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The association of clinically relevant variables with chest radiograph lung disease burden quantified in real-time by radiologists upon initial presentation in individuals hospitalized with COVID-19

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Title:

The association of clinically relevant variables with prospectively quantified chest radiograph lung disease burden upon initial presentation in persons hospitalized with COVID-19

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Declarations of Interest:

None.

Highlights:

- Real-time quantified coronavirus disease 2019 (COVID-19) lung disease burden on presentation chest radiograph is a novel approach to lung disease burden collection and can be adapted for real-time use in many lung diseases.
- An absence of opacities in COVID-19 may be associated with poor oral intake and a prerenal state.
- An increased Charlson Comorbidity Index (CCI > 5) was associated with non-severe chest radiograph findings.
- Chest radiographs that demonstrated disease versus no disease or severe disease versus not severe disease were more likely to have mild, moderate, or severe O2 impairment, history of lung or renal disease, and/or elevated respiratory rate.
- Chest radiographs that demonstrated any disease or severe disease were more likely to have low albumin, high lactate dehydrogenase, and high ferritin.

Abstract:

Objectives: We aimed to correlate lung disease burden on presentation chest radiographs (CXR), quantified at the time of study interpretation, with clinical presentation in patients hospitalized with coronavirus disease 2019 (COVID-19).

Material and methods:

This retrospective cross-sectional study included 5833 consecutive adult patients, aged 18 and older, hospitalized with a diagnosis of COVID-19 with a CXR quantified in real-time while hospitalized in 1 of 12 acute care hospitals across a multihospital integrated healthcare network

between March 24, 2020, and May 22, 2020. Lung disease burden was quantified in real-time by 118 radiologists on 5833 CXR at the time of exam interpretation with each lung annotated by the degree of lung opacity as clear (0%), mild (1–33%), moderate (34–66%), or severe (67–100%). CXR findings were classified as (1) clear versus disease, (2) unilateral versus bilateral, (3) symmetric versus asymmetric, or (4) not severe versus severe. Lung disease burden was characterized on initial presentation by patient demographics, co-morbidities, vital signs, and lab results with chi-square used for univariate analysis and logistic regression for multivariable analysis.

Results: Patients with severe lung disease were more likely to have oxygen impairment, an elevated respiratory rate, low albumin, high lactate dehydrogenase, and high ferritin compared to non-severe lung disease. A lack of opacities in COVID-19 was associated with a low estimated glomerular filtration rate, hypernatremia, and hypoglycemia.

Conclusions: COVID-19 lung disease burden quantified in real-time on presentation CXR was characterized by demographics, comorbidities, emergency severity index, Charlson Comorbidity Index, vital signs, and lab results on 5,833 patients. This novel approach to real-time quantified chest radiograph lung disease burden by radiologists needs further research to understand how this information can be incorporated to improve clinical care for pulmonary-related diseases.. An absence of opacities in COVID-19 may be associated with poor oral intake and a prerenal state as evidenced by the association of clear CXRs with a low eGFR, hypernatremia, and hypoglycemia..

Keywords:

chest radiograph (CXR); coronavirus disease 2019 (COVID-19); lung disease; disease severity; severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)

1. Introduction:

Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus, has resulted in millions of deaths worldwide.[1] The virus primarily affects the lungs and leads to respiratory failure.[2,3] Chest radiographs (CXRs) are the first-line imaging modality utilized to assess the extent of lung involvement in this, as well as other, infectious respiratory diseases.[4-6] Age and comorbidities such as kidney disease and chronic lung disease are associated with disease severity and mortality in individuals hospitalized with COVID-19, though the association of CXR disease severity with these variables remains unclear. Further, a patient's hydration status may limit the ability of a CXR to accurately represent the radiographic disease severity,[7] and, as a result, the clinical disease burden in

dehydrated or hypovolemic patients. At the time of radiologist interpretation, CXR findings—to help understand disease severity of COVID-19 upon hospital admission in various populations with variable presentations—need further exploration, especially in hospital settings.

Prior studies found that CXRs were predictive for patient-centered outcomes in patients with COVID-19.[8-16] However, these prior studies evaluated CXR retrospectively in research settings under ideal conditions or with artificial intelligence (AI)—both difficult to accomplish in real-time settings in diverse environments. In our institution, we developed a mechanism used on nearly 40,000 CXRs to quantify lung disease burden in real-time by radiologists at the time of exam interpretation. This method can become an important research/clinical/operations tool as it may provide predictive abilities to assist efficient patient triage. The association between emergency department (ED) CXR disease severity and clinically relevant variables in patients admitted for COVID-19 is incompletely understood. The purpose of this study is to correlate clinical presentation with COVID-19 lung disease burden on presentation CXRs, quantified in real-time by radiologists at the time of initial exam interpretation. This novel approach to real-time lung disease burden collection can be adapted for use in many real-time lung diseases.

2. Material and methods:

2.1 Study design, setting, and population:

This retrospective cross-sectional study included consecutive adult patients (i.e., aged 18 and older) with a diagnosis of COVID-19 and a CXR quantified in real-time while hospitalized in 1 of 12 acute care hospitals across a multihospital integrated healthcare network in the New York metropolitan region between March 24, 2020, and May 22, 2020. Diagnosis of COVID-19 was

confirmed by a positive result on at least one polymerase chain reaction test during hospitalization. During the time of the study at our institution, all ED patients and inpatients with single-view CXRs had them quantified in real-time at the time of exam interpretation by the performing radiologist. Only the first radiograph, per patient, was included in the analysis. The study was performed with institutional review board (IRB) approval and waiver of informed consent.

2.2 Data source:

Data was obtained from the radiology information system (RIS) and the enterprise inpatient electronic health record (EHR; Sunrise Clinical Manager, Allscripts, Chicago, IL).

2.3 Image acquisition, image analysis and data capture:

CXRs were obtained in either the posteroanterior (PA) view or the anteroposterior (AP) view. All patients were asked to take a deep breath in and hold it for exam acquisition, if possible. PA exam protocol uses automatic exposure control. AP exam protocol uses manual technique using preset settings based on patient size (small, medium, and large) that is picked by the technologist (approximate average of 2.5 mAs and 90 KV).Lung disease burden was quantified in real-time by radiologists at the time of exam interpretation with each lung annotated by the degree of opacity via visual inspection: clear (0%), mild (1–33%), moderate (34–66%), or severe (67–100%) (Figure 1).This was performed using discrete fields in the radiology reporting software (via a pop-up) upon a radiologist's finalization of a CXR report on nearly 40,000 CXRs with results stored in a secure database. If the radiologist reported lung opacity in the report using the reporting system template, the data was stored in the radiology database without the use of a

pop-up. Radiologists were not blinded to patient medical records at the time of image interpretation.

