The Performance of Chest CT in Evaluating the Clinical Severity of COVID-19 Pneumonia: Identifying Critical Cases Based on CT Characteristics

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Objectives: The aim of this study was to assess the clinical severity of COVID-19 pneumonia using qualitative and/or quantitative chest computed tomography (CT) indicators and identify the CT characteristics of critical cases.

Materials and Methods: Fifty-one patients with COVID-19 pneumonia including ordinary cases (group A, n = 12), severe cases (group B, n = 15), and critical cases (group C, n = 24) were retrospectively enrolled. The qualitative and quantitative indicators from chest CT were recorded and compared using Fisher exact test, one-way analysis of variance, Kruskal-Wallis H test, and receiver operating characteristic analysis.

Results: Depending on the severity of the disease, the number of involved lung segments and lobes, the frequencies of consolidation, crazy-paving pattern, and air bronchogram increased in more severe cases. Qualitative indicators including total severity score for the whole lung and total score for crazy-paving and consolidation could distinguish groups B and C from A (69% sensitivity, 83% specificity, and 73% accuracy) but were similar between group B and group C. Combined qualitative and quantitative indicators could distinguish these 3 groups with high sensitivity (B + C vs A, 90%; C vs B, 92%), specificity (100%, 87%), and accuracy (92%, 90%). Critical cases had higher total severity score (>10) and higher total score for crazy-paving and consolidation (>4) than ordinary cases, and had higher mean lung density (≦779 HU) and full width at half maximum (≦128 HU) but lower relative volume of normal lung density (≧50%) than ordinary/severe cases. In our critical cases, 8 patients with relative volume of normal lung density smaller than 40% received mechanical ventilation for supportive treatment, and 2 of them had died.

Conclusions: A rapid, accurate severity assessment of COVID-19 pneumonia based on chest CT would be feasible and could provide help for making management decisions, especially for the critical cases.

Key Words: COVID-19, SARS-CoV-2, quantitative chest CT, computed tomography, viral pneumonia

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Conflicts of interest and sources of funding: This work was supported, in part, by Overseas Research Project of Science and Technology Talent of Henan Health Commission, and positive CT findings of pneumonia. Severe cases are defined as those who had a respiratory rate of less than or equal to 30 times per minute, oxygen saturation of less than or equal to 93% at rest, arterial oxygen partial pressure (PaO2)inspired oxygen (FiO2) of less than or equal to 300 mm Hg (1 mm Hg = 0.133 kPa), or significant progress in chest CT findings of pneumonia within 24 to 48 hours of less than or equal to 50%. Critical cases are defined as those who are admitted to the intensive care unit for mechanical ventilation or had a FiO2 of...
at least 60% or more. Finally, 51 patients were included with demographics and clinical characteristics recorded. The flowchart of patient selection is shown in Figure 1.

CT Protocol

All examinations represented the initial CT scans for every individual patient. All CT images were acquired at the end of inhalation using a 256-row CT scanner (Revolution CT; GE Healthcare, Waukesha, WI) with detector configuration of 256 × 0.625 mm or using a 192-slice CT scanner (Somatom Force; Siemens Healthineers, Forchheim, Germany) with detector collimation of 192 × 0.6 mm. Other acquisition parameters for these 2 scanners were set as follows: tube voltage of 120 kV, automatic tube current modulation of 100 to 300 mA (AutoM, GE Healthcare; CareDose 4D, Siemens Healthineers), pitch of 0.99 to 1.375, and matrix of 512 × 512.

Images were reconstructed at slice thickness/interval of 1 to 1.25 mm with a hybrid adaptive statistical iterative reconstruction (40% level) using stand (mediastinal) and bone plus (lung) kernels (GE Healthcare) or with an advanced modeled iterative reconstruction (strength 3) using Br40 (mediastinal) and B157 (lung) kernels (Siemens Healthineers). The mediastinal and lung window width and level were set as 350/40 HU and 1500/−700 HU (GE Healthcare) or 400/40 HU and 1500/−500 (Siemens Healthineers), respectively, to evaluate the abnormalities in the mediastinum and lung parenchyma.

