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# Relationship between chest CT scan findings with SOFA score, CRP, comorbidity, and mortality in ICU patients with COVID-19

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## Abstract

**Objective:** This study aimed to investigate the relationship between chest computed tomography (CT) scan findings with sequential organ failure assessment (SOFA) score, C-reactive protein (CRP), comorbidity, and mortality in intensive care unit (ICU) patients with coronavirus disease 19 (COVID-19).

**Method:** Adult patients (≥18 years old) with COVID-19 who were consecutively admitted to the Imam-Reza Hospital, Tabriz, East-Azerbaijan Province, North-West of Iran between March 2020 and August 2020 were screened and total of 168 patients were included. Demographic, clinical, and mortality data were gathered. Severity of disease was evaluated using the SOFA score system. CRP levels were measured and chest CT scans were performed.

**Results:** Most of patients had multifocal and bilateral ground glass opacity (GGO) pattern in chest CT scan. There were significant correlations between SOFA score on admission with multifocal and bilateral GGO ($P = .010$ and $P = .011$, respectively). Significant relationships were observed between unilateral and bilateral GGO patterns with CRP ($P = .049$ and $P = .046$, respectively). There was significant relationship between GGO patterns with comorbidities including overweight/obesity, heart failure, cardiovascular diseases, and malignancy ($P < .05$). No significant relationships were observed between chest CT scan results with mortality ($P > .05$).

**Conclusion:** Multifocal bilateral GGO was the most common pattern. Although chest CT scan characteristics were significantly related with SOFA score, CRP, and comorbidity in ICU patients with COVID-19, a relationship with mortality was not significant.

## 1 | INTRODUCTION

In December 2019, an outbreak of cases of pneumonia caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified in Wuhan, China.[1] The disease has been termed coronavirus disease 19 (COVID-19) and rapidly develops throughout the globe.[1] On March 2020, the World Health Organization (WHO) announced the new coronavirus outbreak to be a pandemic.[2] The clinical severity of COVID-19 varies from asymptomatic to acute

respiratory distress syndrome (ARDS) and multiple organ dysfunctions needing respiratory support such as non-invasive ventilation and/or mechanical ventilation and admission to the intensive care unit (ICU).[3] Approximately 20% of the COVID-19 patients develop severe illness after admission to the hospital.[4] Mortality rate ranges from 16-78 percent in critically ill patients with COVID-19.[5] The high Sequential Organ Failure Assessment (SOFA) score on admission can be a significant predictor of developing severe illness in hospital and is considered as a risk factor for COVID-19

mortality.[6-10] Furthermore, underlying diseases such as obesity, diabetes mellitus, chronic respiratory disease, cardiovascular disease, hypertension and cancer have an association with higher risk of mortality.[11,12]

Most patients with COVID-19 present pneumonia thus computed tomography (CT) scanning of the thorax can be a useful tool in screening and diagnosis.[13] Chest CT scan is able to present typical radiological findings of COVID-19 even before the appearance of clinical symptoms.[14-16] Moreover, chest CT scan is a sensitive method in comparison with reverse transcription polymerase chain reaction (RT-PCR) and assists physicians to identify COVID-19 patients who initially had negative RT-PCR results.[14,17] The typical chest CT scan indicates numerous ground glass opacity (GGO) and/or consolidations in a peripheral distribution, which also presents the severity of pulmonary inflammation.[18-20] It has been reported that consolidation and GGO on chest CT scans are more common in non-survivors than survivors.[8,21] In addition, majority of the patients with COVID-19 have bilateral infiltrates on chest CT scans.[11] Due to its availability, chest CT scan may help first-line triage of patients admitting to the hospital.[22] Chest CT scan is also helpful in assessing the severity and progression of disease, monitoring the clinical course as well as assessing the treatment.[23,24] Elevation in consolidative opacities and GGO as well as interstitial septal thickening on chest CT scan is associated with exacerbating pneumonia.[15,25] Chest CT features of COVID-19 pneumonia have been studied mostly in Chinese individuals; however, radiological manifestations should be clarified in other populations and areas around the world that have a quickly increasing number of confirmed cases.

SARS-CoV-2 infection is a multifaceted disease; therefore a reliable and appropriate biomarker is required to show changes in pattern of lung involvement and predict the severity of COVID-19 pneumonia. C-reactive protein (CRP) can be useful in the early diagnosis of pneumonia,[26] and patients with severe pneumonia had high CRP concentrations. Recently, studies have indicated that CRP has a positive association with severe dengue infection.[27,28] Changes in CRP have been demonstrated in COVID-19 patients, but little is known about its correlation with disease severity.[29,30] According to the research in COVID-19 patients, CRP concentration increased as the disease progressed and positive correlation was observed between CRP concentration with lung lesion and disease severity.[31] Furthermore, serum high-sensitivity CRP concentration and CT scores have a good consistency, and their combination can effectively evaluate disease progression and therapeutic effects.[32]

Since Iran has the largest number of approved COVID-19 cases in Asia after China and to the best of our knowledge, there is no study investigating the relationship between chest CT scan characteristics with SOFA score, CRP, comorbidity, and mortality in Iranian COVID-19 patients, current study designed to assess the chest CT scan features in ICU patients with COVID-19 and to find whether there is a relationship between the chest CT scan features with SOFA score, CRP, comorbidity, and mortality.

**What's known**

Chest CT scan can be a useful tool in screening and diagnosis and is able to present typical radiological findings of COVID-19 even before the appearance of clinical symptoms. Chest CT scan is also helpful in assessing the severity and progression of disease, monitoring the clinical course as well as assessing the treatment.

**What's new**

Multifocal bilateral GGO was the most common pattern in chest CT scan. There were significant correlations between SOFA score on admission with multifocal and bilateral GGO. Significant relationships were observed between unilateral and bilateral GGO patterns with CRP. There was significant relationship between GGO patterns with comorbidities including overweight/obesity, heart failure, cardiovascular diseases, and malignancy. No significant relationships were observed between chest CT scan results with mortality.

## 2 | METHODS

### 2.1 | Study patients

Adult patients (≥18 years old) with COVID-19 according to the WHO interim guidance[33] who were consecutively admitted to the Imam-Reza Medical Research and Training Hospital, Tabriz, East-Azerbaijan Province, North-West of Iran between March 2020 and August 2020 were screened and total of 168 ICU patients diagnosed by PCR COVID-19 positive and typical CT scan pattern in PCR negative patients were included in this research. Imam-Reza Medical Research and Training Hospital is the main in Tabriz city, East-Azerbaijan Province, which is one of the high-risk regions in the North-West of Iran. This hospital is affiliated to the Tabriz University of Medical Sciences, Tabriz, Iran. The research protocol was confirmed by the Institutional Review Board and Medical Ethics Committee of Tabriz University of Medical Sciences (ethics code: IR.TBZMED.REC.1399.016). Written informed consents were collected from the patients or their families.

