Visual Classification of Three Computed Tomography Lung Patterns to Predict Prognosis of COVID-19: A Retrospective Study

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Abstract

**Background:** Quantitative evaluation of radiographic images has been developed and suggested for the diagnosis of coronavirus disease 2019 (COVID-19). However, there are limited opportunities to use these image-based diagnostic indices in clinical practice. Our aim in this study was to evaluate the utility of a visually-based classification of pulmonary findings from computed tomography (CT) images among COVID-19 patients that we developed, with the following three patterns defined: peripheral, multifocal, and diffuse findings of pneumonia. We also evaluated the prognostic value of this classification to predict the severity of COVID-19.

**Methods:** This was a single-center retrospective cohort study of patients hospitalized with COVID-19 between January and September 2020, who presented with suspicious findings on CT lung images (n=69). We compared the association between the three predefined patterns (peripheral, multifocal, and diffuse) and admission to the intensive care unit, tracheal intubation, and death. The following demographic and clinical variables were compared between the three groups: sex, age, respiratory rate, pulse rate, blood pressure, temperature, oxygen saturation, partial pressure of oxygen, white blood cell count, lymphocyte count, neutrophil count, c-reactive protein, lactate dehydrogenase, Krebs von den Lungen-6 antigen, D-dimer, platelet count, steroid administration, heparin administration, favipiravir administration, Acute Physiology and Chronic Health Evaluation-II score, and sequential organ failure assessment score.

**Results:** Patients with a diffuse pattern were intubated more frequently and for a longer duration than patients with a peripheral or multifocal pattern. The following clinical variables were significantly different between the diffuse pattern and peripheral and multifocal groups: body temperature, lymphocyte count, neutrophil count, c-reactive protein, lactate dehydrogenase, Krebs von den Lungen-6 antigen, D-dimer, and steroid and Avigan administration.

**Conclusions:** Our simple visual assessment of CT images can predict a systemic cytokine storm, a resulting decrease in respiratory function, and the need for supplemental respiratory ventilation among patients with COVID-19.

**Background**

Since the first outbreak of coronavirus disease 2019 (COVID-19), numerous patients have been admitted to the hospital with respiratory symptoms. Clinical manifestations of COVID-19 range from asymptomatic or mild upper respiratory tract disease to severe interstitial pneumonia with respiratory failure, requiring oxygen support and intubation [1]. More than a year after the worldwide COVID-19 outbreak, there are no signs of the pandemic abating.

Numerous clinical and imaging markers of disease severity have been reported. Among imaging markers, computed tomography (CT) provides the most sensitive radiological technique for the diagnosis of COVID-19, revealing diffuse lung alterations, ranging from ground-glass opacity to consolidation [2, 3]. In
addition, different radiological lung patterns are manifested over the course of the disease. There has been research using quantitative methods to evaluate lung CT images to derive various image analysis scores, suggesting the possibility of predicting the severity of the disease [4, 5]. However, there are limited opportunities in clinical practice to use these quantitative image analysis approaches [6–9]. To address this limitation, we recently conducted a single-center retrospective study of patients with COVID-19 at St Luke's International Hospital, Tokyo to investigate if a simple visual assessment of CT images could predict the severity of COVID-19. We identified three patterns of pneumonia findings based on visual analysis of CT images, which could be associated with disease severity. Our primary objective in this study was to investigate the reliability of classification of these patterns and their utility in predicting the clinical outcomes of COVID-19 outcomes.

Methods

Study oversight

This retrospective study was approved by the institutional review board of St. Luke's International Hospital (20-R220). Informed consent was waived owing to the retrospective study design. We used our hospital’s electronic medical record database to retrospectively identify 224 consecutive patients who had been admitted to the hospital with a diagnosis registered as “COVID-19” or “suspected of COVID-19” from January 2020 to September 2020. Only patients with a COVID-19 diagnosis confirmed by reverse transcription-polymerase chain reaction were selected. Patients in whom a pretreatment CT examination was not available as well as those with a history of lung resection were excluded. Patients with no abnormal lung findings on pretreatment CT were also excluded. Ultimately, 69 consecutive patients with COVID-19 were included in our analysis (Fig. 1).