Qualitative Image Analyses

All the chest CT images were analyzed by 2 radiologists (J.B.G. [a senior thoracic radiologist with more than 30 years’ experience] and R.Z. [a thoracic radiologist with 8 years’ experience]) without access to clinical or laboratory findings. According to previously published articles for COVID-19, the CT image findings of ground glass opacity (GGO), consolidation, crazy-paving pattern, septal thickening, and pulmonary fibrosis were included in calculating the severity score of each lobe, which was classified from score 0 to score 4 with an increment of 25%, respectively. Total severity scores for the whole lung were the sum of 5 lung lobe scores (0–20 scores).

Because previous reports showed that the main CT manifestations of COVID-19 pneumonia at baseline were bilateral, peripheral, and basal GGO and consolidation, and developed into crazy-paving and consolidation with multifocal involvement at the peak of lung involvement, we took the sum extent of crazy-paving and consolidation involving the lung as an index to evaluate the progression of pneumonia. Crazy-paving pattern is defined as consisting of scattered or diffuse ground glass attenuation with superimposed interlobular septal thickening and intralobular lines, whereas consolidation is defined as a uniform increase of lung parenchyma with obscuration of the underlying vessels. The sum involvement of crazy-paving and consolidation of each lobe was scored using the aforementioned scoring criteria, and the sum of the 5 lobes was taken as the total lung scores (0–20 scores).

Quantitative Image Analyses

All the reconstructed images were transferred to the workstation for pulmonary quantitative analyses using CT Pulmo 3D software (CT Pulm3D-Syngo.via VB20; Siemens Healthineers). After loading the CT data, an automatic segmentation mode of lung parenchyma (left and right lung mode) was applied and then manual adjustment, if necessary, was made to ensure accurate lung segmentation. For the segmented lung, the volume (milliliters), relative volume (percent), mean lung density (MLD) (Hounsfield unit), and full width at half maximum (FWHM) (Hounsfield unit) were measured within the preset threshold range of −950 HU and −200 HU. The setting of the threshold range is based on the findings that CT values of normal parenchyma range from −950 HU to −750 HU while those in vessels or pneumonia are ≥−200 HU, from the instructions of the manufacturer, previous studies, and our practical experience. The evaluation index method was displayed by quantifying the percentage of the voxels below the low attenuation value (LAV) (threshold of −950 HU) and above the high attenuation value (HAV) (threshold of −200 HU). The FWHM parameter marks the width of frequency distribution at half of the maximum CT value, representing the heterogeneity of lung tissue density.

A subrange analysis method was used to display the relative volume of the segmented lung within a predetermined HU range, which was −1000 to −200 HU (in 8 colors representing 8 subranges). Percentile analysis was used to calculate and display relative volume (Hounsfield unit) within predefined percentage values of the lung segmentation (0%–100%), representing the cumulative number of voxels. Considering that the threshold of GGO has been reported to range from −800 to −500 HU, the threshold range of normal CT values in our study was finally set at between −950 HU and −800 HU instead of −950 to −750 HU to assess the relative volume of residual normal lung density of COVID-19 pneumonia.

To facilitate readers to better understand the performance of lung quantitative analysis methods on pneumonia, we included normal lung CT images from another 10 cases collected retrospectively for the comparison.