### 2.2 | Data collection

Demographic and clinical characteristics were gathered using a data collection form. The demographic data including age, sex, and smoking; comorbidities including hypertension, diabetes, chronic respiratory disease, coronary artery disease, heart failure, cardiovascular disease, chronic renal failure, malignancy, rheumatologic disease, and chronic liver disease; clinical symptoms including cough, fever, dyspnea, myalgia, fatigue, hemoptysis, chill, headache, sore throat,

anorexia, nausea/vomiting, anosmia, taste loss, and diarrhea; vital signs including blood pressure, respiratory rate, heart rate, blood $O_2$ saturation, and body temperature as well as mortality (survived or died) were gathered. The SOFA score system was used to determine severity of disease with higher scores reflecting more severe illness.[34] Blood samples were also collected on admission and CRP levels were measured by immunoturbidimetry method. Due to wide variation in CRP level, we classified it into three categories: 1+: <10 mg/dL, 2+: 10-50 mg/dL, and 3+: >50 mg/dL.[35] The date of disease onset was ascertained as the day when the first symptom was appeared.

## 2.3 | Chest CT scan

Chest CT scans were conducted by a multi-detector CT scanner 16 slice (Siemens, Munich, Germany) with detailed parameters as below: tube voltage, 120 kV; tube current, standard (60-120 mAs); slice thickness, 1-1.5 mm; reconstruction interval, 1-1.5 mm. The CT scans were conducted beginning from the apex to the lowest part of the lungs in a deep inspiration. Patients were supine in the CT scanner with arms above their head. An expert radiologist (Dr Mohammad Kazem Tarzamni, Professor of Radiology with 25 year experience) analyzed and interpreted the CT scans. Pattern of lung involvement in chest CT scan of COVID-19 patients was divided into 8 categories: Unifocal GGO, Multifocal GGO, Unilateral GGO, Bilateral GGO, Unifocal Consolidation, Multifocal Consolidation, Unilateral Consolidation, and Bilateral Consolidation.

## 2.4 | Statistical analysis

Statistical analysis was carried out by SPSS 16.0 software (SPSS, Chicago, IL). The normal distribution of variables was assessed using the Kolmogorov-Smirnov test. Categorical variables were presented as number with percentage. Continuous variables were expressed as mean ±SD or median (interquartile range), as appropriate. Comparisons between groups were made by Chi-square test, Independent sample t-test, or Mann-Whitney U test, as appropriate. Correlations between variables were determined by Spearman correlation analysis. $P < .05$ was defined statistically significant.

## 3 | RESULTS

Total of 168 ICU patients with COVID-19 were studied. Baseline characteristics of patients are presented in Table 1.

As presented in Table 2, most of patients who had multifocal and bilateral GGO pattern on chest CT scans had SOFA scores <5 on admission (day 1). Significant relationships were only observed between the SOFA score classification on admission (day 1) with multifocal and bilateral GGO ($P = .016$ and $P = .044$, respectively).

**TABLE 1** Baseline characteristics of COVID-19 patients

| Characteristics | All patients (n = 168) |
|---|---|
| Age (year) | 62.65 ± 17.34 |
| Sex | |
|   Male | 102 (61) |
|   Female | 66 (39) |
| Smoking | 24 (15) |
| SOFA score | 5.14 ± 3.39 |
| CRP | |
|   1+ | 43 (26) |
|   2+ | 38 (23) |
|   3+ | 36 (21) |
|   High | 11 (7) |
| Comorbidity | |
|   Overweight/Obesity | 81 (79) |
|   Hypertension | 76 (47) |
|   Diabetes | 40 (25) |
|   Coronary artery disease | 22 (14) |
|   Chronic respiratory disease | 20 (12) |
|   Chronic renal failure | 17 (11) |
|   Heart failure | 15 (9) |
|   Cardiovascular disease | 13 (8) |
|   Malignancy | 10 (6) |
|   Rheumatologic disease | 5 (3) |
|   Chronic liver disease | 3 (2) |
| Clinical symptoms | |
|   Dyspnea | 127 (76) |
|   Cough | 91 (54) |
|   Myalgia | 48 (29) |
|   Fever (temperature ≥37.3°C) | 47 (28) |
|   Fatigue | 45 (27) |
|   Chill | 35 (21) |
|   Anorexia | 18 (11) |
|   Headache | 17 (10) |
|   Nausea/Vomiting | 17 (10) |
|   Sore throat | 15 (9) |
|   Anosmia | 14 (8) |
|   Taste loss | 13 (8) |
|   Diarrhea | 6 (4) |
|   Hemoptysis | 6 (4) |
| Vital signs | |
|   Systolic blood pressure (mmHg) | 121.91 ± 19.21 |
|   Diastolic blood pressure (mmHg) | 73.11 ± 13.95 |
|   Respiratory rate (breaths/min) | 25.10 ± 7.35 |
|   Heart rate (beats/min) | 96.06 ± 17.12 |
|   Blood $O_2$ saturation (%) | 83.43 ± 11.49 |

(Continues)

**TABLE 1** (Continued)

| Characteristics | All patients (n = 168) |
|---|---|
| Body temperature (°C) | 37.27 ± 0.75 |
| Chest CT scan | |
| Unifocal GGO | |
| Yes | 8 (5) |
| No | 160 (95) |
| Multifocal GGO | |
| Yes | 98 (58) |
| No | 70 (42) |
| Unilateral GGO | |
| Yes | 6 (4) |
| No | 162 (96) |
| Bilateral GGO | |
| Yes | 100 (60) |
| No | 68 (40) |
| Unifocal Consolidation | |
| Yes | 4 (2) |
| No | 164 (98) |
| Multifocal Consolidation | |
| Yes | 55 (33) |
| No | 113 (67) |
| Unilateral Consolidation | |
| Yes | 4 (2) |
| No | 164 (98) |
| Bilateral Consolidation | |
| Yes | 60 (36) |
| No | 108 (64) |
| Multifocal Bilateral GGO | |
| Yes | 54 (32) |
| No | 114 (68) |
| Multifocal Bilateral Consolidation | |
| Yes | 18 (11) |
| No | 150 (89) |
| Multifocal Bilateral GGO Consolidation | |
| Yes | 42 (25) |
| No | 126 (75) |

*Note:* Continuous variables were reported as mean ±SD or median (IQR) while categorical variables were expressed as frequency (percentage).
Abbreviations: COVID-19, Coronavirus disease 19; CRP, C-reactive protein; CT, Computed tomography; GGO, ground glass opacity; SOFA, Sequential Organ Failure Assessment.

Table 3 presents correlations between chest CT scan with SOFA scores on admission (day 1) and on day 5 in study patients. According to Table 3, there were only significant correlations between SOFA score on admission (day 1) with multifocal and bilateral GGO (P = .010 and P = .011, respectively). In addition, there were significant correlations between SOFA scores on admission (day 1)

and on day 5 with multifocal bilateral GGO (P = .035 and P = .044, respectively).