CT protocols

CT imaging was performed using either a 256-detector scanner (Revolution CT, GE Healthcare) or 64-detector scanners (Optima CT660, GE Healthcare). The parameters for CT examinations performed on the Revolution CT unit were as follows: 120-kV tube voltage, 50 to 650 mA tube current, 80 mm collimation, 0.992 pitch, 320 mm field of view (FOV), and 512×512 matrix. Parameters for the Optima CT660 unit were as follows: 120-kV tube voltage, 50 to 560 mA tube current, 40 mm collimation, 0.984 pitch, 320 mm FOV, and 512×512 matrix. An unenhanced scan was obtained for all patients. The dose length product was 525.54 ± 290.7 mGy-cm, with a volume CT dose index of 11.21 ± 3.75 mGy.

CT findings

Pulmonary opacities were classified into peripheral, multifocal, and diffuse patterns according to the classification by Akira et al. [10]. Parenchymal opacification predominantly appeared in the subpleural peripheral zone in the peripheral pattern. In contrast, multiple parenchymal opacifications were apparent in both central and peripheral regions in the multifocal pattern. Diffuse patterns revealed generalized pulmonary involvement, with or without heterogeneity (Fig. 2). Further CT findings included consolidation,
linear opacities, reversed halo sign, and crazy-paving sign. Definition of these CT findings were based on the uniform terms for thoracic imaging by the Fleishner society [11]. We also assessed the number of affected lobes.

All CT assessments were reviewed by two radiologists, with 5 and 8 years of experience, who were blinded to clinical patient data. These two radiologists had been potentially involved with the original CT examinations in the clinical setting. For the study, CT assessment were performed off-site, at least 3 months after the initial clinical assessment. The CT images were randomized for assessment to prevent recall bias. Discrepancies in classification of CT findings between the two radiologists were resolved by consensus.

Quantitative analysis

The dataset was anonymized and exported to a dedicated segmentation suite for medical image computing (GE Healthcare, USA), equipped with a semi-automated segmentation algorithm (Thoracic Volume Computer-Assisted Reading software). The aforementioned software performed a first-pass automated segmentation. Lung volumes were then manually perfected using three-dimensional tools, such as spherical brushes or erasers. A complete segmentation included both lungs with interstitial structures, segmentary vessels, and bronchi. The major pulmonary arteries and bronchi, all mediastinal structures, eventual pleural effusion, and lung masses (e.g., tumors, fungal disease) were excluded. We extracted the lung volumes and calculated the percentage of the total volume affected, according to different Hounsfeld unit (HU) intervals, into non-aerated (NNL) (% NNL, density between 100 to −100 HU), poorly aerated (PAL) (% PAL, −101 to −500 HU), normally aerated (NAL) (% NAL, −501 to −900 HU), and hyperinflated (−901 to −1,000 HU) [7]. The additional “compromised lung” (% CL) volume was calculated as the sum of % PAL and % NNL (−500 to 100 HU) (Fig. 2). The authors in charge of the segmentation (T.S. and D.U.) were unaware of the laboratory and clinical parameters or hospitalization outcomes of patients. Conflicts were resolved by a consensus. The principal investigator reviewed and confirmed all segmentations before data entry. We recorded the time required to complete each analysis.

Data sources

We used chart review to obtain clinical information, including physical examination findings, laboratory data, and clinical course. Moreover, we collected data for the date of onset, the date of CT imaging, the time between onset and CT scan, the date of hospitalization, the duration of hospitalization, the presence of tracheal intubation, the duration of tracheal intubation, a history of intensive care unit (ICU) admission, and death. The following clinical information was collected: respiratory rate, oxygen saturation (SpO2), partial pressure of oxygen (PaO2), pulse rate, systolic blood pressure, diastolic blood pressure, body temperature, white blood cell count, lymphocyte count, neutrophil count, platelet count, C-reactive protein (CRP), lactate dehydrogenase (LDH), Krebs von den Lungen-6 antigen (KL-6), D-dimer, and if the patient was receiving steroids, heparin, or favipiravir.

