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ORIGINAL RESEARCH

Infectious Disease

Radiographic findings of SARS-CoV-2 infection

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Abstract

Study objective: The 2019–20 coronavirus pandemic is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19). This study was undertaken to identify and compare findings of chest radiography and computed tomography among patients with SARS-CoV-2 infection.

Methods: This retrospective study was undertaken at a tertiary care center. Eligible subjects included consecutive patients age 18 and over with documented SARS-CoV-2 infection between March and July 2020. The primary outcome measures were results of chest radiography and computed tomography among patients with documented SARS-CoV-2 infection.

Results: Among 724 subjects, most were admitted to a medical floor (46.4%; N = 324) or admitted to an ICU (10.9%; N = 76). A substantial number of subjects were intubated during the emergency department visit or inpatient hospitalization (15.3%; N = 109). The majority of patients received a chest radiograph (80%; N = 579). The most common findings were normal, bilateral infiltrates, ground-glass opacities, or unilateral infiltrate. Among 128 patients who had both chest radiography and computed tomography, there was considerable disagreement between the 2 studies (52.3%; N = 67; 95% confidence interval: 43.7% to 61.0%).). The presence of bilateral infiltrates (infiltrates or ground-glass opacities) was associated with clinical factors including older age, ambulance arrivals, more urgent triage levels, higher heart rate, and lower oxygen saturation. Bilateral infiltrates were associated with poorer outcomes, including higher rate of intubation, greater number of inpatient days, and higher rate of death.

Conclusions: Common radiographic findings of SARS-CoV-2 infection include infiltrates or ground-glass opacities. There was considerable disagreement between chest radiography and computed tomography. Computed tomography was more accurate in defining the extent of involved lung parenchyma. The presence of bilateral infiltrates was associated with morbidity and mortality.

1 | INTRODUCTION

1.1 | Background

The 2019–20 coronavirus pandemic is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19). The pandemic was recognized by the World Health Organization on March 11, 2020. As of November 16, 2020 more than 54 million people have been infected with SARS-2-CoV-2, with over 1.3 million deaths worldwide.[1] There have been over 10 million cases and over 245,000 total deaths in the United States in 2020.[2] In the United States, age, racial, ethnic, and sex-related differences in health outcomes from SARS-CoV-2 infection are recognized. African American race, increasing age, multiple comorbidities, public insurance, residence in a low-income area, and obesity were associated with increased odds of hospital admission.[3]

SARS-CoV-2 infection may present with a myriad of clinical presenting signs and symptoms, including constitutional, pulmonary, gastrointestinal (GI), or central nervous system (CNS) involvement.[4] Clinical manifestations of disease range from asymptomatic infections to fulminant disease, sepsis, respiratory failure, and death. Approximately 5% of infected patients and 20% of those hospitalized require intensive care, and more than 75% of hospitalized patients require supplemental oxygen.[5]

1.2 | Importance

Chest radiography (CXR) and computed tomography (CT) are commonly used to assess pulmonary infection.[6] Radiographic findings of pulmonary SARS-CoV-2 infection may include consolidation, ground-glass opacities (GGO), or a mixed radiographic appearance.[7,8,9,10] Other less common findings have been reported, including crazy paving pattern, fibrous stripes, subpleural lines, architectural distortion, air bronchogram sign, vascular thickening, nodules, lymphadenopathy, and pleural effusion.[4] Peripheral and posterior lungs are commonly affected.[11] Temporal changes in radiographic appearance have been described, with a peak at 10–12 days from symptom onset.[12] Radiographic findings may precede positive SARS-CoV-2 test positivity.[13] A recent database review identified wide variability in sensitivity of radiography and CT among COVID-19 infections.[14]

1.3 | Goals of this investigation

This study was undertaken to identify and compare findings of CXR and CT among patients with SARS-CoV-2 infection.