Table 4 shows relationship between chest CT scan and mortality with CRP in study patients. According to Table 4, most patients with GGO patterns on chest CT scans had CRP 1+. Significant relationships were observed between unilateral and bilateral GGO patterns on chest CT scans with CRP (P = .049 and P = .046, respectively).

As demonstrated in Table 5, significant relationships were observed between unifocal, unilateral, and bilateral GGO patterns on chest CT scans with overweight/obesity (P = .006, P = .045, and P = .034, respectively). Furthermore, significant relationships were observed between multifocal and bilateral GGO patterns on chest CT scans with heart failure (P = .001 and P = .001, respectively). In addition, there were significant relationships between unifocal, multifocal, unilateral, and bilateral GGO patterns on chest CT scans with cardiovascular diseases (P = .041, P = .005, P = .027 and P = .003, respectively). Significant relationships were also observed between unifocal and unilateral GGO patterns on chest CT scans with malignancy (P = .012 and P = .006, respectively). Significant relationship was also observed between multifocal bilateral GGO pattern with cardiovascular diseases (P = .041).

According to Table 6, no significant relationships were observed between chest CT scan results with mortality (P >.05).

## 4 | DISCUSSION

To the best of our knowledge, this is the first study to assess the relationship between chest CT scan findings with SOFA score, CRP, comorbidity, and mortality in ICU patients with COVID-19 in East-Azerbaijan Province, which is one of the high-risk regions in the North-West of Iran. Consistent with previous studies,[18-20,36-44] our research indicated that multifocal and bilateral GGO were the most common patterns on chest CT scans. Furthermore, multifocal and bilateral consolidation were more prevalent than unifocal and unilateral consolidation patterns. A GGO pattern has been suggested to be a very common feature in COVID-19 pneumonia as 100% of individuals whose diagnosis was affirmed by RT-PCR had this feature.[38] Also, there was no significant difference in the CT scan features between subjects with confirmed COVID-19 who needed admission and subjects who were discharged.[38] Since a GGO pattern can be present in different phases of the disease,[45-47] thereby being the most common radiologic feature. The appearance of GGO can be attributable to COVID-19 pathophysiology. The SARS-CoV-2 virus invades the pulmonary interstitium at the end of the lobular bronchioles and spreads to the distal end. The lesion emanates in the secondary pulmonary lobule, appearing as a round ground-glass appearance on CT and then expands to become as confluent GGO.[48] A GGO pattern can cause partial filling of the alveoli that is related with the viral infections pathogenesis.[49] It has been reported that GGO with or without consolidation are major characteristics of the COVID-19. These characteristics are highly indicative of acute interstitial pneumonia of the disease and are consistent with its histopathological

**TABLE 2** Relationship between chest CT scan and SOFA scores in study patients

| Chest CT scan | SOFA score on Day 1 | | | P-value[*] | SOFA score on Day 5 | | | P-value[*] |
|---|---|---|---|---|---|---|---|---|
| | <5 | 5-10 | >10 | | <5 | 5-10 | >10 | |
| Unifocal GGO | | | | .625 | | | | .655 |
| Yes | 3 (38) | 5 (63) | 0 (0) | | 1 (25.0) | 3 (75.0) | 0 (0) | |
| No | 78 (49) | 75 (47) | 7 (4) | | 27 (36) | 41 (54) | 8 (10) | |
| Multifocal GGO | | | | **.016** | | | | .564 |
| Yes | 54 (55) | 42 (43) | 2 (2) | | 18 (40) | 23 (51) | 4 (9) | |
| No | 27 (39) | 38 (54) | 5 (7) | | 10 (29) | 21 (60) | 4 (11) | |
| Unilateral GGO | | | | .501 | | | | .872 |
| Yes | 1 (20) | 5 (80) | 0 (0) | | 1 (33) | 3 (67) | 0 (0) | |
| No | 80 (50) | 75 (46) | 7 (4) | | 27 (36) | 41 (54) | 8 (10) | |
| Bilateral GGO | | | | **.044** | | | | .465 |
| Yes | 55 (55) | 43 (43) | 2 (2) | | 19 (40) | 24 (51) | 4 (9) | |
| No | 26 (38) | 37 (55) | 5 (7) | | 9 (27) | 20 (61) | 4 (12) | |
| Unifocal Consolidation | | | | .095 | | | | .822 |
| Yes | 2 (50) | 1 (25) | 1 (25) | | 1 (33) | 2 (67) | 0 (0) | |
| No | 79 (48) | 79 (48) | 6 (4) | | 27 (35) | 42 (55) | 8 (10) | |
| Multifocal Consolidation | | | | .370 | | | | .643 |
| Yes | 26 (47) | 25 (46) | 4 (7) | | 9 (29) | 19 (61) | 3 (10) | |
| No | 55 (49) | 55 (49) | 3 (3) | | 19 (39) | 25 (51) | 5 (10) | |
| Unilateral Consolidation | | | | .095 | | | | .822 |
| Yes | 2 (50) | 1 (25) | 1 (25) | | 1 (33) | 2 (67) | 0 (0) | |
| No | 79 (48) | 79 (48) | 6 (4) | | 27 (35) | 42 (55) | 8 (10) | |
| Bilateral Consolidation | | | | .481 | | | | .934 |
| Yes | 28 (47) | 28 (47) | 4 (6) | | 12 (33) | 20 (56) | 4 (11) | |
| No | 53 (49) | 52 (48) | 3 (3) | | 16 (36) | 24 (55) | 4 (9) | |
| Multifocal Bilateral GGO | | | | .077 | | | | .215 |
| Yes | 31 (57) | 23 (43) | 0 (0) | | 11 (50) | 9 (41) | 2 (9) | |
| No | 50 (44) | 57 (50) | 7 (6) | | 17 (30) | 35 (60) | 6 (10) | |
| Multifocal Bilateral Consolidation | | | | .172 | | | | .766 |
| Yes | 6 (33) | 10 (56) | 2 (11) | | 4 (31) | 7 (54) | 2 (15) | |
| No | 75 (50) | 70 (47) | 5 (3) | | 24 (36) | 37 (55) | 6 (9) | |
| Multifocal Bilateral GGO Consolidation | | | | .773 | | | | .799 |
| Yes | 22 (52) | 18 (43) | 2 (5) | | 7 (30) | 14 (61) | 2 (9) | |
| No | 59 (47) | 62 (49) | 5 (4) | | 21 (37) | 30 (53) | 6 (10) | |

*Note:* Bold values are statistically significant ($P < .05$).

Data were expressed as frequency (percentage).

Abbreviations: CT, Computed tomography; GGO, ground glass opacity; SOFA. Sequential Organ Failure Assessment.

$P < .05$ was considered significant.