Statistical analyses
To evaluate the reproducibility of the classification, we calculated the interobserver reliability for each finding using the Cohen kappa value. The following ratings were used to interpret the kappa value: poor, $< 0.40$; moderate, $0.40–0.59$; good, $0.60–0.80$; and excellent, $> 0.80$.

The association between the three CT patterns and compromised lung (\% CL) was evaluated using the Kruskal–Wallis test. The association between the three CT patterns and ICU admission, intubation management, and death was assessed using the chi-squared test. The Kruskal–Wallis test was used to compare the duration of hospitalization, duration of intubation, and time from the onset to CT scan between the three CT patterns. Univariate and multivariate logistic regression analyses were performed to evaluate the association between each CT finding and intubation. The correlation between the CT patterns and clinical information was calculated. A parametric Fisher analysis of variance (ANOVA) was used for between-pattern comparison of clinical variables with a normal distribution (pulse rate, systolic blood pressure, diastolic blood pressure, body temperature, neutrophil count, platelet count, CRP, and D-dimer); a Kruskal–Wallis test was used for variables with a non-normal distribution (respiratory rate, SpO2, PaO2, white blood cell count, lymphocyte count, neutrophil count, LDH, KL-6, Acute Physiology and Chronic Health Evaluation-II score, and sequential organ failure assessment [SOFA] score). Differences in the use of steroids, heparin, and Avigan between the three patterns were evaluated using the chi-squared test. Subsequently, we conducted the Bonferroni test and Mann-Whitney U test as a post-hoc test. All statistical analyses were performed using Stata 16.1 (StataCorp LP). A p-value $< 0.05$ was considered statistically significant.

**Results**

Pretreatment CT images for each patient were classified into one of our three patterns: diffuse, multifocal, and peripheral. There was good interobserver reproducibility in the classification of images ($\kappa = 0.74$).

There were differences in the rate of ICU admission, tracheal intubation, and death between the three patterns (chi-squared test, $p = 0.07$, $p < 0.0001$, and $p = 0.06$, respectively), with the difference in the rate of tracheal intubation alone being significant. Further, each pattern was associated with a different duration of hospitalization, duration of tracheal intubation, and the time from the onset to CT scan (Kruskal-Wallis, $p = 0.09$, $p = 0.0001$, and $p = 0.80$, respectively); the difference in the duration of tracheal intubation alone was significant (Fig. 3). These variables were also significantly different between the peripheral and diffuse patterns and between the multifocal and diffuse patterns (Mann-Whitney U test, $p = 0.003$ and $p = 0.001$, respectively).

There was a significant difference between the three CT patterns and volume of compromised lung (\% CL) (Kruskal–Wallis test, $p = 0.003$; Fig. 4). On post-hoc analysis, using the Mann-Whitney U test, there was a significant difference in \% CL between the peripheral and diffuse patterns and between the multifocal and diffuse patterns ($p = 0.001$ and $p = 0.002$, respectively).

On ANOVA, there was a significant correlation among temperature, CRP, and D-dimer between the three patterns ($p < 0.05$ each). The Kruskal–Wallis test revealed a significant correlation among the lymphocyte...
count, neutrophil count, LDH, and KL-6 (p < 0.05). Steroids and favipiravir administration correlated with a diffuse CT pattern (chi-squared, p < 0.05) (Table 1).
Table 1
Demographic and clinical data stratified according to the three CT patterns (peripheral, multifocal, and diffuse)

