), sputum (11)
Klebsiella pneumoniae	8	Blood culture (2), sputum (5), urine culture (1)
Pseudomonas aeruginosa	7	Sputum (2), BAL (1), urine culture (4)
Enterobacter species	6	Blood culture (2), sputum (1), BAL (1), urine culture (2)
Stenotrophomonas species	4	Sputum (3), BAL (1)
Aspergillus species	3	Sputum (2), serology (1)
Citrobacter species	3	Sputum (2), BAL (1)
Haemophilus influenzae	3	Sputum (3)
Serratia species	3	Blood culture (2), sputum (1)
Klebsiella oxytoca	2	sputum (2)
Proteus species	2	Sputum (1), urine culture (1)
Pseudomonas non-aeruginosa	2	Sputum (2)
Other Streptococcus o species	2	Blood culture (1), sputum (1)
Achromobacter xylosoxidans	1	BAL (1)
Acinetobacter species	1	Sputum (1)
Aerococcus sanguinicola	1	Urine culture (1)
Klebsiella varicola	1	Blood culture (1)
Mycobacterium avium	1	Sputum (1)
Streptococcus pyogenes	1	Blood culture (1)

Abbreviations: BAL, bronchoalveolar lavage; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*; NP, nasopharyngeal; OP, oropharyngeal.

Table 7. Cardiac and cardiovascular events in patients hospitalized with SARS-CoV-2 CAP.

Variable	n (%)
New arrhythmia	69 (7)
Cardiac arrest	33 (3)
Heart failure	31 (3)
Acute myocardial infarction	29 (3)
Pulmonary embolism	23 (2)
Acute worsening of chronic arrhythmia	15 (1)
Pulmonary edema	15 (1)
Deep vein thrombosis	15 (1)
Cerebrovascular accident	12 (1)
Cardiogenic shock	6 (1)
Myocarditis	1 (<1)
Any event	180 (18)

Charlson comorbidity index showed a significant linear relationship with in-hospital mortality; as each score or index increased, mortality increased as well. CURB-65 score differentiated risk of death during hospitalization, from 6% risk of death in patients with a score of 0 to 57% risk of death for patients with a score of 5. A Charlson comorbidity index score of 5 was observed in 32% of patients and accounted for 20% of in-hospital mortality. The associated 10-year survival for a Charlson Comorbidity Index score of 5 is 21%, suggesting a poor prognosis for long-term outcomes.[6] The relationship between severity of disease indices and mortality shown in our study makes the utilization of these tools crucial for patient management and prognosis. Similar studies have shown that the PSI, CURB-65, and the Charlson comorbidity index can predict in-hospital mortality; however, validation in SARS-CoV-2 CAP patients remains controversial.[22, 23]

In the present study, we assessed six binary outcomes and seven time-to-event outcomes. Compared to our previously published data from March through July 2020, the mean length of hospital stay remained around 7 days for patients who were discharged alive; however, the in-hospital mortality rate increased from 17% to 19%. In comparison to early pandemic data, there were decreases in ICU admission (39.4% *vs.* 35.7%), invasive mechanical ventilation use (25.2% *vs.* 22.2%), development of a cardiovascular event during hospitalization (19% *vs.* 18%), development of septic shock (13.4% *vs.* 9.7%), and development of ARDS (15.5% *vs.* 4.4%). These lower rates show the importance of proper assessment of clinical outcomes of SARS-CoV-2 CAP and therapeutic interventions for ongoing research efforts. Similar findings were noted in studies comparing the clinical outcomes of patients hospitalized early in the pandemic to later, showing significant decreases in IMV use and cardiovascular events and small or nonsignificant increases in mortality.[24-26]

Strengths

The epidemiological data in our study, including demographic characteristics, socioeconomic characteristics, and health behaviors, are derived from a hospital system that serves a population highly representative of the general United States population.[27] Another strength of our study is our inclusion criteria, selecting only SARS-CoV-2 CAP. The common discussion of COVID-19 has focused on cases and the case fatality rate, regardless of organ involvement. Hence, comparing studies becomes more difficult when patients with and without pneumonia are analyzed together. The wide range of clinical outcomes evaluated in our study, including binary and time-to-event outcomes, increases the internal validity of the results. Lastly, the timing of this data collection period (September 2020 through March 2021), coincides with the emergence of the SARS-CoV-2 Delta variant in the US; hence, our findings can help to elucidate the clinical characteristics of this new variant and its differences from earlier variants.