2.4. Lung disease burden classification/outcomes:

The following 4 outcomes were defined based on the opacities of the left and right lungs in the CXRs: (1) clear versus disease, (2) unilateral versus bilateral, (3) symmetric versus asymmetric, and (4) not severe versus severe (see Supplement Table 4 for definitions). Only binomial outcomes were considered, and patients that were labeled "clear" were only used in the analysis of clear versus disease (see Supplement Table 4). Patients without opacities were not used in the analysis of unilateral versus bilateral, symmetric versus asymmetric and not severe versus severe lung disease burden. Because of human error and potential overlapping categories, we allowed for symmetric disease to include the same category in each lung or one category away.

2.5 Independent variables:

We collected data on patient demographics, comorbidities, vital signs, and lab results and reported them as categorical variables. We used patient-reported race and ethnicity to categorize patients into 1 of 5 groups for race (Asian, Black, White, Other, Unknown/Declined) and one of three groups for ethnicity (Ethnicity Unknown/Declined; Ethnicity Hispanic or Latino, Ethnicity Not Hispanic or Latino).

Comorbidities were chosen based on data from previous publications[17-20] and included the following diagnoses based on Tenth Revision (ICD-10) coding: congestive heart failure (CHF), lung disease, kidney disease, diabetes, coronary artery disease (CAD), and hypertension (HTN).

We identified the following comorbidities by International Statistical Classification of Disease and Related Health Problems, Tenth Revision (ICD-10) coding (see Supplement Table 1 for ICD-10 codes): coronary artery disease (CAD) , hypertension, lung disease, kidney disease, diabetes (DM), or heart failure (HF).

We calculated the Charlson Comorbidity Index (CCI) as a measure of total comorbidity burden and categorized results into 3 groups: 0–5, 6–10, or greater than 10. The emergency severity index (ESI), a tool for EDs at the time of triage, is scored from 1 (most urgent) to 5 (least urgent). The estimated glomerular filtration rate (eGFR) was extracted from the EHR.

Systolic blood pressure (SBP), diastolic blood pressure (DBP), respiratory rate (RR), temperature (Temp), and heart rate (HR) were categorized as low, normal, and high (see Supplement Table 2). Oxygen (O2) impairment was defined as none, mild, moderate, or severe based on the level of oxygen saturation (SpO2) and supplemental oxygen requirements (oxygen delivery method) (see Supplement Table 3). The lab results other than d-dimer and C-reactive protein (CRP) were categorized as being low, normal, or high based on the predefined ranges from the specific assays that were performed. D-dimer and CRP were categorized as normal or high.

2.6 Data analysis:

Nearest-neighbor interpolation of vitals and labs to the time of radiograph was performed. The time-varying measurements that include vital signs and lab results were interpolated using

nearest-neighbor interpolation to the time of the first CXR in a series of CXRs for each patient. Nearest neighbor interpolation can select values recorded before or after the time of the CXR and was used regardless of the duration between the time of the radiograph and the time of the measurement, even though most of the measurement occurred within a short time after the CXR was taken (see Supplemental Table 4). Some lab values were not measured at all for certain patients and were assigned to the category "not recorded."

2.7 Outcome analysis:

Univariate analysis was performed using chi-square and multivariate analysis was performed using logistic regression. Some measurements were labeled as "not recorded," and this resulted in degenerate patterns of missingness (the input matrix for the multivariate analysis was not full rank) because these missing measurements were not missing completely at random. This problem was alleviated by removing Eosinophil and Alanine Aminotransferase from the analysis.

The 95% confidence intervals (CIs) on the adjusted odds ratios (ORs) were determined using the adjusted log OR coefficients, adding and subtracting 1.96 times the standard error, and exponentiating the result. All analyses were performed using MATLAB 2019b and its statistics and machine learning toolbox (Mathworks, Natick, MA).

3. Results:

3.1 Patient population:

A total of 5,833 patients were included in this study; of these, 2427 (41.6%) were female (see Table 1). The age distribution was 360 (6.2%), 1485 (25.5%), 2685 (46.0%), 1303 (22.3%) who

were respectively aged 18–40, 41–60, 61–80, and 81–106 years. Overall, 1149 (19.7%) were Black, 1208 (20.7%) were Hispanic or Latino, and 1353 (23.2%), had a CCI of 6 or higher. The 5,833 CXRs on these patients were interpreted by 118 radiologists. The mean and median number of CXRs interpreted by each radiologist was 49.4 and 28.5 respectively. There were 4,819 AP CXR, 40 PA CXR, and 973 CXR of unknown (either AP or PA orientation).

3.2 Outcomes:

Overall, patients were more likely to have disease compared to a clear CXR, bilateral compared to unilateral CXR findings, symmetric compared to asymmetric CXR disease, and severe compared to not severe CXR disease (see Table 2). Missing data is reported in Table 4 and Supplement Table 6.

3.2.1 CXR lung disease burden: clear versus disease:

Patients with a clear CXR compared to any disease on CXR were more likely to be of an age of 18–40 years relative to 60–80 years (OR 0.46, 95% CI 0.33, 0.65, $p < 0.001$) and Black relative to White (OR 0.78 [95% CI 0.62, 0.98], $p < 0.05$). Further, they were more likely to have low platelets (OR 0.66 [95% CI 0.52, 0.84], $p < 0.001$), low eGFR (OR 0.70 [95% CI 0.54, 0.91], $p < 0.01$), low glucose (OR 0.46 [95% CI 0.22, 0.96], $p < 0.05$), high sodium (OR 0.72 [95% CI 0.54, 0.97], $p < 0.05$), and high monocytes (OR 0.78 [95% CI 0.62, 0.97], $p < 0.05$) (see Table 3).

Patients with CXR that demonstrates disease compared to no disease were more likely to have a history of lung disease (OR 1.92 [95% CI 1.52, 2.42], $p < 0.001$); a history of renal disease (OR 1.67 [95% CI 1.15, 2.43], $p < 0.01$); mild, moderate, and severe O2 impairment (OR 2.27 [95% CI 1.83, 2.83], $p < 0.001$, OR 3.97 [95% CI 2.82, 5.60], $p < 0.001$, OR 4.47 [95% CI 2.68, 7.45],

p < 0.001), respectively; elevated respiratory rate (OR 1.84 [95% CI 1.48, 2.28], p < 0.001); low hemoglobin (OR 1.36 [95% CI 1.12, 1.66], p < 0.01); low albumin (OR 1.70 [95% CI 1.40, 2.06], p < 0.001); low lymphocytes (OR 1.32 [95% CI 1.09, 1.59], p < 0.01; high neutrophil OR 0.75 [95% CI 0.58, 0.98], p < 0.05); high Aspartate Aminotransferase (AST) (OR 1.40 [95% CI 1.16, 1.69], p < 0.001); high CRP (OR 3.00 [95% CI 2.15, 4.18], p < 0.001); high lactate dehydrogenase (OR 1.90 [95% CI 1.43, 2.54], p < 0.001); high d-dimer (OR 1.31 [95% CI 1.04, 1.63], p < 0.05); and high ferritin (OR 1.74 [95% CI 1.37, 2.22], p < 0.001).