Statistical Analyses

Analyses were done with SPSS software version 16.0 and MedCalc software version 15.2.2, with P value less than 0.05 indicating a statistical difference. Continuous variables were presented as mean and standard deviation (SD) if normally distributed, and as median and interquartile range (IQR) values if nonnormally distributed, whereas categorical variables were described as frequency rates and percentages. The normality of continuous variables was tested for using Shapiro-Wilk tests. Comparisons among the groups were performed using Fisher exact test (for categorical data), one-way analysis of variance using Fisher exact test (for categorical data), one-way analysis of variance, and two-way analysis using Fisher exact test (for categorical data), one-way analysis of variance.
TABLE 1. Demographics and Clinical Characteristics of Patients With COVID-19 Pneumonia

| Parameter                        | All Patients (n = 51) | Group A (n = 12) | Group B (n = 15) | Group C (n = 24) | P†  |
|----------------------------------|----------------------|-----------------|-----------------|-----------------|-----|
| Sex, male/female                 | 29/22                | 7/5             | 8/7             | 14/10           | 0.948 |
| Age, y*                          | 54 ± 17              | 36 ± 10         | 47 ± 14         | 58 ± 27         | 0.046 |
| Exposure history                 | 43 (84%)             | 12 (100%)       | 13 (87%)        | 18 (75%)        | 0.872 |
| Initial signs and RLU52322symptoms of onset |                     |                 |                 |                 | 0.764 |
| Fever                            | 50 (98%)             | 11 (92%)        | 15 (100%)       | 24 (100%)       |     |
| Dyspnea                          | 12 (24%)             | 1 (8%)          | 4 (27%)         | 7 (29%)         |     |
| Fatigue                          | 16 (31%)             | 5 (42%)         | 5 (33%)         | 6 (25%)         |     |
| Dry cough                        | 22 (43%)             | 2 (17%)         | 8 (53%)         | 12 (50%)        |     |
| Underlying disease               | 17 (33%)             |                 |                 |                 | 0.002 |
| Chronic pulmonary disease        | 3 (6%)               | 0               | 2 (13%)         | 13 (31%)        |     |
| Cardiovascular disease           | 8 (16%)              | 0               | 2 (13%)         | 6 (25%)         |     |
| Cerebrovascular disease          | 5 (10%)              | 0               | 2 (13%)         | 3 (13%)         |     |
| Malignant tumor                  | 1 (2%)               | 1 (8%)          | 0               | 0               |     |
| Comorbidities                    |                      |                 |                 |                 |     |
| Acute respiratory distress syndrome | 20 (39%)            | 0               | 6 (40%)         | 13 (54%)        | 0.032 |
| Treatment                        |                      |                 |                 |                 |     |
| High flow nasal cannula          | 25 (49%)             | 2 (17%)         | 6 (40%)         | 17 (71%)        | <0.001 |
| Mechanical ventilation           | 7 (14%)              | 0               | 8 (33%)         | 3 (13%)         | 0.310 |
| ICU admission                    | 23 (45%)             | 0               | 7 (47%)         | 16 (67%)        | <0.001 |

Note: Data are the numbers with the percentage in parentheses except where specified.

Exposure history indicates the history of cases exposed to infected individuals or epidemic areas.

*Data are presented as mean ± SD. †Difference among groups A to C.

COVID-19, coronavirus disease 2019; ICU, intensive care unit.

RESULTS

Patient Characteristics

The demographics and clinical characteristics of all patients are summarized in the Table 1. In the full cohort, the mean age was 54 ± 17 years (range, 25–94), with no sex difference (29 [57%] men and 22 [43%] women). The most common symptoms at symptom onset were fever (50 [98%] patients) and dry cough (22 [43%]), with 17 patients (33%) who had underlying diseases. Twenty patients (39%) suffered from acute respiratory distress syndrome, of which 13 were transferred from other hospitals (6 in group B and 7 in group C). Patients in group C were much older (58 ± 27 years) than group A (36 ± 10 years) (P = 0.036), and had more cases of underlying diseases (12 [50%]) and acute respiratory distress syndrome (13 [54%]) than groups A and B (A, 1 [8%] and none; B, 4 [26%] and 6 [40%], respectively) (P < 0.05).