2 | METHODS

2.1 | Study design and setting

This retrospective study was undertaken at a tertiary care center. The study institution's emergency department is a Level 1 trauma center with an annual census of ≈95,000. The study was approved by the Wright State University Institutional Review Board.

2.2 | Selection of participants

Eligible subjects included patients age 18 and over with documented SARS-CoV-2 infection between March and July 2020, who were seen in our ED or admitted to our institution. Documented infection was defined for this study as positive reverse transcription-polymerase chain reaction (RT-PCR) test at our institution or documented positive COVID-19 test from another institution (undefined test). Subjects were identified by our institution's infectious disease database of SARS-CoV-2 positive cases. Subjects were excluded if they were under age 18. A priori, a minimum sample size of 366 patients was selected based on producing a 2-sided 95% confidence interval (CI) with a width equal to $\pm$10% when the sample proportion is 60%.

2.3 | Interventions and methods of measurement

Data were extracted manually from the electronic medical record, including ED and inpatient records. Data were extracted by study authors, who were trained on medical record chart extraction. We defined all study data and variables before initiating the study and trained our data abstractors regarding study definitions and data entry. Medical student authors were trained with general training and at least 2 collaborative chart reviews and regular weekly chart audits. Resident and faculty authors were trained regarding chart abstraction and reviewed at weekly chart audits. For eligible subjects, we extracted demographic information, triage vital signs and oxygenation, comorbidities, COVID-19 test results, CXR reports, CT reports, and ED and inpatient hospital course and disposition. All chart abstractions were reviewed by the principal investigator at least weekly, and missing data and discrepancies were remedied.

2.4 | Outcome measures

The primary outcome measures were results of CXR and CT among patients with documented SARS-CoV-2 infection. Radiograph

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The Bottom Line

This study evaluated computed tomography (CT) and radiograph findings in over 700 coronavirus disease 2019 (COVID-19) polymerase chain reaction positive patients presenting to a large urban emergency department. Radiograph and CT findings diverged in 52% of cases with 43% of all plain radiographs interpreted as normal. These findings underscore the limitations of plain radiography and provide clinically relevant information regarding the accuracy of imaging in COVID-19 patients.

interpretations as recorded by attending radiologists in electronic medical records were reviewed and recorded and discrepancies were categorized. The term "bilateral infiltrates" was defined as a radiologist report of bilateral infiltrates or opacities. The term "no bilateral infiltrates" was defined as all other readings, including normal, or unilateral infiltrate. Secondary outcome measures were intubation, hospital days, and final disposition. Triage categories were based on Emergency Severity Index (ESI), which ranks acuity using 5 levels, with 1 being most urgent and 5 being non-urgent. Multiple studies have demonstrated this 5-level ESI to be reliable and valid.[15,16,17]

2.5 | Primary data analysis

Continuous data are presented with medians, interquartile ranges, and 95% CIs and compared between subgroups using Mann Whitney Wilcoxon tests. Categorical data are presented with frequency counts, percentages, and 95% CIss and compared between groups (ie, bilateral infiltrates vs no bilateral infiltrates, died vs discharged alive) using chi-square or Fisher's exact tests. Data were analyzed using SAS (version 9.4; SAS Institute, Inc., Cary, NC).

3 | RESULTS

3.1 | Characteristics of study subjects

A total of 724 subjects were identified with documented SARS-CoV-2 infection at our institution between March and July 2020. A slight majority were female (52.6%; N = 381). Subjects arrived by walk-in (50.1%; N = 357) or ambulance (49.9%; N = 356). The majority of subjects were triaged as Level 2 or Level 3. The most common preexisting medical conditions were hypertension (51.3%; N = 370) and diabetes (29.4%; N = 212) (Table 1).