3.2.2 CXR lung disease burden: severe versus not severe:

Patients without severe disease on CXR were more likely to have CCI 6–10, CCI >10 (OR 0.75 [95% CI 0.62, 0.92], p < 0.01, OR 0.71 [95% CI 0.51, 0.98], p < 0.05), low platelets (OR 0.80 [95% CI 0.66, 0.97], p < 0.05), and high blood area nitrogen (BUN) (OR 0.82 [95% CI 0.69, 0.98], p < 0.05).

Patients with severe disease on CXR were more likely to be Hispanic (OR 1.33 [95% CI 1.09, 1.63], p < 0.01) and more likely to have prior lung disease (OR 1.31 [95% CI 1.11, 1.55], p < 0.01); renal disease (OR 1.33 [95% CI 1.00, 1.75], p < 0.05); mild, moderate, and severe O2 impairment (OR 2.21 [95% CI 1.86, 2.62], p < 0.001, OR 4.13 [95% CI 3.37, 5.08], p < 0.001, OR 3.78 [95% CI 2.90, 4.91], p < 0.001); elevated respiratory rate (RR) (OR 1.34 [95% CI 1.16, 1.55], p < 0.001); high bicarbonate (OR 1.48 [95% CI 1.04, 2.10], p < 0.05); low albumin (OR 1.54 [95% CI 1.34, 1.79], p < 0.001); low lymphocytes (OR 1.25 [95% CI 1.09, 1.44], p < 0.01); high lactate dehydrogenase (OR 1.61 [95% CI 1.22, 2.12], p < 0.001); and high ferritin (OR 1.40 [95% CI 1.13, 1.75], p < 0.01).

For univariable results, refer to Supplement Table 6. For multivariable results of unilateral versus bilateral and asymmetric versus asymmetric disease, refer to Table 3.

4. Discussion:

This retrospective cross-sectional study shows the ability to correlate clinical presentation with COVID-19 lung disease burden on presentation CXRs using image quantified in real-time by radiologists at the time of initial exam interpretation. Patients with CXRs that demonstrated disease (compared to no disease) or severe disease (compared to no severe disease) were more likely to be older, have mild or moderate O2 impairment, as well as known markers associated with more severe COVID-19,[17-19,21-25] such as underlying lung and renal disease, severe O2 impairment, elevated respiratory rate, low albumin, high lactate dehydrogenase, and high ferritin. No differences were found between male and female sex.

While prior studies have evaluated chest imaging in the setting of COVID-19, they have not quantified lung disease burden in real-time by a radiologist at the time of exam exam interpretation. Some of these studies evaluated CXR lung disease burden retrospectively in research settings under ideal conditions, while other studies used AI. Both retrospective studies and AI are difficult to implement clinically in real-time settings in diverse environments. Specifically, the RALE[26] and BRIXIA [27]scores. For example, the RALE score divides the lungs into 4 zones and gives each a consolidation score from 0-4 and a density score from 1-3. The BRIXIA score divides the lungs into 6 zones and gives each a score from 0-3. Given the cumbersome nature of obtaining these scores it was not practical to obtain them in real-time. Further, a recent meta-analysis of CXR scores in COVID did not assess if the scores were

obtained in real-time or retrospectively[28]. Also, the largest series in the meta-analysis had 636 patients and was obtained retrospectively[29]. This is compared to our methodology that was able to obtain scores on nearly 40,000 CXR in real-time, with 5,833 used for this study.

Our method allowed radiologists to quantify lung disease burden on a large volume of CXRs, at the time of exam interpretation, with minimal disruption to work-flow during a time of unprecedented stress. Radiologists typically do not quantify degree of lung opacity on CXR reports. We show that this annotation scheme can be helpful to provide a standardized mechanism for providers to understand degree of disease. Further research is needed to understand how this information can be incorporated to improve clinical care for pulmonary-related diseases.

We were also able to develop a logic that combined patient oxygen saturation with oxygen delivery methods to fully account for the level of O2 impairment. To the best of our knowledge, we are the first to use quantified lung disease burden in real-time by radiologists at the time of exam interpretation, combine these findings with oxygen saturation and oxygen delivery (i.e., to convey severity of oxygen impairment), and associate these findings with any CXR evidence of COVID-19 (compared to no disease) and severe CXR disease (compared to non-severe).

Interestingly, our findings suggest that the lack of opacities in COVID-19 may be associated with poor oral intake and a prerenal state as evidenced by the association of clear CXRs with a low eGFR, hypernatremia, and hypoglycemia. This may suggest that during the period of illness from a SARS-CoV-2 infection, patients' oral intake was unable to keep pace with the

physiologic demands of the body. This is further supported by the association of a high BUN with non-severe CXR disease. A previous study looking at the association of hydration status with CXR findings of pneumonia revealed that improvement in hydration status resulted in worsening opacities on subsequent CXRs.[7] This is an important finding as it illustrates the potential to misdiagnose vulnerable patients as not having COVID-19 pneumonia when, in fact, the disease may not be apparent and has the potential to rapidly progress.

In addition to previously reported associations between a past medical history of renal disease and an elevated LDH with the presence of any COVID-19 lung findings on CXR, we also found that a past medical history of lung disease, O2 impairment, elevated respiratory rate, low albumin, and high ferritin on initial presentation to the hospital was associated with signs of COVID-19 on CXR (compared to no disease) and severe COVID-19 CXR disease.[30,31] Further, we are the first to show an association of increased comorbidity burden (CCI > 5) with non-severe CXR findings—a result that needs to be explored further as an increased CCI has been associated with increased mortality.[2,32] Therefore, CXR disease severity may not correlate with mortality risk in select populations. Future studies will need to evaluate the associations between patient demographics, clinical variables, COVID-19 lung disease burden quantified real-time on presentation CXR, and patient-centered outcomes such as mechanical ventilation and mortality. Our study has some limitations. Our approach used logistic regression which accounts for linear relationships between variables. While nonlinear interactions are common in models that analyze medical images our study did not focus on the analysis of medical images but instead focused on relationships between radiologist annotated features such as opacities and clinical characteristics, which in our patient population and other studies have been shown to exhibit mostly linear

interactions[29,33-35]. The participants in this study were recruited from a single multihospital healthcare system and the data were analyzed retrospectively. Lung disease on CXRs were quantified by many radiologists, however, inter-reader variability was not evaluated. Further, the CXR was quantified in 4 discrete levels (i.e., negative, mild, moderate, severe) but was converted to binary outcomes, such as severe versus not severe and clear versus disease, that may be more clinically useful. However, the human eye cannot distinguish between the lung disease burden categories perfectly. Radiology experience was not collected or accounted for which is another limitation. The accuracy of Charlson Comorbidity Index is susceptible to a number of factors such as: possible ICD-10 coding errors and incomplete medical histories. Finally, research is needed to understand how real-time quantified lung disease burden can be adapted to be clinically useful for non–COVID-19 pulmonary disease.