*P values indicate comparison between groups (Chi-square).

results that COVID-19 pneumonia involves both parenchyma and interstitial lung tissue.[50] In addition, GGO and consolidation are more common in patients who needed ICU admission. These findings indicate that chest CT scan can be a helpful risk stratification tool for admitted patients, and via applying a simple procedure for scoring the abnormal results in each location, radiologists can give

critical information about at-risk patients who need ICU admission. Moreover, the chest CT scan can predict the prognosis of patients.[51] Based on our study, a GGO pattern was more valuable than a consolidation pattern in predicting the prognosis of COVID-19 patients which was in line with Lin et al[52] who indicated the value of the CT scan in diagnosis and evaluation of COVID-19. Additional studies are

| Chest CT scan | SOFA score on Day 1 (n = 168) | | SOFA score on Day 5 (n = 80) | |
|---|---|---|---|---|
| | r | P-value* | r | P-value* |
| Unifocal GGO | 0.008 | .917 | 0.075 | .509 |
| Multifocal GGO | 0.199 | **.010** | 0.196 | .082 |
| Unilateral GGO | 0.088 | .256 | 0.095 | .404 |
| Bilateral GGO | 0.196 | **.011** | 0.196 | .082 |
| Unifocal Consolidation | 0.004 | .963 | 0.059 | .605 |
| Multifocal Consolidation | 0.039 | .620 | 0.170 | .132 |
| Unilateral Consolidation | 0.004 | .963 | 0.059 | .605 |
| Bilateral Consolidation | 0.035 | .656 | 0.112 | .325 |
| Multifocal Bilateral GGO | 0.162 | **.035** | 0.226 | **.044** |
| Multifocal Bilateral Consolidation | 0.127 | .102 | 0.192 | .088 |
| Multifocal Bilateral GGO Consolidation | 0.056 | .467 | 0.008 | .941 |

*Note:* P < .05 was considered significant.

Abbreviations: CT, Computed tomography; GGO, ground glass opacity; SOFA, Sequential Organ Failure Assessment.

*Spearman rank correlation coefficient.

warranted to completely understand the prognostic power of this finding in patients with COVID-19.

Our study preliminarily demonstrated a significant correlation between chest CT scan features including multifocal and bilateral GGO patterns with SOFA score on admission (day 1). In addition, significant correlations were noticed between multifocal bilateral GGO with SOFA scores on admission (day 1) and on day 5. These findings indicate that in more severe disease, more abnormalities can be observed on chest CT scan. The SOFA score is an important index to reflect the state and degree of multiple organ dysfunctions[11] and can predict the severity and outcome of the disease.[53,54] In a study by Francone et al,[55] CT score was significantly higher in critical and severe patients than in mild stage subjects which was consistent with our research. In addition, Shen et al[56] found that CT imaging was helpful in classifying disease severity as a larger proportion of scans from critically ill patients presented bilateral lung involvement compared with mild cases. In another study on COVID-19 patients, higher CT scores had a significant relationship with more severe disease.[57] Wu et al[40] also suggested that chest CT scan could be used to assess the severity of the disease and had a considerable function in clinical practice. Therefore, it seems that CT is the main procedure to determine the severity of the disease and can be used to identify disease progression. The main benefit of the CT scan is that the test is available immediately and results are accessible directly after scanning. This benefit depends on the accessibility of a CT scan, personnel and a well-designed approach to perform these scans.

Increased inflammatory parameters, such as CRP were reported in COVID-19.[31,44,55,58-60] CRP is a non-specific acute-phase protein as well as a sensitive biomarker of inflammation, infection, and tissue destruction.[61] Increased CRP concentrations may reflect the extent of inflammation or extensive tissue

damage and are usually noticed in viral pneumonia.[62,63] According to our study, there was a significant relationship between chest CT scan features including unilateral and bilateral GGO patterns with serum CRP. Our research was consistent with Zhu et al[64] who indicated that chest CT scan results significantly positively correlated with CRP concentrations. Furthermore, Zhang et al[44] and Xiong et al[65] reported that CRP had a significant positive correlation with the severity of pneumonia assessed on CT scan. Francone et al[55] indicated a statistically significant correlation between CT score and CRP which was in line with our study. Moreover, Tan et al[60] stated a positive correlation between CRP with CT scores which was similar to present study. Chen et al[66] also found a positive correlation between plasma CRP level and CT grading. Furthermore, it has been reported that serum CRP concentration and CT scores have a good consistency, and their combination can effectively evaluate disease progression and therapeutic effects.[32]

Our study preliminarily demonstrated significant relationships between chest CT scan features including GGO patterns with comorbidities, such as overweight/obesity, heart failure, cardiovascular diseases, and malignancy. To our surprise, this research did not reveal significant relationship between chest CT scan features with preexisting hypertension and diabetes mellitus. There are limited reports about the relationship between chest CT scan manifestations and comorbidities. Our study was supported by Liu et al[67] who reported that preexisting chronic diseases were correlated with the higher disease severity and increased admittance to ICU. However, another study conducted by Asai et al[68] did not find any correlation between the underlying diseases and radiological characteristics which was in contrast with our study. This discrepancy might be due to differences in sample size and characteristics of studied patients. The sample size included in

**TABLE 4** Relationship between chest CT scan and C-reactive protein in study patients (n = 168)

| Chest CT scan | C-reactive protein | | | | P-value[*] |
| --- | --- | --- | --- | --- | --- |
| | 1+ | 2+ | 3+ | High | |
| Unifocal GGO | | | | | .722 |
| Yes | 3 (38) | 1 (13) | 1 (13) | 1 (13) | |
| No | 37 (23) | 37 (23) | 33 (21) | 10 (6) | |
| Multifocal GGO | | | | | .063 |
| Yes | 26 (27) | 20 (20) | 14 (14) | 5 (5) | |
| No | 14 (20) | 18 (26) | 20 (29) | 6 (9) | |
| Unilateral GGO | | | | | **.049** |
| Yes | 2 (40) | 1 (20) | 1 (20) | 1 (20) | |
| No | 38 (24) | 37 (23) | 33 (20) | 10 (6) | |
| Bilateral GGO | | | | | **.046** |
| Yes | 26 (26) | 20 (20) | 14 (14) | 6 (6) | |
| No | 14 (21) | 18 (27) | 20 (29) | 5 (7) | |
| Unifocal Consolidation | | | | | .386 |
| Yes | 2 (50) | 1 (25) | 0 (0) | 1 (25) | |
| No | 38 (23) | 37 (23) | 34 (21) | 10 (6) | |
| Multifocal Consolidation | | | | | .233 |
| Yes | 10 (18) | 16 (29) | 8 (15) | 2 (4) | |
| No | 30 (27) | 22 (20) | 26 (23) | 9 (8) | |
| Unilateral Consolidation | | | | | .386 |
| Yes | 2 (50) | 1 (25) | 0 (0) | 1 (25) | |
| No | 38 (23) | 37 (23) | 34 (21) | 10 (6) | |
| Bilateral Consolidation | | | | | .094 |
| Yes | 10 (17) | 19 (32) | 8 (13) | 3 (5) | |
| No | 30 (28) | 19 (18) | 26 (24) | 8 (7) | |
| Multifocal Bilateral GGO | | | | | .095 |
| Yes | 19 (35) | 7 (13) | 9 (17) | 3 (6) | |
| No | 21 (18) | 31 (27) | 25 (22) | 8 (7) | |
| Multifocal Bilateral Consolidation | | | | | .118 |
| Yes | 2 (11) | 8 (44) | 5 (28) | 0 (0) | |
| No | 38 (25) | 30 (20) | 29 (19) | 11 (7) | |
| Multifocal Bilateral GGO Consolidation | | | | | .113 |
| Yes | 7 (17) | 11 (26) | 4 (10) | 3 (7) | |
| No | 33 (26) | 27 (21) | 30 (24) | 8 (6) | |
| Mortality | | | | | .556 |
| Survived | 26 (26) | 22 (22) | 21 (21) | 8 (8) | |
| Died | 16 (21) | 16 (21) | 15 (20) | 4 (5) | |