Quantitative Indicators

Comparisons of quantitative analyses and image examples are shown in Table 3 and Figure 2. A normal lung CT group (n = 10) was included for the quantitative comparison with the other 3 COVID-19 pneumonia groups. Patients in group C had significantly lower total lung volumes, higher MLD, higher FWHM, and higher HAV than the other 3 groups (all P < 0.001), but showed similar LAV values to them. No statistical differences in the quantitative indicators were found between groups A and B except MLD, which was higher in group B than group A (P = 0.038). The percentile analysis showed that relative volume of normal lung density (from −950 HU to −800 HU) within the total segmented lung was 43.01% (SD, 13.42) variance, or the Kruskal-Wallis H test (for continuous data). Using clinical stages as the reference standard, the sensitivity, specificity, accuracy, and the associated area under the receiver operating characteristic curve (AUC) with 95% confidence interval (CI) of qualitative and quantitative indicators were calculated.
in group C, which was significantly lower than those in the other 3 groups (group A: 87.83% [SD, 6.73]; group B: 62.25% [SD, 14.80]; normal group: 88.91% [SD, 3.35]) (all \( P < 0.001 \)) (Fig. 3). Compared with the normal group, the relative volume of normal lung density was lower in group B (\( P < 0.001 \)) but was similar to group A, with the latter 2 groups significantly different from each other (\( P = 0.03 \)).

Identification of Different Clinical Stages With CT Indicators

By using the receiver operating characteristic curves, the threshold values of statistically significant parameters were determined to optimize both the sensitivity and the specificity for differentiating each group from the other 2 groups (Table 4). For example, patients in groups C were significantly different from groups A and B with a higher number of involved lung segments (>8, sensitivity and specificity of 100% and 37%), higher total severity score (>10, 67% and 74%), higher total score for crazy-paving and consolidation (>4, 87% and 44%), higher MLD (>−779 HU, 100%, and 85%), higher FWHM (>116 HU, 83% and 81%), and lower relative volume of normal lung density (\( \leq 50\% \), 83% and 92%). As the intermediate stage between group A and group C, group B was similar to these 2 groups in qualitative indicators except for the total score for crazy-paving and consolidation, which is significantly different from group A (threshold value of 8, sensitivity and specificity of 92% and 40%). Compared with group B, group C showed higher MLD (>−779 HU, sensitivity and specificity of 100% and 73%) and FWHM (>128 HU, 75% and 80%) but lower relative volume of normal lung density (\( \leq 50\% \), 83% and 80%), whereas group A showed lower MLD (<−816 HU, 92% and 80%) and FWHM (<102 HU, 92% and 67%) but higher relative volume of normal lung density (>80%, 92% and 100%) (Table 5).

In short, using qualitative indicators could not differentiate group C from group B, but quantitative indicators could distinguish them. Based on the results of qualitative and quantitative indicators to distinguish the 3 groups, a summary diagram was drawn with the illustrations attached for each group (Fig. 4).

### TABLE 2. Comparison of CT Image Findings Among Different Groups

| Parameter | Group A (n = 12) | Group B (n = 15) | Group C (n = 24) | \( P^* \) |
|-----------|----------------|----------------|----------------|-------|
| Unilateral/bilateral | 8 (67%)/4 (33%) | 2 (13%)/13 (87%) | 0/24 (100%) | <0.001 |
| No. involved segments* | 9 (3–13) | 14 (7–18) | 17 (12–18) | 0.018 |
| Involved lobes | 0–2/3–5 | 8 (67%)/4 (33%) | 3 (20%)/12 (80%) | 0/24 (100%) | <0.001 |
| Total severity score* | 6 (2–9) | 9 (4–14) | 12 (9–17) | <0.001 |
| Total score for crazy-paving and consolidation* | 4 (2–7) | 8 (5–12) | 9 (6–14) | <0.001 |
| Lesion distribution | | | | 0.040 |
| Ground glass opacity | 8 (67%) | 9 (60%) | 13 (54%) | 0.097 |
| Consolidation | 7 (58%) | 14 (93%) | 22 (92%) | 0.002 |
| Crazy-paving pattern | 6 (50%) | 11 (73%) | 20 (83%) | 0.001 |
| Air bronchogram | 3 (25%) | 9 (75%) | 20 (83%) | <0.001 |
| Septal thickening | 7 (58%) | 11 (73%) | 18 (75%) | 0.210 |
| Pulmonary fibrosis | 1 (8%) | 6 (40%) | 6 (25%) | 0.549 |
| Pleural effusion | 0 | 2 (13%) | 8 (33%) | 0.019 |
| From onset of symptoms to CT scan, d* | 4 (1–7) | 8 (4–13) | 10 (6–14) | 0.007 |