5. Conclusion:

COVID-19 lung disease burden quantified in real-time on presentation CXR was characterized by clinical variables on thousands of patients. This novel approach to real-time lung disease burden collection can be adapted for real-time use in many lung diseases.

We found that an absence of opacities in COVID-19 may be associated with poor oral intake and a prerenal state as evidenced by the association of clear CXRs with a low eGFR, hypernatremia, and hypoglycemia.. This important finding demonstrates the potential to misclassify severity of lung disease burden for vulnerable patients. Further, we provided evidence that a past medical history of lung disease, O2 impairment, elevated respiratory rate, low albumin, and high ferritin on initial presentation to the hospital was associated with signs of COVID-19 on CXR (compared to no disease) and severe COVID-19 CXR disease (compared to non-severe).

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Figures:

Figure 1a: 54 year old male with dyspnea and clear lungs bilaterally.

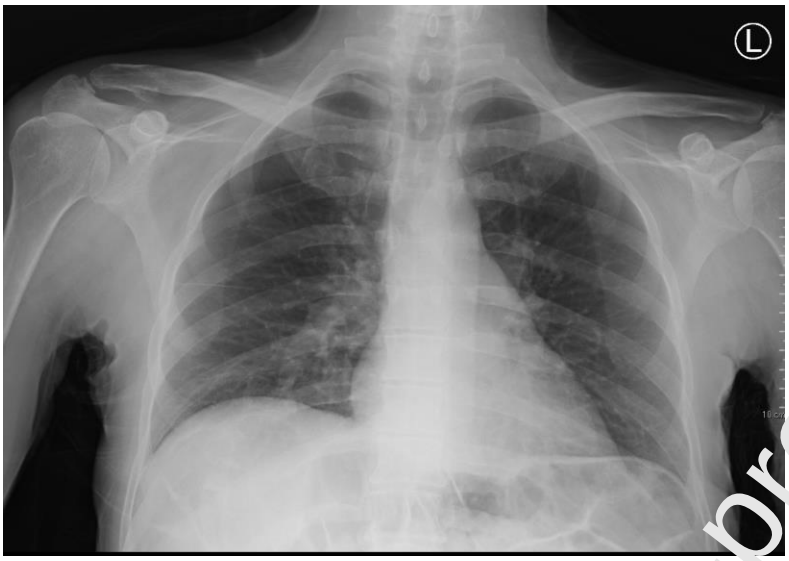


Figure 1b: 60 year old male with fever, cough, and dyspnea and mild disease bilaterally with subtle bilateral lung opacities.

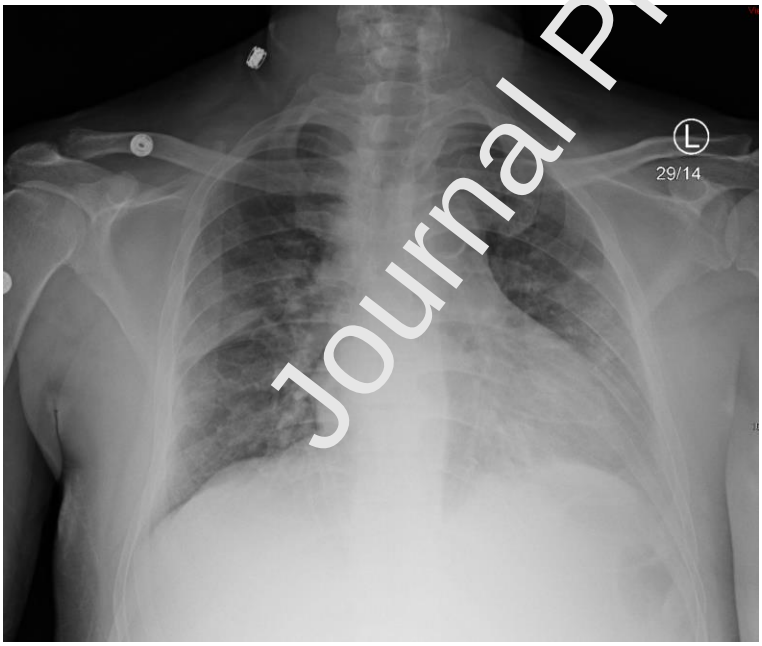


Figure 1c: 53 year old male with dyspnea and moderate disease bilaterally with ill-defined patchy and linear opacities bilaterally.

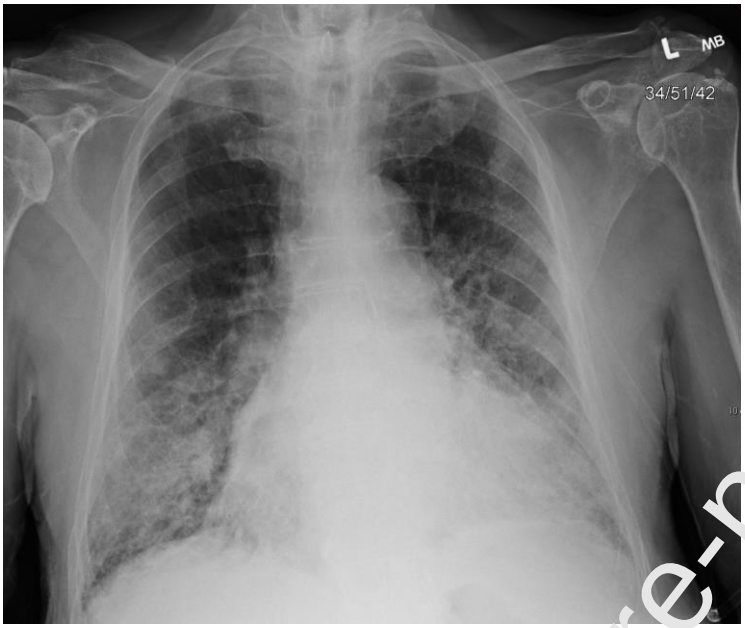
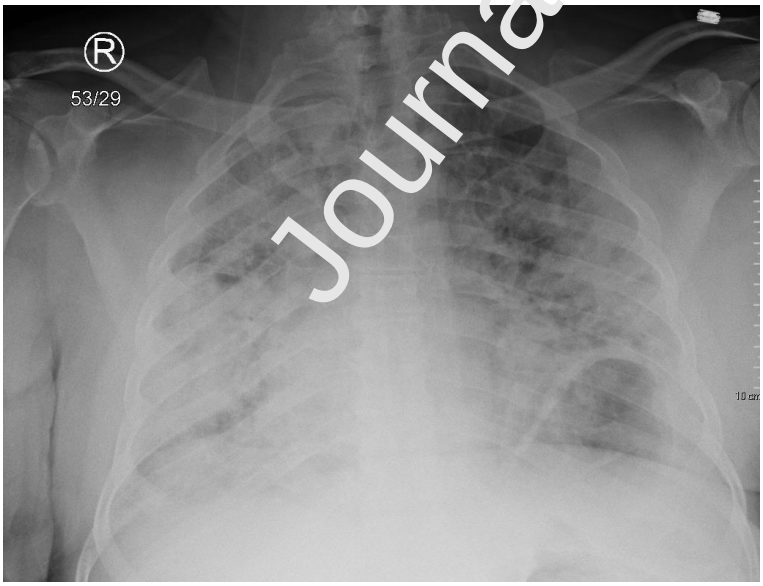


Figure 1d: 73 year old male with cough, fever, and dyspnea with severe disease bilaterally as seen by patchy and consolidative bilateral lung opacities.