*Note:* Data were expressed as frequency (percentage).

Abbreviations: CT, Computed tomography; GGO, ground glass opacity.

*P* < .05 was considered significant.

[*]*P* values indicate comparison between groups (Chi-square).

present study was larger than Asai et al[68] research and the results may be more convincing. It has been reported that comorbidities lead to an impaired body function and weakened immune system, thereby causing individuals to be more vulnerable to the coronavirus. Chronic diseases share several common features with infectious disorders and their complications, such as endothelial dysfunction, the pro-inflammatory state, and alterations in the innate immune response.[69-71] More investigations

**TABLE 5** Relationship between chest CT scan and comorbidities in study patients

| Chest CT scan | Overweight/Obesity | | | Hypertension | | | Diabetes | | | Heart failure | | | CVD | | | Malignancy | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Yes | No | P* | Yes | No | P* | Yes | No | P* | Yes | No | P* | Yes | No | P* | Yes | No | P* |
| **Unifocal GGO** | | | .006 | | | .584 | | | .509 | | | .639 | | | .041 | | | .012 |
| Yes | 1 (25) | 3 (75) | | 3 (37) | 5 (63) | | 1 (14) | 6 (86) | | 1 (14) | 6 (86) | | 2 (29) | 5 (71) | | 2 (29) | 5 (71) | |
| No | 80 (82) | 18 (18) | | 73 (47) | 81 (53) | | 39 (25) | 115 (75) | | 14 (9) | 141 (91) | | 11 (7) | 144 (93) | | 8 (5) | 147 (95) | |
| **Multifocal GGO** | | | .059 | | | .871 | | | .737 | | | .001 | | | .005 | | | .993 |
| Yes | 53 (86) | 9 (14) | | 45 (46) | 52 (54) | | 25 (26) | 72 (74) | | 3 (3) | 94 (97) | | 3 (3) | 94 (97) | | 6 (6) | 91 (94) | |
| No | 28 (70) | 12 (30) | | 31 (48) | 34 (52) | | 15 (23) | 49 (77) | | 12 (18) | 53 (82) | | 10 (15) | 55 (85) | | 4 (6) | 61 (94) | |
| **Unilateral GGO** | | | .045 | | | .608 | | | .620 | | | .728 | | | .027 | | | .006 |
| Yes | 1 (33) | 2 (67) | | 2 (40) | 4 (60) | | 2 (40) | 4 (60) | | 0 (0) | 6 (100) | | 2 (40) | 4 (60) | | 2 (40) | 4 (60) | |
| No | 80 (81) | 19 (19) | | 74 (47) | 82 (53) | | 38 (25) | 117 (75) | | 15 (10) | 141 (90) | | 11 (7) | 145 (93) | | 8 (5) | 148 (95) | |
| **Bilateral GGO** | | | .034 | | | .430 | | | .823 | | | .001 | | | .003 | | | .941 |
| Yes | 55 (86) | 9 (14) | | 44 (44) | 55 (56) | | 24 (24) | 75 (76) | | 3 (3) | 96 (97) | | 3 (3) | 96 (97) | | 6 (6) | 93 (94) | |
| No | 26 (68) | 12 (32) | | 32 (51) | 31 (49) | | 16 (26) | 46 (74) | | 12 (19) | 51 (81) | | 10 (16) | 53 (84) | | 4 (6) | 59 (94) | |
| **Unifocal Consolidation** | | | 0.299 | | | 0.634 | | | 0.731 | | | 0.577 | | | 0.606 | | | .654 |
| Yes | 1 (50) | 1 (50) | | 1 (33) | 2 (67) | | 1 (33) | 2 (67) | | 0 (0) | 3 (100) | | 0 (0) | 3 (100) | | 0 (0) | 3 (100) | |
| No | 80 (80) | 20 (20) | | 75 (47) | 84 (53) | | 39 (25) | 119 (75) | | 15 (10) | 144 (91) | | 13 (8) | 146 (92) | | 10 (6) | 149 (94) | |
| **Multifocal Consolidation** | | | 0.072 | | | 0.119 | | | 0.166 | | | 0.250 | | | 0.152 | | | .817 |
| Yes | 28 (90) | 3 (10) | | 30 (56) | 24 (44) | | 17 (32) | 37 (68) | | 3 (6) | 51 (94) | | 2 (4) | 52 (96) | | 3 (6) | 51 (94) | |
| No | 53 (75) | 18 (25) | | 46 (43) | 62 (57) | | 33 (22) | 84 (78) | | 12 (11) | 96 (89) | | 11 (10) | 97 (90) | | 7 (6) | 101 (94) | |
| **Unilateral Consolidation** | | | .299 | | | .634 | | | .731 | | | .577 | | | .606 | | | .654 |
| Yes | 1 (50) | 1 (50) | | 1 (33) | 2 (67) | | 1 (33) | 2 (67) | | 0 (0) | 3 (100) | | 0 (0) | 3 (100) | | 0 (0) | 3 (100) | |
| No | 80 (80) | 20 (20) | | 75 (47) | 84 (53) | | 39 (25) | 119 (75) | | 15 (9) | 144 (91) | | 13 (8) | 146 (92) | | 10 (6) | 149 (94) | |
| **Bilateral Consolidation** | | | 0.119 | | | 0.116 | | | 0.173 | | | 0.180 | | | 0.109 | | | .693 |
| Yes | 30 (88) | 4 (12) | | 32 (55) | 26 (45) | | 18 (31) | 40 (69) | | 3 (5) | 55 (95) | | 2 (3) | 56 (97) | | 3 (5) | 55 (95) | |
| No | 51 (75) | 17 (25) | | 44 (42) | 60 (58) | | 22 (21) | 81 (79) | | 12 (12) | 92 (88) | | 11 (11) | 93 (89) | | 7 (7) | 97 (93) | |

(Continues)