|                        | Total (n = 69) | Peripheral pattern (n = 29) | Multifocal pattern (n = 28) | Diffuse pattern (n = 12) | p-value |
|------------------------|---------------|-----------------------------|----------------------------|--------------------------|---------|
| Male sex (%)           | 21 (30%)      | 11 (38%)                    | 7 (25%)                    | 3 (25%)                  | 0.52    |
| Age (years)            | 57.8 (47–72)  | 55.2 (42–69)                | 58.9 (49–72.5)             | 61.8 (44–75)             | 0.43    |
| Respiratory rate (breaths per min) | 20.71 (16–24) | 18.9 (16–20)                | 22.1 (16–27.5)             | 21.8 (18–24.5)           | 0.10    |
| Pulse rate (per min)   | 87.17 (80–96) | 87.1 (80–98)                | 86.1 (77–94)               | 89.8 (83.5–100.5)        | 0.75    |
| Systolic BP (mmHg)     | 122.82 (113–130) | 120.1 (112–130)            | 127.7 (119–134)            | 118.0 (107–129)          | 0.06    |
| Diastolic BP (mmHg)    | 76.71 (68–86) | 73.6 (66–82)                | 80.5 (70–90)               | 75.1 (62–86.5)           | 0.16    |
| Body temperature (°C)  | 37.5 (36.9–38) | 37.5 (36.8–37.8)           | 37.7 (37.2–38.25)          | 37.1 (36.45–37.6)        | 0.04    |
| WBC (×1000) (/µL)      | 5.97 (4–7.1)  | 5.8 (3.4–7.5)               | 5.6 (3.8–6.55)             | 7.3 (5.6–8.7)            | 0.10    |
| Lymphocyte count (/µL) | 889.95 (598–1190) | 1210.1 (852.6–1602)       | 1003.4 (560.5–978.8)       | 672.4 (328–1190)         | 0.01    |
| Neutrophil count (/µL) | 3859.45 (2252–4902.8) | 3478.3 (1788.4–4650.5)     | 3597.9 (2532.7–4438.2)     | 5842.2 (3062.7–7526.4)   | 0.02    |
| CRP (mg/dL)            | 7.82 (1.43–11.92) | 5.83 (0.47–9.87)           | 7.59 (1.905–11.71)         | 13.3 (9.41–17.76)        | 0.005   |
| LDH (IU/L)             | 320.15 (213–388) | 247.6 (184–302)            | 314.8 (233.5–396.5)        | 511.9 (358–629)          | < 0.001 |
| KL6 (U/mL)             | 408.28 (214–526.5) | 244.6 (190–234)           | 293.4 (206–352)            | 813.9 (473.5–1094.5)     | 0.002   |
| SpO2 (%)               | 95.59 (95–97)  | 95.9 (95–98)                | 96.1 (95–97.5)             | 93.8 (91.5–96.5)         | 0.08    |
| PaO2 (mmHg)            | 96.38 (72.55–121) | 95.8 (84.1–101)           | 98.5 (72.55–121)           | 93.7 (72.1–132)          | 0.86    |
| Platelet (×10³/µL)     | 192.59 (158–229) | 191.7 (149–242)           | 187.8 (160–217.5)          | 207.0 (146–229)          | 0.66    |

APACHE-II, Acute Physiology and Chronic Health Evaluation-II; BP, blood pressure; CRP, C-reactive protein; CT, computed tomography; LDH, lactate dehydrogenase; KL6, Krebs von den Lungen-6 antigen; PaO2, partial pressure of oxygen; SOFA, sequential organ failure assessment; SpO2, oxygen saturation; WBC, white blood cell
|                  | Total (n = 69) | Peripheral pattern (n = 29) | Multifocal pattern (n = 28) | Diffuse pattern (n = 12) | p-value |
|------------------|---------------|-----------------------------|-----------------------------|--------------------------|---------|
| D-dimer (µg/mL)  | 4.18 (0.6–1.8) | 1.5 (0–1.6)                 | 0.99 (0–1.1)                | 16.8 (1.5–25.9)          | <0.001  |
| Steroid          | 48 (69.57%)   | 15 (52%)                    | 12 (43%)                    | 12 (100%)                | 0.01    |
| Heparin          | 48 (69.57%)   | 17 (59%)                    | 22 (79%)                    | 9 (75%)                  | 0.24    |
| Favipiravir      | 14 (20.29%)   | 2 (7%)                      | 7 (25%)                     | 5 (42%)                  | 0.03    |
| APACHE-II score  | 16.78 (13–19) | 15 (11.5–18)                | 16.3 (13–19)                | 19.3 (15.5–23)           | 0.37    |
| SOFA score       | 5.48 (3–7)    | 4.5 (3–5.5)                 | 5.1 (3–6)                   | 7 (5–9)                  | 0.17    |