Tables:

Table 1: Demographics

Category	N (%)
Age	
18-40	360 (6.2%)
41-60	1485 (25.5%)
61-80	2685 (46.0%)
81-106	1303 (22.3%)
Gender	
Female	2427 (41.6%)
Male	3406 (58.4%)
Race	
Asian	524 (9.0%)
Black	1149 (19.7%)
Unknown/Declined	268 (4.6%)
Other	1553 (26.6%)
White	2339 (40.1%)
Ethnicity	
Unknown/Declined	374 (6.4%)
Hispanic or Latino	1208 (20.7%)
Not Hispanic or Latino	4251 (72.9%)
Charlson Comorbidity Index 0-5	2199 (37.7%)
6-10	1353 (23.2%)
> 10	404 (6.9%)
not recorded	1877 (32.2%)
Heart Failure	
No	3505 (60.1%)
Yes	455 (7.8%)
not recorded	1873 (32.1%)
Lung Disease	
No	1652 (28.3%)
Yes	2308 (39.6%)
not recorded	1873 (32.1%)
Kidney Disease	
No	3326 (57.0%)
Yes	634 (10.9%)
not recorded	1873 (32.1%)
Diabetes	
No	2400 (41.1%)
Yes	1560 (26.7%)
not recorded	1873 (32.1%)
Coronary artery disease	
No	3352 (57.5%)
Yes	608 (10.4%)
not recorded	1873 (32.1%)
Hypertension	
No	3548 (60.8%)
Yes	412 (7.1%)
not recorded	1873 (32.1%)
Heart rate	
< 60	189 (3.2%)
60-99	3936 (67.5%)
> 99	1333 (22.9%)

not recorded	375 (6.4%)
Emergency severity index 1	202 (3.5%)
2	2258 (38.7%)
3	1394 (23.9%)
4	26 (0.4%)
not recorded	1953 (33.5%)
O2 impairment	
normal	1893 (32.5%)
mild	1655 (28.4%)
moderate	1153 (19.8%)
severe	750 (12.9%)
not recorded	372 (6.4%)
Systolic Blood Pressure	
low	428 (7.3%)
normal	4905 (84.1%)
high	109 (1.9%)
not recorded	391 (6.7%)
Diastolic Blood Pressure	
low	917 (15.7%)
normal	4411 (75.6%)
high	113 (1.9%)
not recorded	392 (6.7%)
Respiratory Rate	
low	38 (0.7%)
normal	2724 (46.7%)
high	2690 (46.1%)
not recorded	381 (6.5%)
Temperature	
low	245 (4.2%)
normal	4461 (76.5%)
high	738 (12.7%)
not recorded	389 (6.7%)
Hemoglobin	
Low	2807 (48.1%)
Normal	2861 (49.0%)
High	133 (2.3%)
not recorded	32 (0.5%)
White blood cell count	
Low	290 (5.0%)
Normal	3239 (55.5%)
High	2266 (38.8%)
not recorded	38 (0.7%)
Red cell distribution width	
Low	4 (0.1%)
Normal	3539 (60.7%)
High	2257 (38.7%)
not recorded	33 (0.6%)
Platelet count	
Low	809 (13.9%)
Normal	4284 (73.4%)
High	706 (12.1%)
not recorded	34 (0.6%)
Estimated glomerular filtration rate	
Low	2199 (37.7%)
Normal	3555 (60.9%)

not recorded	79 (1.4%)
Glucose	
Low	64 (1.1%)
Normal	747 (12.8%)
High	4943 (84.7%)
not recorded	79 (1.4%)
Blood urea nitrogen	
Low	209 (3.6%)
Normal	2555 (43.8%)
High	2990 (51.3%)
not recorded	79 (1.4%)
Bicarbonate (CO2)	
Low	1517 (26.0%)
Normal	4018 (68.9%)
High	219 (3.8%)
not recorded	79 (1.4%)
Sodium	
Low	1561 (26.8%)
Normal	3497 (60.0%)
High	696 (11.9%)
not recorded	79 (1.4%)
Creatinine	
Low	248 (4.3%)
Normal	3379 (57.9%)
High	2127 (36.5%)
not recorded	79 (1.4%)
Potassium	
Low	562 (9.6%)
Normal	4668 (80.0%)
High	524 (9.0%)
not recorded	79 (1.4%)
Albumin	
Low	3345 (57.3%)
Normal	2393 (41.0%)
High	3 (0.1%)
not recorded	92 (1.6%)
Alkaline phosphatase	
Low	105 (1.8%)
Normal	4361 (74.8%)
High	1275 (21.9%)
not recorded	92 (1.6%)
Lymphocyte	
Low	3267 (56.0%)
Normal	2368 (40.6%)
High	108 (1.9%)
not recorded	90 (1.5%)
Monocyte	
Low	10 (0.2%)
Normal	4474 (76.7%)
High	1259 (21.6%)
not recorded	90 (1.5%)
Neutrophil	
Low	96 (1.6%)
Normal	2813 (48.2%)
High	2834 (48.6%)

not recorded	90 (1.5%)
Bilirubin	
Low	195 (3.3%)
Normal	5133 (88.0%)
High	413 (7.1%)
not recorded	92 (1.6%)
Aspartate Aminotransferase Low	52 (0.9%)
Normal	2562 (43.9%)
High	3127 (53.6%)
not recorded	92 (1.6%)
C-reactive protein	
Normal	252 (4.3%)
High	5007 (85.8%)
not recorded	574 (9.8%)
Lactate Dehydrogenase	
Low	6 (0.1%)
Normal	432 (7.4%)
High	3848 (66.0%)
not recorded	1547 (26.5%)
D-Dimer	
Normal	1446 (24.8%)
High	3784 (64.9%)
not recorded	603(10.4%)
Ferritin	
Low	18 (0.3%)
Normal	697 (11.9%)
High	4519 (77.5%)
not recorded	599 (10.3%)