Note: Data are the numbers with the percentage in parentheses except where specified. *Data are presented as median (IQR). **Difference among groups A to C. CT, computed tomography.

| Groups | Volume, mL | MLD, HU | FWHM, HU | LAV, % | HAV, % |
|--------|------------|---------|----------|--------|--------|
| Normal group (n = 10) | 4850 (761) | −863.91 (45.7) | 73.00 (9.01) | 1.57 (0.56) | 1.49 (0.24) |
| Group A (n = 12) | 4651 (1000) | −833.82 (16.41) | 81.90 (16.12) | 2.07 (1.80) | 1.53 (0.24) |
| Group B (n = 15) | 3884 (913) | −775.70 (58.31) | 112.30 (45.47) | 1.68 (0.87) | 2.44 (1.55) |
| Group C (n = 24) | 2231 (639) | −691.71 (54.18) | 140.80 (36.09) | 0.74 (0.63) | 5.71 (1.98) |

Note: Data are expressed as mean (SD).  
The threshold for the lung volume calculation was set ranging from −950 HU to −200 HU.  
*Difference among normal groups, groups A to C.  
COVID-19, coronavirus disease 2019; MLD, mean lung density; FWHM, full width at half maximum; LAV, low attenuation value; HAV, high attenuation value.
Combined use of the qualitative and quantitative indicators showed higher sensitivity (90%), specificity (100%), and accuracy (92%) in distinguishing groups B and C from group A than qualitative indicators alone (sensitivity, specificity, and accuracy: 69%, 83%, and 73%; \( P < 0.001 \)) (Table 6). Based on the qualitative results of distinguishing groups B and C from group A, we further achieved sensitivity of 92%, specificity of 87%, and accuracy of 90% to distinguish group C from group B using the quantitative indicators (Fig. 5).

**DISCUSSION**

The novel coronavirus SARS-CoV-2, the seventh member of the Coronaviridae family, leads to a very high case fatality rate of COVID-19, varying by country, age, and the presence of underlying disease.\(^1\)\(^4\) It is difficult to obtain the exact mortality at present as the COVID-19 is still spreading across the world and posing a significant global health threat because of its high infectiousness and lack of specialized treatments. Because the mainstay of treatment for COVID-19 pneumonia has been supportive care, early identification of clinical stages is essential for initial management, especially for critical patients who are related to high mortality\(^4\) and need aggressive treatments and intensive care treatment.