We performed separate statistical analyses for patients with and without tracheal intubation (Table 2), with comparison of their clinical information. Respiratory rate, white blood cell count, lymphocyte count, neutrophil count, CRP, LDH, KL-6, SpO2, D-dimer, steroid, favipiravir, and SOFA were significantly correlated with intubation (p < 0.05; Table 3). On univariate logistic regression analysis, the following factors were different between patients with and without intubation: the three CT patterns, compromised lung (% CL), affected lobes, consolidation, and crazy-paving appearance. Of these, the CT pattern and % CL alone were significant (CT pattern, p = 0.00; odds ratio [OR], 3.52; [95% confidence interval [CI], 1.17–4.12]; % CL, p = 0.004; OR, 2.85; [95% CI, 0.02–0.12]). On multivariate analysis, the three CT patterns alone were retained as an independent predictive factor of intubation (p = 0.02; OR, 2.34; [95% CI, 0.2–2.27]; Table 4). The three CT patterns predicted the tracheal intubation, with an area under the receiver operating characteristic (ROC) curve of 0.77 (Fig. 5).
|                                | Intubation (-) (n = 50) | Intubation (+) (n = 19) | p-value |
|--------------------------------|-------------------------|-------------------------|---------|
| Peripheral pattern (%)         | 26 (52%)                | 3 (16%)                 | 0.006   |
| Multifocal pattern (%)         | 21 (42%)                | 6 (32%)                 | 0.43    |
| Diffuse pattern (%)            | 3 (6%)                  | 9 (47%)                 | < 0.001 |
| Compromised lung (% CL)        | 12.36 (5.98–15.67)      | 23.86 (11.75–32.49)     | 0.004   |
| Affected lobes                 | 4.76 (4–6)              | 5.74 (6–6)              | 0.01    |
| GGO (%)                        | 49 (98%)                | 19 (100%)               | 0.54    |
| Consolidation (%)              | 36 (72%)                | 18 (95%)                | 0.04    |
| Linear opacities (%)           | 46 (93%)                | 18 (95%)                | 0.70    |
| Reversed halo (%)              | 1 (3%)                  | 0 (0%)                  | 0.54    |
| Crazy-paving (%)               | 24 (48%)                | 14 (74%)                | 0.06    |
| Emphysema (%)                  | 4 (8%)                  | 3 (16%)                 | 0.34    |
| Fibrosis (%)                   | 1 (2%)                  | 0 (0%)                  | 0.54    |
| Fatty liver (%)                | 20 (40%)                | 11 (58%)                | 0.18    |