Table 2: CXR results

Category	N (%)
Lung disease burden	
Clear (0%)	893 (15.3%)
Mild (1-33%)	2380 (40.8%)
Moderate (34-66%)	1757 (30.1%)
Severe (67-100%)	803 (13.8%)
Total	5833 (100.0%)
Clear versus Disease	
Clear	893 (15.3%)
Disease	4940 (84.7%)
Total	5833 (100.0%)
Lung Burden Laterality	
Clear	893 (15.3%)
Unilateral	699 (12.0%)
Bilateral	4241 (72.7%)

Total	5833 (100.0%)
Unilateral	699 (14.1%)
Bilateral	4241 (85.9%)
Total (excluding clear)	4940 (100.0%)
Lung Burden Severity	
Clear	893 (15.3%)
Not Severe	2380 (40.8%)
Severe	2560 (43.9%)
Total	5833 (100.0%)
Not Severe	2380 (48.2%)
Severe	2560 (51.8%)
Total (excluding clear)	4940 (100.0%)
Symmetry	
Symmetric	4719 (95.5%)
Asymmetric	221 (4.5%)
Total	4940 (100.0%)

Table 3: Multivariable analysis

category	Clear Versus Disease	Unilateral Versus Bilateral	Symmetric Versus Asymmetric	Not Severe Versus Severe
Age				
18-40	**0.46 (0.33, 0.65)****	0.73 (0.49, 1.09)	1.45 (0.79, 2.67)	1.29 (0.95, 1.75)
41-60	0.80 (0.64, 1.01)	1.00 (0.79, 1.28)	0.72 (0.48, 1.06)	1.15 (0.97, 1.35)
61-80	Reference	Reference	Reference	Reference
81-106	0.98 (0.78, 1.23)	0.83 (0.66, 1.04)	1.02 (0.70, 1.50)	1.03 (0.86, 1.23)
Sex				
Female	0.88 (0.73, 1.06)	0.90 (0.74, 1.09)	1.34 (0.98, 1.82)	0.87 (0.76, 1.00)
Male	Reference	Reference	Reference	Reference
Race				
Asian	1.16 (0.82, 1.63)	1.12 (0.81, 1.56)	0.67 (0.38, 1.19)	0.94 (0.74, 1.18)
Black	**0.78 (0.62, 0.98)***	1.20 (0.94, 1.54)	0.73 (0.48, 1.10)	0.97 (0.80, 1.16)
Unknown/Declined	0.81 (0.45, 1.45)	1.20 (0.66, 2.19)	0.81 (0.35, 1.88)	1.20 (0.81, 1.79)
Other	1.14 (0.86, 1.52)	1.14 (0.86, 1.52)	1.06 (0.69, 1.61)	0.94 (0.77, 1.14)
White	Reference	Reference	Reference	Reference
Ethnicity				
Unknown/Declined	1.26 (0.75, 2.11)	1.22 (0.73, 2.04)	1.16 (0.60, 2.24)	0.79 (0.56, 1.10)
Hispanic or Latino	1.34 (0.99, 1.81)	**1.44 (1.06, 1.95)***	**0.56 (0.35, 0.91)***	**1.33 (1.09, 1.63)****
Not Hispanic or Latino	Reference	Reference	Reference	Reference
CCI				
0-5	Reference	Reference	Reference	Reference
6-10	0.80 (0.61, 1.05)	**0.64 (0.48, 0.85)****	0.68 (0.44, 1.07)	**0.75 (0.62, 0.92)****
> 10	0.66 (0.44, 1.01)	**0.55 (0.36, 0.85)****	0.71 (0.35, 1.43)	**0.71 (0.51, 0.98)***
not recorded	Inf (0.00, Inf)	0.42 (0.04, 4.43)	0.00 (0.00, Inf)	0.00 (0.00, Inf)
Heart Failure				
No	Reference	Reference	Reference	Reference
Yes	0.85 (0.60, 1.19)	**1.69 (1.13, 2.51)****	0.65 (0.34, 1.26)	1.31 (1.00, 1.72)
not recorded	0.00 (0.00, Inf)	3.11 (0.27, 36.35)	Inf (0.00, Inf)	Inf (0.00, Inf)