3.2 | Main results

Most patients were seen in the ED (96.4%; N = 698). Most were admitted to a medical floor (46.4%; N = 324) or admitted to an ICU (10.9%;

TABLE 1 Characteristics of 724 subjects with SARS-CoV-2 infection

	Median (interquartile Range) or n (%)
Age (y)	54.0 (35.0, 68.0)
Gender	
Male	343 (47.4)
Female	381 (52.6)
Mode of arrival	
Walk-in	357 (50.1)
Ambulance	356 (49.9)
Emergency Severity Index triage level	
1 or 2	207 (30.2)
3	358 (52.3)
4 or 5	120 (17.5)
Past medical history	
Asthma	90 (12.5)
Chronic obstructive pulmonary disease	91 (12.6)
Heart disease	167 (23.2)
Hypertension	370 (51.3)
Diabetes	212 (29.4)
Other lung disease	30 (4.6)
Triage vital signs	
Temperature (degrees Fahrenheit)	99.0 (98.4, 100.1)
Blood pressure (systolic mm Hg)	133.5 (119.0, 147.0)
Heart rate	92.5 (81.0, 104.0)
Respiratory rate	18.0 (16.0, 20.0)
O2 saturation	96.0 (94.0, 98.0)
ED disposition	
Discharged home	297 (42.6)
Admit med/surg	324 (46.4)
Admit ICU	76 (10.9)
Skilled nursing facility	1 (0.1)
Intubated	109 (15.3)
Inpatient days (for subjects with 1 or more days)	7.0 (4.0, 12.0)
Hospital disposition	
Discharged home	575 (79.4)
Skilled nursing facility	98 (13.5)
Expired	51 (7.0)

SARS-CoV-2, severe acute respiratory syndrome coronavirus 2

N = 76). Others were discharged home (42.6%; N = 297) or discharged to a skilled nursing facility (<1%; N = 1). A substantial number of subjects were intubated during the ED visit or inpatient hospitalization (15.3%; N = 109).

The majority of patients received a chest radiograph (80%; N = 579). The most common findings were normal, bilateral infiltrates, GGO, or unilateral infiltrate (Figures 1 and 2). Normal radiographs were found in
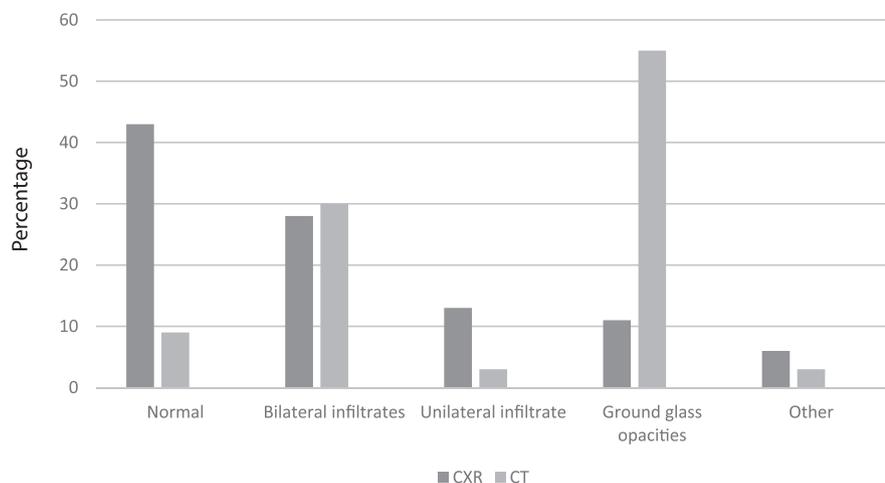
FIGURE 1 Radiographic findings among subjects with SARS-CoV-2 infection. CT, computed tomography; CXR, chest radiography; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2
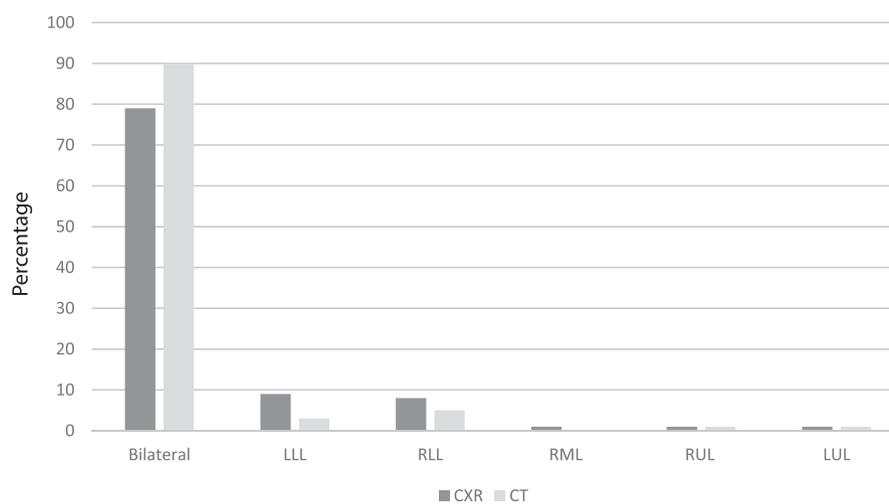