CT, computed tomography; GGO, ground-glass opacity
|                                | Intubation (-) (n = 50) | Intubation (+) (n = 19) | p-value |
|--------------------------------|-------------------------|-------------------------|---------|
| Male sex (%)                   | 17 (34%)                | 4 (66%)                 | 0.30    |
| Age (years)                    | 57.4 (35–82)            | 58.9 (47–72)            | 0.75    |
| Respiratory rate (breaths per min) | 19.7 (16–20)         | 23.5 (18–28)            | 0.003   |
| Pulse rate (per min)           | 85.8 (79–96)            | 90.8 (80–101)           | 0.19    |
| Systolic BP (mmHg)             | 122.4 (112–130)         | 124 (116–132)           | 0.67    |
| Diastolic BP (mmHg)            | 76.6 (67–86)            | 77.1 (68–87)            | 0.88    |
| Body temperature (°C)          | 37.42 (36.9–37.8)       | 37.7 (37.3–38)          | 0.14    |
| WBC (×1000) (/µL)              | 5.6 (4.6–5)             | 6.9 (3.6–8.9)           | 0.01    |
| Lymphocyte count (/µL)         | 1174.428 (780–1350)     | 683.7158 (413–936)      | 0.002   |
| Neutrophil count (/µL)         | 3375.539 (2029–4526)    | 5103.8 (2657–6675)      | 0.02    |
| CRP (mg/dL)                    | 5.47 (0.97–9.87)        | 13.63 (9.08–10.24)      | < 0.001 |
| LDH (IU/L)                     | 272.95 (199–307)        | 436.89 (342–510)        | < 0.001 |
| KL6 (U/mL)                     | 274.47 (209–289)        | 559.93 (221–885)        | 0.04    |
| SpO2 (%)                       | 96.3 (95–98)            | 93.74 (93–97)           | 0.002   |
| PaO2 (mmHg)                    | 92.14 (71.5–115)        | 100.17 (81.6–132)       | 0.37    |
| Platelet (×10³/µL)             | 193.94 (158–238)        | 189.2632 (146–222)      | 0.77    |
| D-dimer (µg/mL)                | 1.52 (0.1–1.15)         | 10.1 (0.9–6.3)          | 0.005   |
| Steroid (%)                    | 31 (62%)                | 17 (89%)                | 0.03    |
| Heparin (%)                    | 33 (66%)                | 15 (79%)                | 0.3     |
| Favipiravir (%)                | 7 (14%)                 | 7 (37%)                 | 0.04    |
| APACHE-II score                | 16.2 (13–18)            | 17.12 (13–22)           | 0.73    |
| SOFA score                     | 4.1 (2–5)               | 6.29 (4–8)              | 0.05    |

APACHE-II, Acute Physiology and Chronic Health Evaluation-II; BP, blood pressure; CRP, C-reactive protein; KL6, Krebs von den Lungen-6 antigen; LDH, lactate dehydrogenase; PaO2, partial pressure of oxygen; SOFA, sequential organ failure assessment; SpO2, oxygen saturation; WBC, white blood cell

**Discussion**
Patients with a diffuse pattern of findings on pretreatment lung CT were more frequently intubated and had a prolonged duration of intubation. COVID-19 pneumonia has an extremely variable prognosis. While 80% of patients are either asymptomatic or have mild symptoms, 20% develop severe or profound disease and eventually die [12]. The identification of prognostic factors at an early stage of the disease could help guide clinicians in providing an optimal treatment path based on patient-specific characteristics, as well as predict more precisely where medical resources are most required.

CT imaging of the lungs plays an important role in the care of patients infected with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), with the prognostic value of CT having been evaluated in several studies [8, 13–16]. However, most of these studies are from China, Europe, and the United States, with no information available for patient cohorts in Japan. In addition, several researchers have used image analysis software to quantify CT findings, making these impractical in daily clinical practice [17, 18]. Practicality in clinical practice was our motivation to develop and to evaluate the prognostic value of our visually-based assessment of CT lung findings (peripheral, multifocal, and diffuse) in a hospital patient cohort in Tokyo, Japan, a city with a particularly high SARS-CoV-2 prevalence. COVID-19 pneumonia shares a similar pathogenesis to acute exacerbation of interstitial pneumonia (AE-IP). Volume loss because of alveolar collapse is the primary cause of traction bronchiectasis in COVID-19 pneumonia. However, the extent of involved alveoli and mucosa may expand with disease progression. In addition, inflammation-related damage to the bronchial walls may lead to fibrosis, bronchiectasis, and bronchial wall thickening. Thus, COVID-19 is associated with acute respiratory distress syndrome and may produce CT findings similar to AE-IP [8, 15, 16]. Akira et al. reported that the prognosis of AEs in IP could be predicted by classifying findings on lung CT images into peripheral, multifocal, and diffuse patterns [10].