Lung Disease				
No	Reference	Reference	Reference	Reference
Yes	**1.92 (1.52, 2.42)*** **	**1.56 (1.23, 1.97)*** **	0.85 (0.59, 1.23)	**1.31 (1.11, 1.55)** **
not recorded	none	none	none	none
Kidney Disease				
No	Reference	Reference	Reference	Reference
Yes	**1.67 (1.15, 2.43)** **	0.85 (0.59, 1.23)	1.53 (0.85, 2.76)	**1.33 (1.00, 1.75)* **
not recorded	none	none	none	none
Diabetes				
No	Reference	Reference	Reference	Reference
Yes	1.07 (0.85, 1.35)	1.18 (0.92, 1.50)	1.05 (0.73, 1.52)	1.02 (0.86, 1.20)
not recorded	none	none	none	none
CAD				
No	Reference	Reference	Reference	Reference
Yes	0.83 (0.61, 1.11)	1.04 (0.75, 1.43)	0.84 (0.49, 1.44)	0.90 (0.71, 1.13)
not recorded	none	none	none	none
Hypertension				
No	Reference	Reference	Reference	Reference
Yes	0.97 (0.63, 1.50)	1.76 (1.09, 2.83)*	1.13 (0.56, 2.31)	1.15 (0.83, 1.61)
not recorded	none	none	none	none
Heart Rate				
Low	0.65 (0.42, 1.01)	1.25 (0.73, 2.15)	1.18 (0.54, 2.55)	0.80 (0.55, 1.17)
Normal	Reference	Reference	Reference	Reference
High	0.95 (0.76, 1.20)	0.82 (0.66, 1.03)	1.16 (0.82, 1.63)	0.96 (0.82, 1.12)
not recorded	0.95 (0.04, 22.55)	4.71 (0.26, 86.75)	4.31 (0.07, 270.44)	0.90 (0.09, 8.50)
ESI				
1	0.63 (0.17, 2.33)	0.34 (0.07, 1.75)	0.36 (0.06, 2.19)	1.39 (0.50, 3.88)
2	1.05 (0.32, 3.45)	0.56 (0.12, 2.59)	0.48 (0.09, 2.46)	1.23 (0.47, 3.25)
3	1.03 (0.31, 3.35)	0.60 (0.15, 2.88)	0.34 (0.07, 1.77)	1.19 (0.45, 3.14)
4	Reference	Reference	Reference	Reference
not recorded	1.64 (0.39, 6.84)	0.38 (0.07, 2.11)	1.18 (0.19, 7.26)	1.02 (0.34, 3.08)
O2 impairment				
normal	Reference	Reference	Reference	Reference
mild impairment	**2.27 (1.83, 2.83)*** **	**1.87 (1.50, 2.32)*** **	0.96 (0.65, 1.42)	**2.21 (1.86, 2.62)*** **
moderate impairment	**3.97 (2.82, 5.60)*** **	**2.83 (2.11, 3.81)*** **	1.18 (0.76, 1.84)	**4.13 (3.37, 5.08)*** **
severe impairment	**4.47 (2.68, 7.45)*** **	**5.15 (3.24, 8.18)*** **	**0.52 (0.29, 0.96)* **	**3.78 (2.90, 4.91)*** **
not recorded	1.55 (0.36, 6.77)	1.09 (0.20, 6.03)	0.11 (0.01, 1.43)	2.21 (0.44, 11.00)
SBP				
Low	0.80 (0.55, 1.17)	0.83 (0.58, 1.20)	1.28 (0.74, 2.23)	0.84 (0.65, 1.09)
Normal	Reference	Reference	Reference	Reference
High	0.65 (0.35, 1.18)	1.83 (0.85, 3.98)	0.75 (0.24, 2.33)	0.79 (0.46, 1.34)
not recorded	0.00 (0.00, Inf)	0.00 (0.00, Inf)	Inf (0.00, Inf)	Inf (0.00, Inf)
DBP				
Low	1.02 (0.78, 1.35)	1.09 (0.83, 1.43)	0.71 (0.45, 1.11)	1.06 (0.88, 1.29)
Normal	Reference	Reference	Reference	Reference
High	1.27 (0.66, 2.45)	0.60 (0.32, 1.13)	1.41 (0.54, 3.65)	0.98 (0.59, 1.62)
not recorded	Inf (0.00, Inf)	Inf (0.00, Inf)	0.00 (0.00, Inf)	0.00 (0.00, Inf)
RR				
Low	1.47 (0.51, 4.18)	5.24 (0.67, 40.74)	1.31 (0.29, 6.04)	1.67 (0.76, 3.71)
Normal	Reference	Reference	Reference	Reference
High	**1.84 (1.48, 2.28)*** **	**1.23 (1.01, 1.51)* **	0.98 (0.71, 1.36)	**1.34 (1.16, 1.55)*** **
not recorded	0.95 (0.12, 7.73)	0.30 (0.03, 3.27)	0.18 (0.00, 8.31)	0.42 (0.07, 2.61)
Temperature				
Low	0.70 (0.45, 1.09)	0.77 (0.48, 1.23)	1.60 (0.83, 3.05)	0.91 (0.65, 1.26)
Normal	Reference	Reference	Reference	Reference
High	0.93 (0.70, 1.25)	0.86 (0.65, 1.12)	**2.09 (1.44, 3.03)*** **	1.04 (0.86, 1.26)
not recorded	0.78 (0.20, 3.06)	4.16 (0.38, 45.76)	2.81 (0.28, 28.02)	2.29 (0.61, 8.61)
Hemoglobin				
Low	**1.36 (1.12, 1.66)** **	1.04 (0.85, 1.28)	0.95 (0.69, 1.32)	1.16 (1.00, 1.34)
Normal	Reference	Reference	Reference	Reference
High	0.64 (0.39, 1.07)	0.82 (0.46, 1.45)	0.61 (0.18, 2.05)	**0.62 (0.40, 0.97)* **

not recorded	0.00 (0.00, Inf)	Inf (0.00, Inf)	0.92 (0.00, Inf)	Inf (0.00, Inf)
WBC				
Low	0.99 (0.65, 1.50)	0.92 (0.60, 1.40)	1.01 (0.50, 2.07)	0.99 (0.70, 1.39)
Normal	Reference	Reference	Reference	Reference
High	1.21 (0.91, 1.60)	0.78 (0.57, 1.05)	0.86 (0.56, 1.31)	1.16 (0.95, 1.41)
not recorded	Inf (0.00, Inf)	Inf (0.00, Inf)	0.00 (0.00, Inf)	**15.65 (1.51, 162.73)***
RCDW				
Low	0.36 (0.02, 5.51)	Inf (0.00, Inf)	0.00 (0.00, Inf)	0.38 (0.03, 4.75)
Normal	Reference	Reference	Reference	Reference
High	0.91 (0.74, 1.10)	0.94 (0.77, 1.15)	1.20 (0.87, 1.66)	1.09 (0.93, 1.26)
not recorded	0.25 (0.00, Inf)	0.00 (0.00, Inf)	2.53 (0.00, Inf)	0.00 (0.00, Inf)
Platelet				
Low	**0.66 (0.52, 0.84)*****	**0.76 (0.59, 0.97)***	1.28 (0.86, 1.91)	**0.80 (0.66, 0.97)***
Normal	Reference	Reference	Reference	Reference
High	0.87 (0.65, 1.15)	1.33 (0.97, 1.82)	0.86 (0.53, 1.39)	1.00 (0.82, 1.22)
not recorded	Inf (0.00, Inf)	Inf (0.00, Inf)	0.00 (0.00, Inf)	Inf (0.00, Inf)
eGFR Low	**0.70 (0.54, 0.91)****	0.94 (0.72, 1.24)	1.14 (0.72, 1.79)	0.89 (0.72, 1.09)
eGFR Normal	Reference	Reference	Reference	Reference
eGFR not recorded	**12.00 (2.44, 58.93)****	0.00 (0.00, Inf)	Inf (0.00, Inf)	Inf (0.00, Inf)
Glucose				
Low	**0.46 (0.22, 0.96)***	1.54 (0.57, 4.17)	0.39 (0.05, 3.03)	0.98 (0.53, 1.84)
Normal	Reference	Reference	Reference	Reference
High	0.96 (0.76, 1.22)	1.18 (0.92, 1.52)	1.06 (0.68, 1.66)	0.95 (0.77, 1.16)
not recorded	none	none	none	none
BUN				
Low	1.11 (0.71, 1.73)	1.20 (0.72, 2.00)	0.68 (0.26, 1.79)	1.08 (0.76, 1.55)
Normal	Reference	Reference	Reference	Reference
High	0.85 (0.67, 1.08)	0.80 (0.62, 1.02)	1.23 (0.83, 1.81)	**0.82 (0.69, 0.98)***
not recorded	none	none	none	none
CO2				
Low	0.92 (0.74, 1.13)	1.01 (0.81, 1.24)	0.83 (0.58, 1.19)	0.98 (0.84, 1.15)
Normal	Reference	Reference	Reference	Reference
High	0.88 (0.55, 1.40)	0.95 (0.58, 1.56)	1.28 (0.66, 2.50)	**1.48 (1.04, 2.10)***
not recorded	none	none	none	none
Sodium				
Low	0.96 (0.78, 1.18)	0.92 (0.75, 1.14)	1.10 (0.79, 1.54)	0.99 (0.85, 1.15)
Normal	Reference	Reference	Reference	Reference
High	**0.72 (0.54, 0.97)***	**0.58 (0.43, 0.76)*****	0.69 (0.43, 1.11)	**0.56 (0.45, 0.69)*****
not recorded	none	none	none	none
Creatinine				
Low	1.25 (0.73, 2.09)	1.34 (0.77, 2.33)	0.91 (0.41, 1.98)	1.22 (0.87, 1.70)
Normal	Reference	Reference	Reference	Reference
High	1.05 (0.80, 1.37)	0.86 (0.65, 1.13)	0.98 (0.62, 1.54)	0.82 (0.66, 1.01)
not recorded	none	none	none	none
Potassium				
Low	0.94 (0.70, 1.27)	**0.74 (0.55, 0.98)***	**1.76 (1.16, 2.68)****	0.82 (0.67, 1.02)
Normal	Reference	Reference	Reference	Reference
High	1.12 (0.82, 1.54)	0.80 (0.59, 1.09)	1.13 (0.70, 1.84)	1.10 (0.87, 1.38)
not recorded	none	none	none	none
Albumin				
Low	**1.70 (1.40, 2.06)*****	1.22 (1.00, 1.48)	**1.68 (1.19, 2.38)****	**1.54 (1.34, 1.79)*****
Normal	Reference	Reference	Reference	Reference
High	0.00 (0.00, Inf)	Na	Na	Na
not recorded	**0.10 (0.02, 0.44)****	Inf (0.00, Inf)	0.00 (0.00, Inf)	0.00 (0.00, Inf)
Alkaline phosphatase				
Low	0.80 (0.43, 1.51)	1.24 (0.64, 2.41)	0.97 (0.34, 2.79)	0.96 (0.61, 1.53)
Normal	Reference	Reference	Reference	Reference
High	0.83 (0.66, 1.03)	1.16 (0.92, 1.47)	1.07 (0.76, 1.52)	1.11 (0.94, 1.30)
not recorded	none	none	none	none
Lymphocyte				
Low	**1.32 (1.09, 1.59)****	**1.56 (1.29, 1.89)*****	**1.42 (1.03, 1.98)***	**1.25 (1.09, 1.44)****