Similar to previous studies,\(^1\)\(^4\) the predisposing conditions for COVID-19 pneumonia in the critical cases tended to be old age (>55 years) and original existing disease (such as chronic pulmonary disease, cardiovascular disease, and cerebrovascular disease), perhaps due to their poor immunity. The predominant abnormal chest CT pattern observed was bilateral and peripheral GGO and consolidation,\(^6\)\(^23\) the frequency of the former was not specific in identifying the cases in different clinical stages. This can be explained by the pathological
findings that early alveolar damage caused by virus invasion into pulmonary interstitium includes alveolar edema, protein exudate, and thickening of the interlobular interstitium,32,33 which will evolve to diffuse alveolar damage with cellular fibromyxoid exudate as the disease progresses to the critical stage,34 both manifesting as GGO. From the ordinary stage to the severe/critical stage, in more severe cases, the number of involved lung segments and lobes, the frequencies of consolidation, crazy-paving pattern, and air bronchogram all increased, making the total severity score for the whole lung and total score for crazy-paving and consolidation significantly higher in the severe/critical cases compared with the ordinary cases. These findings were consistent with previous studies,16,23 showing that the progression of septal thickening, crazy-paving, and lung consolidation were noted in the progression or peak period of pneumonia (1–3 weeks). Progression of consolidation and crazy-paving might represent further infiltration of the lung parenchyma and lung interstitium,5,35 indicating that the virus has invaded the respiratory epithelium, which is characterized by diffuse alveolar damage and necrotizing bronchitis, leading to the alveoli being completely filled with inflammatory exudation. Some of the severe (2 [13%]) and critical cases (8 [33%]) in our study presented with pleural effusion on CT, the presence of which has been shown as a poor prognostic indicator in patients with Middle East respiratory syndrome coronavirus.36 One of our critical cases with bilateral pleural effusion was found dead during our later follow-up. The time interval between the initial CT scan and the symptom onset in the severe/critical cases were longer than that in the ordinary cases, partly might be due to the late initial CT scan for the transferred patients (33% [13/39]) from the county or township hospitals with limited medical equipment and ability, and partly due to the fact that some cases were not hospitalized until their clinical symptoms progressed.

The COVID-19 viral disease is now officially a pandemic, as the World Health Organization announced on March 10, 2020. Chest CT has been widely used as an effective tool for diagnosing patients with COVID-19 pneumonia. However, the diversified CT patterns of COVID-19 pneumonia made it difficult to accurately and quickly assess the clinical severity. Our study demonstrated that severe/critical cases could be distinguished from ordinary cases using the combined qualitative indicators including total severity score for the whole lung and total severity score for the crazy-paving and consolidation. The average relative volume of normal lung density (from −950 HU to −800 HU) within the total segmented lung was 88% in group A, 62% in group B, and 43% in group C, respectively (A). Examples of chest CT coronal images and 3-dimensional volume-rendering (3D-VR) images showed that a 28-year-old man in group A had the peripheral distribution of multiple focal consolidations and ground glass opacities (GGOs) in bilateral lungs, with residual normal lung density of 90% based on the percentile analysis; a 48-year-old woman in group B had multiple patchy consolidations, GGO, and crazy-paving sign, with residual normal lung density of 70%; a 58-year-old man in group C had diffuse consolidation, crazy-paving, and air bronchogram, with residual normal lung density of 20% (B). 3D-VR images clearly showed the distribution of lesions in the lung with the form of high density.
score for crazy-paving and consolidation (sensitivity, specificity, and accuracy: 69%, 83%, and 73%). However, the diversity of virus manifestations and small imaging differences between the critical cases and severe cases make the qualitative indicators insufficient to distinguish them. This shortcoming might be compensated by the quantitative indicators.

Compared with severe cases, critical cases showed higher MLD (>779 HU, sensitivity and specificity of 100% and 73%, respectively) and FWHM (>128 HU, 75% and 80%) but lower relative volume of normal lung density (≤80%, 83% and 80%). The combined quantitative indicators could achieve high sensitivity (92%), specificity (87%), and accuracy (90%) in distinguishing critical cases from severe cases, based on the qualitative results of distinguishing severe/critical cases from ordinary cases. Lung density on CT, positively correlated with the proportion of consolidation,16 might mirror an inflammatory response in the lung.28 FWHM represents the heterogeneity and density distribution of the lung parenchyma, the higher values of which might indicate mixed and diverse inflammatory components. The residual relative volume of normal lung density might be related to the lung function.37 In our critical cases, 8 patients with residual normal lung density smaller than 40% received mechanical ventilation for supportive treatment, 2 of them had died. The substantial difference in the relative volume of residual normal lung density among the 3 groups, indicating the value is associated with the severity of illness and thus prognosis. The similar LAV values of the 3 COVID-19 pneumonia groups to the normal CT groups indicated that no obvious sign of emphysema observed in pneumonia at the initial CT scan, as the setting of the LA V threshold for emphysema was ~950 HU.30 The HAV values increased in more severe cases, indicating an increase in high-density lesions and providing evidence that the total score for crazy-paving and consolidation could be as