FIGURE 2 Location of radiographic findings among subjects with SARS-CoV-2 infection. CT, computed tomography; CXR, chest radiography; LLL, left lower lobe; LUL, left upper lobe; RLL, right lower lobe; RML, right middle lobe; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2

43% of cases that had chest radiographs (N = 249). Among 128 patients who had both CXRy and CT, 61 (47.4%, 95% CI: 39.0%–56.3%) had interpretations of imaging studies that agreed, and 67 (52.3%, 95% CI: 43.7%–61.0%) had a discrepancy. In the majority of the discrepancies, CT demonstrated greater extent of involved parenchyma than plain radiography (92.5%; N = 62) (Table 2). Discordant results were noted throughout the study period, suggesting this phenomenon was not limited to individual radiologists.

The presence of bilateral infiltrates (infiltrate or GGO on CXR and/or CT) was associated with clinical factors including older age, ambulance arrivals, more urgent triage levels, higher heart rate (HR), and lower oxygen saturation. Bilateral infiltrates were associated with poorer outcomes, including higher rate of intubation, greater number of inpatient days, and higher rate of death (Table 3)

4 | LIMITATIONS

This study was conducted at a single institution. Results may not be generalizable to other settings. Chart abstractors were not blinded to the study objective. We relied solely on the radiologist's interpretation of the radiographs and CT. Radiologists may be unaware of the clinical information, which may inform radiographic interpretation. Because of the retrospective study design, there was no protocol for ordering imaging studies. Clinicians may have ordered imaging studies based on factors such as severity of illness or other clinical factors. As RT-PCR was used as the inclusion criterion for this study, patients who had a false negative test were not included in this study. Because of the retrospective nature of this study, there was no standardization of timing of RT-PCR and imaging studies.

TABLE 2 Imaging discrepancies between chest radiography and computed tomography among patients with SARS-CoV-2 Infection

Chest radiograph reading	Computed tomography reading	Percentage (%)	N
Normal	Unilateral infiltrate	7.5	5
Normal	Unilateral ground glass opacities	3.0	2
Normal	Bilateral infiltrate	7.5	5
Normal	Bilateral ground glass opacities	13.4	9
Unilateral infiltrate	Bilateral infiltrate	9.0	6
Unilateral infiltrate	Bilateral ground glass opacities	16.4	11
Unilateral infiltrate	Normal	1.5	1
Bilateral infiltrate	Unilateral ground glass opacities	1.5	1
Bilateral infiltrate	Unilateral infiltrate	1.5	1
Bilateral infiltrate	Bilateral ground glass opacities	29.9	20
Unilateral ground glass opacity	Bilateral ground glass opacities	1.5	1
Bilateral ground glass opacities	Bilateral infiltrates	1.5	1
Congestive heart failure	Bilateral infiltrates	1.5	1
Congestive heart failure	Bilateral ground glass opacities	1.5	1
Other discrepancy		3.0	2
Total discrepancies		100	67