Normal	Reference	Reference	Reference	Reference
High	0.83 (0.47, 1.48)	1.42 (0.71, 2.85)	2.03 (0.76, 5.41)	0.79 (0.48, 1.29)
not recorded	0.54 (0.01, 31.80)	0.00 (0.00, Inf)	0.00 (0.00, Inf)	0.00 (0.00, Inf)
Monocyte				
Low	1.21 (0.12, 12.08)	2.41 (0.20, 29.78)	0.00 (0.00, Inf)	1.62 (0.33, 7.96)
Normal	Reference	Reference	Reference	Reference
High	**0.78 (0.62, 0.97)***	0.95 (0.75, 1.21)	1.35 (0.93, 1.95)	0.88 (0.74, 1.05)
not recorded	1.52 (0.03, 73.20)	Inf (0.00, Inf)	0.00 (0.00, Inf)	Inf (0.00, Inf)
Neutrophil				
Low	1.00 (0.54, 1.87)	**0.48 (0.26, 0.91)***	0.78 (0.21, 2.93)	0.63 (0.34, 1.18)
Normal	Reference	Reference	Reference	Reference
High	0.75 (0.58, 0.98)*	1.30 (0.98, 1.74)	1.32 (0.87, 2.00)	1.05 (0.87, 1.27)
not recorded	1.03 (0.02, 49.48)	2.09 (0.00, Inf)	Inf (0.00, Inf)	Inf (0.00, Inf)
Bilirubin				
Low	0.86 (0.56, 1.32)	0.65 (0.41, 1.03)	**2.06 (1.07, 3.99)***	0.83 (0.58, 1.20)
Normal	Reference	Reference	Reference	Reference
High	0.74 (0.53, 1.03)	1.14 (0.78, 1.65)	0.86 (0.4[illegible] 1.53)	1.04 (0.81, 1.35)
not recorded	none	none	none	none
AST				
Low	1.40 (0.69, 2.83)	0.68 (0.32, 1.46)	0.5[illegible] (0.07, 4.21)	1.08 (0.50, 2.32)
Normal	Reference	Reference	Reference	Reference
High	**1.40 (1.16, 1.69)*****	0.90 (0.74, 1.09)	1.02 (0.75, 1.39)	1.09 (0.95, 1.25)
not recorded	none	none	none	none
CRP				
Normal	Reference	Reference	Reference	Reference
High	**3.00 (2.15, 4.18)*****	1.04 (0.64, 1.[illegible]9)	5.22 (0.71, 38.59)	1.03 (0.70, 1.52)
not recorded	**1.87 (1.21, 2.90)****	0.99 (0.53, 1.[illegible]6)	5.55 (0.64, 47.98)	0.88 (0.51, 1.50)
Lactate Dehydrogenase				
Low	0.05 (0.00, 1.12)	Inf (0.00, Inf)	0.00 (0.00, Inf)	Inf (0.00, Inf)
Normal	Reference	Reference	Reference	Reference
High	**1.90 (1.43, 2.54)*****	**1.7[illegible] 1.24, 2.34)****	1.03 (0.56, 1.91)	**1.61 (1.22, 2.12)*****
not recorded	1.22 (0.91, 1.64)	**1.79 (1.27, 2.53)*****	0.88 (0.44, 1.73)	**1.44 (1.06, 1.94)***
D-Dimer				
Normal	Reference	Reference	Reference	Reference
High	1.31 (1.04, 1.63)*	1.05 (0.83, 1.33)	1.32 (0.87, 2.01)	**1.33 (1.12, 1.57)*****
not recorded	0.83 (0.60, 1.15)	1.34 (0.89, 2.01)	1.77 (0.86, 3.64)	0.86 (0.61, 1.21)
Ferritin				
Low	0.49 (0.16, 1.[illegible]2)	0.70 (0.15, 3.40)	0.00 (0.00, Inf)	0.37 (0.04, 3.29)
Normal	Reference[illegible]	Reference	Reference	Reference
High	**1.74 (1.37, 2.22)*****	**1.93 (1.48, 2.52)*****	1.02 (0.61, 1.70)	**1.40 (1.13, 1.75)****
not recorded	1.15 (0.[illegible]9, 1.67)	0.74 (0.47, 1.15)	0.80 (0.31, 2.04)	0.94 (0.62, 1.41)

Significant variables * <0.05, ** < 0.01, *** < 0.001. CCI-Charlson Comorbidity Index, CAD-Coronary artery disease, ESI-Emergency severity index, SBP-Systolic Blood Pressure, DBP-Diastolic Blood Pressure, RR-Respiratory Rate, WBC-White blood cell count, RCDW-Red cell distribution width, eGFR-Estimated glomerular filtration rate, BUN-Blood urea nitrogen, C02-Bicarbonate, AST-Aspartate Aminotransferase, CRP-C-reactive protein