### TABLE 4. Thresholds, Sensitivities, and Specificities for Distinguishing Each Group From the Other 2 Groups

| Parameter | A (Positive, n = 12) vs B + C (Negative, n = 39) | C (Positive, n = 24) vs A + B (Negative, n = 27) |
|-----------|--------------------------------------------------|--------------------------------------------------|
| AUC (95% CI) | Threshold Value | Sensitivity, % | Specificity, % | Threshold Value | Sensitivity, % | Specificity, % |
| No. involved segments | NS | NS | NS | NS | 0.71 (0.56–0.85) | >8* 100 (24) | 37 (10) |
| Total severity score | 0.72 (0.58–0.86) | ≤10* 83 (10) | 51 (20) | 0.75 (0.60–0.89) | >10* 67 (16) | 74 (20) |
| Total score for crazy-paving and consolidation | 0.75 (0.61–0.89) | ≤4** 58 (7) | 80 (31) | 0.66 (0.51–0.82) | >4** 87 (21) | 44 (12) |
| MLD, HU | 0.96 (0.82–0.98) | ≤–816** 91 (11) | 70 (35) | 0.94 (0.80–0.99) | >–779** 100 (24) | 85 (23) |
| FWHM, HU | 0.87 (0.70–0.96) | ≤102** 91 (11) | 77 (30) | 0.86 (0.70–0.96) | >116** 83 (20) | 81 (22) |
| Rel.vol of normal lung density, % | 0.93 (0.86–1.00) | >80** 91 (11) | 100 (39) | 0.94 (0.80–0.99) | ≤50** 83 (20) | 92 (25) |

Data in parentheses are numbers of corrected diagnoses used to calculate percentages. Sensitivity values are numbers of positive cases used to calculate percentages. Specificity values are numbers of negative cases used to calculate percentages. Number of groups A, B, and C = 12, 15, and 24, respectively.

### TABLE 5. Thresholds, Sensitivities, and Specificities for Distinguishing Group A From Group B and Group C From Group B

| Parameter | A (Positive, n = 12) vs B (Negative, n = 15) | C (Positive, n = 24) vs A + B (Negative, n = 27) |
|-----------|--------------------------------------------------|--------------------------------------------------|
| Threshold Value | Sensitivity, % | Specificity, % | Threshold Value | Sensitivity, % | Specificity, % |
| No. involved segments | NS | NS | NS | NS | NS | NS |
| Total severity score | NS | NS | NS | NS | NS | NS |
| Total score for crazy-paving and consolidation | ≤7* 92 (11) | 40 (6) | NS | NS | NS |
| MLD, HU | ≤–816* 92 (11) | 80 (12) | >–779* 100 (24) | 73 (11) |
| FWHM, HU | ≤102* 92 (11) | 67 (10) | >128* 75 (18) | 80 (12) |
| Rel.vol of normal lung density, % | >80* 92 (11) | 100 (15) | ≤50* 83 (20) | 80 (12) |

Data in parentheses are numbers of patients used to calculate the percentage. Sensitivity values are numbers of positive cases used to calculate percentages. Specificity values are numbers of negative cases used to calculate percentages. *P < 0.05 indicates the difference between each group and the other 2 groups. No significant different differences were found between the cases of group B and the cases of groups A and C.

AUC, area under the receiver operating characteristic curve; CI, confidence interval; NS, no statistical difference; MLD, mean lung density; FWNH, full width at half maximum; Rel.vol, relative volume.
a qualitative indicator for evaluating disease progression. The higher HAV values (above than $-200$ HU) in the critical cases also helped explain why the total lung volume within the preset threshold range of $-950$ HU and $-200$ HU lower than the ordinary/severe cases.