TABLE 5 (Continued)

| Chest CT scan | Overweight/Obesity | | | Hypertension | | | Diabetes | | | Heart failure | | | CVD | | | Malignancy | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Yes | No | P* | Yes | No | P* | Yes | No | P* | Yes | No | P* | Yes | No | P* | Yes | No | P* |
| Multifocal Bilateral GGO | | | .065 | | | .148 | | | .584 | | | .085 | | | **.041** | | | .817 |
| Yes | 33 (89) | 4 (11) | | 21 (39) | 33 (61) | | 12 (22) | 42 (78) | | 2 (4) | 52 (96) | | 1 (2) | 53 (98) | | 3 (6) | 51 (94) | |
| No | 48 (74) | 17 (26) | | 55 (51) | 53 (49) | | 28 (26) | 79 (74) | | 13 (12) | 95 (88) | | 12 (11) | 96 (89) | | 7 (6) | 101 (94) | |
| Multifocal Bilateral Consolidation | | | .110 | | | .188 | | | .217 | | | .638 | | | .213 | | | .280 |
| Yes | 9 (100) | 0 (0) | | 10 (63) | 6 (37) | | 6 (37) | 10 (63) | | 2 (12) | 14 (88) | | 0 (0) | 16 (100) | | 0 (0) | 16 (100) | |
| No | 72 (77) | 21 (23) | | 66 (45) | 80 (55) | | 34 (23) | 111 (77) | | 13 (9) | 133 (91) | | 13 (9) | 133 (91) | | 10 (7) | 136 (93) | |
| Multifocal Bilateral GGO Consolidation | | | .933 | | | .409 | | | .516 | | | .074 | | | .366 | | | .762 |
| Yes | 20 (80) | 5 (20) | | 22 (52) | 20 (48) | | 12 (29) | 30 (71) | | 1 (2) | 41 (98) | | 2 (5) | 40 (95) | | 3 (7) | 39 (93) | |
| No | 61 (79) | 16 (21) | | 54 (45) | 66 (55) | | 28 (24) | 91 (76) | | 14 (12) | 106 (88) | | 11 (9) | 109 (91) | | 7 (6) | 113 (94) | |

Note: Bold values are statistically significant ($P < .05$).

Data were expressed as frequency (percentage).

Abbreviations: CT, Computed tomography; CVD, Cardiovascular disease; GGO, ground glass opacity.

$P < .05$ was considered significant.

*P values indicate comparison between groups (Chi-square).

**TABLE 6** Relationship between chest CT scan and mortality in study patients (n = 168)

| Chest CT scan | Mortality | | |
| --- | --- | --- | --- |
| | Survived (n = 94) | Died (n = 74) | P-value* |
| Unifocal GGO | | | .281 |
| Yes | 3 (37) | 5 (63) | |
| No | 91 (57) | 69 (43) | |
| Multifocal GGO | | | .713 |
| Yes | 56 (57) | 42 (43) | |
| No | 38 (54) | 32 (46) | |
| Unifocal GGO | | | .400 |
| Yes | 2 (40) | 4 (60) | |
| No | 92 (57) | 70 (43) | |
| Bilateral GGO | | | .988 |
| Yes | 56 (56) | 44 (44) | |
| No | 38 (56) | 30 (44) | |
| Unifocal Consolidation | | | .437 |
| Yes | 3 (75) | 1 (25) | |
| No | 91 (55) | 73 (45) | |
| Multifocal Consolidation | | | .114 |
| Yes | 26 (47) | 29 (53) | |
| No | 68 (60) | 45 (40) | |
| Unilateral Consolidation | | | .437 |
| Yes | 3 (75) | 1 (25) | |
| No | 91 (56) | 73 (45) | |
| Bilateral Consolidation | | | .138 |
| Yes | 29 (48) | 31 (52) | |
| No | 65 (60) | 43 (40) | |
| Multifocal Bilateral GGO | | | .111 |
| Yes | 35 (65) | 19 (35) | |
| No | 59 (52) | 55 (48) | |
| Multifocal Bilateral Consolidation | | | .123 |
| Yes | 7 (39) | 11 (61) | |
| No | 87 (58) | 63 (42) | |
| Multifocal Bilateral GGO Consolidation | | | .370 |
| Yes | 21 (50) | 21 (50) | |
| No | 73 (58) | 53 (42) | |

*Note:* Data were expressed as frequency (percentage).

Abbreviations: CT, Computed tomography; GGO, ground glass opacity.

$P < .05$ was considered significant.

*P values indicate comparison between groups (Chi-square).

are warranted to evaluate the nature and extent of coexistence between COVID-19 and chronic diseases.

Based on our study, multifocal and bilateral GGO patterns on chest CT scans were more common in survived patients than in death patients, whereas multifocal and bilateral consolidation patterns were more common in death patients than in survived patients. Recent investigations by Zhou et al[8] and Yuan et al[36] showed consolidation and bilateral infiltration were more frequent in patients who died from COVID-19 than patients who survived which was in line with our research. Li et al[72] also reported that consolidations on CT images were more common in death patients than in survived patients which was consistent with our study. Furthermore, another study in COVID-19 adults reported that presence of consolidation pattern was more common in non-survivors compared to survivors.[73] The relation between CT findings and mortality are not completely understood. Present research did not show any significant relationships between chest CT scan results with mortality. Our research was consistent with Asai et al[68] who also indicated no significant association between CT findings with mortality. However, Raoufi et al[74] showed a significant correlation between chest CT scan characteristics and mortality of COVID-19 cases which was in contrast with our study. Furthermore, Hu et al[21] reported that chest CT findings were worsening in patients who died from COVID-19.

This study had some limitations including a single-center study and having small sample size. Thus, additional large-scale multi-center studies would be helpful. Furthermore, we did not follow-up these patients who survived and correlated their chest CT or clinical findings with outcomes. Lastly, no autopsy was conducted in the deceased patients.

## 5 | CONCLUSION

In conclusion, multifocal bilateral GGO was the most common pattern on chest CT scans. Furthermore, multifocal bilateral consolidation was more prevalent than unifocal unilateral consolidation pattern. Although chest CT scan characteristics were significantly related with SOFA score, CRP, and comorbidity in ICU patients with COVID-19, a relationship with mortality was not significant.

### CONFLICT OF INTEREST
The authors declared that they have no conflicts of interests.

### DATA AVAILABILITY STATEMENT
Data available on request from the authors. The data that support the findings of this study are available from the corresponding author upon reasonable request.

### REFERENCES
1. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China 2019. *N Engl J Med*. 2020;382(8):727-733.
2. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen
3. Cascella M, Rajnik M, Cuomo A, Dulebohn SC, Di Napoli R. *Features, evaluation, and treatment of Coronavirus (COVID-19)*. StatPearls Publishing; 2020.

4. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. *Intensive Care Med*. 2020;46(5):846-848.

5. Grasselli G, Zangrillo A, Zanella A, et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the lombardy region, Italy. *JAMA*. 2020;323(16):1574-1581.