SARS-CoV-2, severe acute respiratory syndrome coronavirus 2

5 | DISCUSSION

In this study, we identified 724 subjects with COVID-19 infection at our institution, a tertiary care center in Dayton, Ohio. We found that the majority of patients received a chest radiograph, demonstrating findings including normal, bilateral infiltrates, GGO, or unilateral infiltrates. In our study, we found a high percentage of normal chest radiographs (43%), higher than reported previously in the literature (18%).[14] Among patients who underwent both CXR and CT, there was considerable disagreement of the 2 studies. The presence of bilateral infiltrates was associated with poorer outcomes, including higher rate of intubation, greater number of inpatient days, and higher rate of death.

SARS-CoV-2 infection may cause a variety of clinical symptoms, including pulmonary symptoms. The underlying pathophysiology that leads to typical radiographic findings are largely a reflection of the immune response. SARS-CoV-2 spike proteins bind and enter via angiotensin-converting enzyme 2 (ACE-2) receptors on the apical side of alveolar epithelial cells. Infected cells are then processed by antigen presenting cells, such as dendritic cells and macrophages, and presented to neutrophils and T-cells. As the ACE-2 receptors decrease with age, there is immune senescence as well a robust immune response contributing to the acute damages in the lungs. Inflammatory cells destroy the infected cells and trigger the release of proinflammatory cytokines, primarily interleukin-6 and interleukin-8. Direct damage by neutrophils and cytokines leads to epithelial damage in the alveoli.[18] Damaged lung tissue leads to a collection of fluid and debris displacing air in the pulmonary tree. This collection of material is hyperattenuating on radiographs compared to the surrounding normal lung parenchyma. The focal areas of hyperattenuation reflect the extent of tissue damage, and more diffuse destruction of lung tissue is reflected by broader distribution of lung opacification on chest radiograph.[19]

Acute respiratory distress syndrome (ARDS) may develop, which manifests as diffuse hazy opacification throughout the lung fields on CXR. ARDS is theorized to result from activation of coagulation and inhibition of fibrinolysis within the lung tissue, which leads to deposition of hyperattenuating, fibrin-rich hyaline membrane exudates in the lungs[20].

Imaging in patients with SARS-CoV-2 infection may demonstrate a variety of findings. One study identified GGO as a common finding but also identified normal radiographs in 17.9% of patients with non-severe disease and in 2.9% of those with severe disease. [21] Other studies have identified CXR findings including consolidation, GGO, or less commonly, pleural effusion or pneumothorax.[11,22,23] CT may demonstrate GGO, consolidation, or reticular septal thickening.[24,25] GGO is a common term found in interpretations of imaging when describing COVID-19 pneumonia. GGOs are characterized by areas of hazy increased attenuation of the lung.[26,27] These findings can be to the result of reduction of air or partial filling in the alveolar space, thickening of interstitium, increased perfusion, or a combination.[28] The abnormal filling of reduction of air in the alveolar spaces may be owing to the presence of fluid, blood, or inflammatory cells or a combination of these factors.

Previous studies have demonstrated higher sensitivity of CT compared to CXR in pneumonia.[29] Chest CT has been shown to detect pneumonia-associated findings even in the setting of normal CXR. [30] Chest CT has also been well documented in better diagnosing lung pathology and decreasing overdiagnosis of pneumonia when compared to CXR, indicating a higher specificity. [31] The use of both CXR with a confirmatory chest CT has been shown to improve diagnostic and clinical management of suspected community-acquired pneumonia. [32] In a retrospective study by Ai et al, CT abnormalities with GGO and/or consolidation lesions in the lungs were compared with positive RT-PCR

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TABLE 3 Factors associated with bilateral infiltrates (bilateral or glass opacities) on either CXR or CT