It should be noted that the time interval between the initial CT scan and the symptom onset ranged from 0 to 20 days in our study, and 63% (32/51) of CT scans were not obtained at an early stage (0–5 days).8,9 The evolution of diverse CT imaging findings of COVID-19 pneumonia with time8 and the interobserver variability of imaging assessment would make the visually accurate evaluation or staging of the disease difficult. However, the method of quantitative analysis of pneumonia based on the lung density and volume changes was standard, except for the manual adjustment, if necessary, to ensure the accuracy of automatic lung segmentation using the software, which would make it easier and objective for radiologists to evaluate the extent of disease. Different from previous quantitative studies,14,16,18 which evaluated the extent of the disease by quantifying the CT lung opacification percentage using a deep-learning, computer, or computation-based method, our study assessed the extent of pulmonary changes and the severity of COVID-19 by quantifying the relative volume of normal lung density using a commercial CT Pulmo 3D software, which would provide valuable knowledge and a feasible clinical tool for the management of these patients and broaden the technical spectrum of lung quantitative analysis.

Our study had several limitations. First, only 51 patients were included in our study. We hope that the significant findings presented here will encourage a larger cohort study in the future. Second, the application of CT quantification using specific software limits its widespread clinical application. However, the use of qualitative indicators in distinguishing severe/critical cases from ordinary cases would also provide help for initial management for clinical care. Third, only the initial CT scan was included for analysis; more follow-up time points would be assessed in our next research. Fourth, the correlation of clinical features and outcome with the CT features, especially for the quantitative indicators, has not been assessed in our study; this work is currently in progress.

In conclusion, depending on the severity of the disease, the number of involved lung segments and lobes as well as the frequencies of consolidation, crazy-paving pattern, and air bronchogram increased in more severe cases. Using qualitative indicators alone could distinguish severe/critical cases from ordinary cases but provide little help to differentiate severe cases from critical cases. The combined use of qualitative and quantitative indicators could distinguish cases at different clinical stages and might provide help to facilitate the fast identification and management of critical cases, thus reducing the mortality rate.

FIGURE 4. A summary diagram of identifying ordinary, severe, and critical cases using the qualitative and quantitative indicators. Each stage is attached to 2 axial CT images from 2 separate patients. Rel.vol, relative volume; MLD, mean lung density; FWHM, full width at half maximum.

TABLE 6. The Performance of Combined CT Qualitative and Quantitative Indicators for Identifying Different Groups of COVID-19 Pneumonia

| Indicators | Groups | AUC (95% CI) | P | Sensitivity, % | Specificity, % | Accuracy, % |
|------------|--------|-------------|---|---------------|---------------|-------------|
| Qualitative | B + C (positive, n = 39) vs A (negative, n = 12) | 0.87 (0.71–0.96) | 0.033 | 69 (27) | 83 (10) | 73 (37) |
| Qualitative and quantitative | B + C (positive, n = 39) vs A (negative, n = 12) | 0.99 (0.88–1.00) | <0.001 | 90 (35) | 100 (12) | 92 (47) |
|                           | C (positive, n = 24) vs B (negative, n = 15) | 0.92 (0.73–0.99) | <0.001 | 92 (22) | 87 (13) | 90 (35) |

Note: Data in parentheses are numbers of patients used to calculate the percentage. Data in brackets are 95% confidence intervals.

Sensitivity values are numbers of positive cases used to calculate percentages.

Specificity values are numbers of negative cases used to calculate percentages.

CT, computed tomography; COVID-19, coronavirus disease 2019; AUC, area under the receiver operating characteristic curve; CI, confidence interval.
cases had higher total severity score (>10) and total score for crazy-paving and consolidation (>4) than ordinary cases, and had higher mean lung density (>779 HU) and full width at half maximum (>128 HU) but lower relative volume of normal lung density (≤50%) than ordinary/severe cases. CT imaging findings could help to continuously monitor the treatment effects objectively in the follow-up as well as provide guidance for clinical management and treatment.

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