6. Liu J, Zhang S, Wu Z, et al. Clinical outcomes of COVID-19 in Wuhan, China: a large cohort study. *Ann Intensive Care*. 2020;10(99):1-21.

7. Yao Q, Wang P, Wang X, et al. A retrospective study of risk factors for severe acute respiratory syndrome coronavirus 2 infections in hospitalized adult patients. *Pol Arch Intern Med*. 2020;130(5):390-399.

8. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395(10229):1054-1062.

9. Morrison AR, Johnson JM, Griebe KM, et al. Clinical characteristics and predictors of survival in adults with coronavirus disease 2019 receiving tocilizumab. *J Autoimmun*. 2020;114:1-8.

10. Wang ZH, Shu C, Ran X, Xie CH, Zhang L. Critically Ill patients with coronavirus disease 2019 in a designated ICU: clinical features and predictors for mortality. *Risk Manag Healthc Policy*. 2020;13:833-845.

11. Wu C, Chen X, Cai Y, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. *JAMA Intern Med*. 2020;180(7):934-943.

12. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med*. 2020;8(5):475-481.

13. Li Y, Xia L. Coronavirus Disease 2019 (COVID-19): role of chest CT in diagnosis and management. *AJR Am J Roentgenol*. 2020;214(6):1-7.

14. Ai T, Yang Z, Hou H, et al. Correlation of chest CT and RT-PCR testing in coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases. *Radiology*. 2020;296(2):E32-40.

15. Pan Y, Guan H, Zhou S, et al. Initial CT findings and temporal changes in patients with the novel coronavirus pneumonia (2019-nCoV): a study of 63 patients in Wuhan, China. *Eur Radiol*. 2020;30(6):3306-3309.

16. Kim JY, Choe PG, Oh Y, et al. The first case of 2019 novel coronavirus pneumonia imported into Korea from Wuhan, China: implication for infection prevention and control measures. *J Korean Med Sci*. 2020;35(5):e61.

17. Huang P, Liu T, Huang L, et al. Use of chest CT in combination with negative RT-PCR assay for the 2019 novel coronavirus but high clinical suspicion. *Radiology*. 2020;295(1):22-23.

18. Liu J, Zheng X, Tong Q, et al. Overlapping and discrete aspects of the pathology and pathogenesis of the emerging human pathogenic coronaviruses SARS-CoV, MERSCoV, and 2019-nCoV. *J Med Virol*. 2020;92(5):491-494.

19. Chung M, Bernheim A, Mei X, et al. CT imaging features of 2019 novel coronavirus (2019-nCoV). *Radiology*. 2020;295(1):230.

20. Song F, Shi N, Shan F, et al. Emerging coronavirus 2019-nCoV pneumonia. *Radiology*. 2020;295(1):210-217.

21. Hu Y, Zhan C, Chen C, Ai T, Xia L. Chest CT findings related to mortality of patients with COVID-19: a retrospective case series study. *PLoS One*. 2020;15(8):1-12.

22. Sverzellati N, Milone F, Balbi M. How imaging should properly be used in COVID-19 outbreak: an Italian experience. *Diagn Interv Radiol*. 2020;26:204-206.

23. Bernheim A, Mei X, Huang M, et al. Chest CT findings in coronavirus disease-19 (COVID-19): relationship to duration of infection. *Radiology*. 2020;295(3):200463.

24. Wang Y, Dong C, Hu Y, et al. Temporal changes of CT findings in 90 patients with COVID-19 pneumonia: a longitudinal study. *Radiology*. 2020;296(2):E55-64.

25. Salehi S, Abedi A, Balakrishnan S, Gholamrezanezhad A. Coronavirus disease 2019 (COVID-19): a systematic review of imaging findings in 919 patients. *AJR Am J Roentgenol*. 2020;215(1):87-93.

26. Warusevitane A, Karunatilake D, Sim J, Smith C, Roffe C. Early diagnosis of pneumonia in severe stroke: clinical features and the diagnostic role of C-reactive protein. *PLoS One*. 2016;11(3):e0150269.

27. Chen CC, Lee IK, Liu JW, Huang SY, Wang L. Utility of C-reactive protein levels for early prediction of dengue severity in adults. *Biomed Res Int*. 2015;2015(2):936062.

28. Eppy E, Suhendro S, Nainggolan L, Rumende CM. The differences between interleukin-6 and c-reactive protein levels among adult patients of dengue infection with and without plasma leakage. *Acta Med Indones*. 2016;48(1):3-9.

29. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA*. 2020;323(11):1061-1069.

30. Yang W, Cao Q, Qin L, et al. Clinical characteristics and imaging manifestations of the 2019 novel coronavirus disease (COVID-19): a multi-center study in Wenzhou city, Zhejiang, China. *J Infect*. 2020;80(4):388-393.

31. Wang L. C-reactive protein levels in the early stage of COVID-19. *Médecine Et Maladies Infectieuses*. 2020;50(4):332-334.

32. Kim SH, Lee JY, Kim DH, et al. Factors related to the initial stroke severity of posterior circulation ischemic stroke. *Cerebrovasc Dis*. 2013;36(1):62-68.

33. WHO. Clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected: interim guidance. 2020. https://apps.who.int/iris/handle/10665/330893

34. Vincent JL, Moreno R, Takala J, et al. On behalf of the Working Group on sepsis-related problems of the European Society of Intensive Care Medicine. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. *Intensive Care Med*. 1996;22(7):707-710.

35. Nehring SM, Goyal A, Bansal P, et al. C Reactive Protein. [Updated 2020 Jun 5]. In: StatPearls [Internet]. StatPearls Publishing; 2021. Available from: https://www.ncbi.nlm.nih.gov/books/NBK441843/

36. Ye Z, Zhang Y, Wang Y, Huang Z, Song B. Chest CT manifestations of new coronavirus disease 2019 (COVID-19): a pictorial review. *Eur Radiol*. 2020;30:4381-4389.

37. Yuan M, Yin W, Tao Z, Tan W, Hu Y. Association of radiologic findings with mortality of patients infected with 2019 novel coronavirus in Wuhan, China. *PLoS One*. 2020;15(3):e0230548.

38. Caruso D, Zerunian M, Polici M, et al. Chest CT features of COVID-19 in Rome, Italy. *Radiology*. 2020;296(2):E79-85.

39. Xu X, Yu C, Qu J, et al. Imaging and clinical features of patients with 2019 novel coronavirus SARS-CoV-2. *Eur J Nucl Med Mol Imaging*. 2020;47(5):1275-1280.

40. Wu J, Wu X, Zeng W, et al. Chest CT findings in patients with corona virus disease 2019 and its relationship with clinical features. *Investig Radiol*. 2020;55(5):257-261.

41. Guan CS, Lv ZB, Yan S, et al. Imaging features of coronavirus disease 2019 (COVID-19): evaluation on thin-section CT. *Acad Radiol*. 2020;27(5):609-613.