	No bilateral infiltrates	Bilateral infiltrates	P value
N	294	344	
Age (y)	47.0 (33.0, 64.0) (CI: 46.9–51.2)	62.5 (48.0, 73.0] (CI: 58.3–62.1)	<0.001
Mode of arrival			<0.001
Walk-in	175 (59.7) (CI: 54.1–65.3)	127 (37.6)(CI: 32.4–42.7)	
Ambulance	118 (40.3) (CI: 34.7–45.9)	211 (62.4)(CI: 57.3–67.6)	
Emergency Severity Index triage level			overall $P < 0.001$*
1 or 2	61 (20.9) (CI: 16.2–25.6)	143 (45.5)(CI: 40.0–51.0)	
3	171 (58.6) (CI: 52.9–64.2)	159 (50.6)(CI: 45.1–56.2)	
4 or 5	60 (20.5) (CI: 15.9–25.2)	12 (3.8)(CI: 1.7–5.9)	
Temperature (degrees Fahrenheit)	99.1 (98.5, 100.0) (CI: 99.3–99.6)	99.1 (98.4, 100.5) (CI: 99.4–99.8)	0.56
Systolic blood pressure (mm Hg)	136.0 (123.0, 149.0) (CI: 134.8–140.4)	132.0 (118.0, 147.0] (CI: 131.3–137.0)	0.08
Heart rate	90.0 (81.0, 103.0) (CI: 90.0–94.3)	95.0 (82.0, 106.0) (CI: 93.3–97.8)	0.02
Respiratory rate	18.0 (16.0, 18.0) (CI: 17.7–20.0)	20.0 (18.0, 22.0) (CI: 19.7–20.7)	<0.001
Oxygen saturation	97.0 (95.0, 98.0) (CI: 96.3–97.0)	94.0 (92.0, 96.0) (CI: 92.5–93.8)	<0.001
Intubated	5 (1.7) (CI: 0.2–3.2)	104 (30.4)(CI: 25.4–35.1)	<0.001
Inpatient days	4.0 (3.0, 8.0) (CI: 5.0–7.1)	8.0 (5.0, 14.0) (CI: 10.7–13.4)	<0.001
Death	3 (1.0) (CI: 0–2.2)	48 (14.0)(CI: 10.3–17.6)	<0.001

Data are presented as median (interquartile range: 25th percentile, 75th percentile) or frequency count and percentage, and 95% confidence interval (lower limit–upper limit).
*All triage levels were significantly different from each other with $P < 0.001$.
CI, confidence interval; CT, computed tomography; CXR, chest radiography SARS-CoV-2, severe acute respiratory syndrome coronavirus 2

tests. CT findings yielded a high sensitivity result of 97% and specificity of 25%.[33]

Our study identified an association of bilateral infiltrates with morbidity and mortality, including higher rate of intubation, greater number of inpatient days, and higher rate of death. This association is congruent with a previous study that identified bilateral and peripheral infiltrates on chest radiographs as one of numerous predictors of mortality, that also included heart failure, peripheral artery disease, crackles at clinical status, respiratory rate, oxygen support needs, C-reactive protein, and bilateral and peripheral infiltrates on chest radiographs.[34]

Future directions for research on this topic may include a prospective analysis of radiographic findings among concurrent CXR and CT and association with clinical outcomes.

In summary, common radiographic findings of SARS-CoV-2 infection include infiltrates orGGO. There was significant disagreement between CXR and CT. We found a higher rate of normal CXR compared to previously reported data, demonstrating the limitations of this imaging technique in COVID-19 infection. CT was more accurate in defining the extent of involved lung parenchyma. The presence of bilateral infiltrates on CXR or CT was associated with morbidity and mortality.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

CM and JMB conceived of the study. CM, SR, HS, JB, AH, JS, BK, JPA, and JMB participated in data collection. CM, JMB and NB supervised the data analysis. All authors contributed to the manuscript and take responsibility for the manuscript as a whole.

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