Limitations

There are a few limitations to acknowledge. The results of this retrospective study may not be generalizable to the overall population; patients who presented to the emergency department with COVID-19 but were discharged home or those who did not seek medical attention may have significantly different characteristics to patients hospitalized with COVID-19 pneumonia. Due to the nature of the study, we were not able to collect more detailed information on non-hospitalized patients with COVID-19 in the city of Louisville; therefore, we could not evaluate the risk of hospitalization or the role of severity scores in predicting ambulatory care.

Conclusion

In conclusion, we observed considerable in-hospital mortality, as nearly one in five patients hospitalized
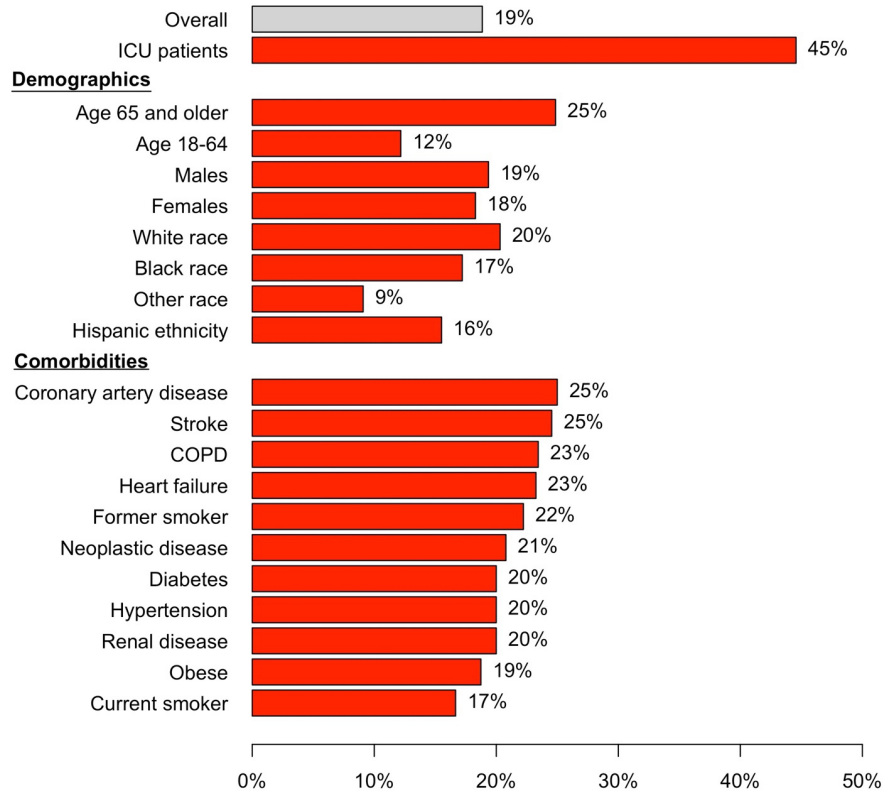
Figure 9. In-hospital mortality rates by intensive care unit admission, demographics, and comorbidities of patients hospitalized with SARS-CoV-2 CAP. The percentage in each group is displayed.

with SARS-CoV-2 CAP died, and nearly one in two patients admitted to the ICU with SARS-CoV-2 CAP died. The elderly, males, and comorbid patients were overrepresented among hospitalized patients with SARS-CoV-2 CAP compared to the Louisville population. These patients were also more likely to require ICU care and had worse clinical outcomes. The most prevalent comorbidities in our population were coronary artery disease, cerebrovascular disease, COPD, hypertension, diabetes, renal disease, and obesity. Future studies of hospitalized patients with SARS-CoV-2 CAP should also collect data on non-hospitalized patients to identify risk factors for hospitalization, as well as conducting analytical studies to examine risk factors and develop new management and treatment strategies for patients hospitalized with SARS-CoV-2 CAP.

Conflict of Interest: All authors declared no conflict of interest in relation to the main objective of this work.

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