42. Han R, Huang L, Jiang H, Dong J, Peng H, Zhang D. Early clinical and CT manifestations of coronavirus disease 2019 (COVID-19) pneumonia. *Am J Roentgenol*. 2020;215(2):338-343.

43. Zhao W, Zhong Z, Xie X, Yu Q, Liu J. Relation between chest CT findings and clinical conditions of coronavirus disease (COVID-19) pneumonia: a multicenter study. *Am J Roentgenol*. 2020;214(5):1-6.

44. Zhang N, Xu X, Zhou LY, et al. Clinical characteristics and chest CT imaging features of critically ill COVID-19 patients. *Eur Radiol*. 2020;30(11):6151-6160.

45. Ding YQ, Bian XW. Analysis of coronavirus disease-19 (COVID-19) based on SARS autopsy. *Chin J Pathol*. 2020;49(4):291-293.

46. Stump B, Cui Y, Kidambi P, Lamattina AM, El-Chemaly S. Lymphatic changes in respiratory diseases: more than just remodeling of the lung? *Am J Respir Cell Mol Biol*. 2017;57(3):272-279.

47. Xu SP, Kuang D, Hu Y, Liu C, Duan YQ, Wang GP. Detection of 2019-nCoV in the pathological paraffin embedded tissue. *Chin J Pathol*. 2020;49:E004.

48. Meng H, Xiong R, He R, et al. CT imaging and clinical course of asymptomatic cases with COVID-19 pneumonia at admission in Wuhan, China. *J Infect*. 2020;8(1):E33-39.

49. Hj K, Lim S, Choe J, Choi SH, Sung H, Do KH. Radiographic and CT features of viral pneumonia. *Radiographics*. 2018;38(3):719-739.

50. Xu Z, Shi L, Wang Y, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. *Lancet Respir Med*. 2020;8(4):420-422.

51. Lee KS. Pneumonia associated with 2019 novel coronavirus: can computed tomographic findings help predict the prognosis of the disease? *Korean J Radiol*. 2020;21(3):257-258.

52. Lin C, Ding Y, Xie B, et al. Asymptomatic novel coronavirus pneumonia patient outside Wuhan: the value of CT images in the course of the disease. *Clin Imaging*. 2020;63(3):7-9.

53. de Grooth HJ, Geenen IL, Girbes AR, Vincent JL, Parienti JJ, Oudemans-van Straaten HM. SOFA and mortality end- points in randomized controlled trials: a systematic review and meta-regression analysis. *Crit Care*. 2017;21(1):38.

54. Raith EP, Udy AA, Bailey M, et al. Prognostic accuracy of the SOFAscore, SIRS criteria, and qSOFA score for in-hospital mortality among adults with suspected infection admitted to the intensive care unit. *JAMA*. 2017; 317(3):290-300.

55. Francone M, Iafrate F, Masci GM, et al. Chest CT score in COVID-19 patients: correlation with disease severity and short-term prognosis. *Eur Radiol*. 2020;30(12):6808-6817.

56. Shen Y, Zheng F, Sun D, et al. Epidemiology and clinical course of COVID-19 in Shanghai, China. *Emerg Microbes Infect*. 2020;9(1):1537-1545.

57. Li K, Wu J, Wu F, et al. The clinical and chest CT features associated with severe and critical COVID-19 pneumonia. *Investig Radiol*. 2020;55(6):327-331.

58. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020;395(10223):507-513.

59. Liu F, Li L, Xu M, et al. Prognostic value of interleukin-6, C-reactive protein, and procalcitonin in patients with COVID-19. *J Clin Virol*. 2020;127:104370.

60. Tan C, Huang Y, Shi F, et al. C-reactive protein correlates with computed tomographic findings and predicts severe COVID-19 early. *J Med Virol*. 2020;92(7):856-862.

61. Pepys MB, Hirschfield GM. C-reactive protein: a critical update. *J Clin Invest*. 2013;111(2):1805-1812.

62. Tsang OT, Chau TN, Choi KW, et al. Coronavirus-positive nasopharyngeal aspirate as predictor for severe acute respiratory syndrome mortality. *Emerg Infect Dis*. 2003;9(11):1381-1387.

63. Ahn S, Kim WY, Kim SH, et al. Role of procalcitonin and C-reactive protein in differentiation of mixed bacterial infection from 2009 H1N1 viral pneumonia. *Influenza Other Respi Viruses*. 2011;5(6):398-403.

64. Zhu J, Chen C, Shi R, Li B. Correlations of CT scan with high-sensitivity C-reactive protein and D-dimer in patients with coronavirus disease 2019. *Pak J Med Sci*. 2020;36(6):1397-1401.

65. Xiong Y, Sun D, Liu Y, et al. Clinical and high-resolution CT features of the COVID-19 infection: comparison of the initial and follow-up changes. *Invest Radiol*. 2020;55(6):332-339.

66. Chen W, Zheng KI, Liu S, Yan Z, Xu C, Qiao Z. Plasma CRP level is positively associated with the severity of COVID-19. *Ann Clin Microbiol Antimicrob*. 2020;19(1):1-7.

67. Liu H, Chen S, Liu M, Nie H, Lu H. Comorbid chronic diseases are strongly correlated with disease severity among COVID-19 patients: a systematic review and meta-analysis. *Aging Dis*. 2020;11(3):668-678.

68. Asai N, Sakanashi D, Nakamura A, et al. Clinical manifestations and radiological features by chest computed tomographic findings of a novel coronavirus disease-19 pneumonia among 92 patients in Japan. *J Microbiol Immunol Infect*. 2020;54(4):748-751.

69. Htun NSN, Odermatt P, Eze IC, Boillat-Blanco N, D'Acremont V, Probst-Hensch N. Is diabetes a risk factor for a severe clinical presentation of dengue?– review and meta-analysis. *PLoS Negl Trop Dis*. 2015;9(4):e0003741.

70. Limonta D, Torres G, Capó V, Guzmán MG. Apoptosis, vascular leakage and increased risk of severe dengue in a type 2 diabetes mellitus patient. *Diab Vasc Dis Res*. 2008;5(3):213-214.

71. Dharmashankar K, Widlansky ME. Vascular endothelial function and hypertension: insights and directions. *Curr Hypertens Rep*. 2010;12(6):448-455.

72. Li Y, Yang Z, Ai T, Wu S, Liming X. Association of "initial CT" findings with mortality in older patients with coronavirus disease 2019 (COVID-19). *Eur Radiol*. 2020;30(11):6186-6193.

73. Li K, Chen D, Chen S, et al. Predictors of fatality including radiographic findings in adults with COVID-19. *Respir Res*. 2020;21(1):1-10.

74. Raoufi M, Safavi Naini SAA, Azizan Z, et al. Correlation between chest computed tomography scan findings and mortality of COVID-19 cases; a cross sectional Study. *Arch Acad Emerg Med*. 2020;8(1):e57.