In our study, we applied the same classification to patients with COVID-19 and evaluated if these three patterns were predictive of patients’ clinical course. Our findings show that a diffuse pattern was associated with the highest risk for tracheal intubation and need for prolonged duration on intubation. In addition to the three CT patterns, we also examined the compromised lung (% CL), number of lung lobes with lesions, presence of consolidation, and presence of crazy-paving appearance. Only the three CT patterns were retained as an independent predictor of tracheal intubation on multivariate logistic regression analysis, with patients with a diffuse pattern being at the highest risk for intubation and a prolonged duration of intubation. The patterns, however, did not predict the risk of ICU admission or death. Our comparison of clinical variables (body temperature, lymphocyte count, neutrophil count, CRP, LDH, KL6, D-dimer, and steroid or Avigan administration) between the three CT patterns identified the risk for a systemic cytokine storm associated with the diffuse pattern, which led to a marked decrease in respiratory function and the need for assisted ventilation. The aggressive use of steroids and Avigan in patients with severe COVID-19 may have prevented a significant difference in mortality. However, the reason for the lack of an association between mortality and the length of hospital stay and the three CT patterns is unclear. Nonetheless, the study population presumably included some of the earliest patients following the pandemic, and the treatment methods were inconsistent, thereby resulting in a lack of correlation between mortality and the length of hospital stay. We intend to collect more data in the future to clarify the association between CT findings and mortality.
The limitations of our study should be acknowledged in the interpretation of our results. First, this was a single-center retrospective study with a small sample size. Second, only Japanese patients from the city of Tokyo were included. As such, the risk of bias related to viral factors, such as host factors and genomic variation, cannot be discounted. We do note the benefit of a single center for ensuring a uniform assessment of images. Lastly, the inclusion criteria were limited to patients with pulmonary lesions on the initial CT scan; patients with no abnormalities on the initial CT scan were not included.

**Conclusions**

Our simple visual assessment of CT images can predict a systemic cytokine storm, a resulting decrease in respiratory function, and the need for supplemental respiratory ventilation among patients with COVID-19.

**Abbreviations**

AE-IP, acute exacerbation of interstitial pneumonia

CL, compromised lung

CRP, C-reactive protein

FOV, field of view

ICU, intensive care unit

KL-6, Krebs von den Lungen-6 antigen

LDH, lactate dehydrogenase

PaO2, partial pressure of oxygen

SpO2, oxygen saturation

%NNL, non-aerated

%PAL, poorly aerated

%NAL, normally aerated

**Declarations**

*Ethics approval and consent to participate*  This retrospective study was approved by the institutional review board of St. Luke’s International Hospital (20-R220). The requirement for informed consent was waived by the Institutional Review Board owing to the retrospective study design.
Consent for publication: Not applicable.

Availability of data and materials: The datasets during and/or analysed during the current study available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

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Authors’ contributions: DY and KI analyzed and interpreted the patient data regarding COVID-19. SO provided statistical advice for this manuscript. MM and YK were a major contributor in writing the manuscript. All authors read and approved the final manuscript.

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Figures
Consecutive patients hospitalized with the diagnosis of COVID-19 (n = 224)

- Excluded (n = 146)
  - Patients who have not performed CT scans

Consecutive patients diagnosed with COVID-19, CT scan performed, and hospitalized (n = 78)

- Excluded (n = 6)
  - Chest CT negative for COVID-19 pneumonia

Confirmed patients affected by COVID-19 with positive CT (n = 72)

- Excluded (n = 3)
  - History of lung resection

Final inclusion (n = 69)

Peripheral pattern (n = 29)  Multifocal pattern (n = 28)  Diffuse pattern (n = 12)

Figure 1

Flowchart depicting the patient selection process COVID-19: coronavirus disease 2019, CT: computed tomography
Figure 2

Computed tomography (CT) images for the three patterns of COVID-19 pneumonia. The pulmonary opacities are classified into peripheral, multifocal, and diffuse patterns. (A) In the peripheral pattern, parenchymal opacification appears in the inner peripheral zone. (B) In the multifocal pattern, parenchymal opacification is apparent in the central and peripheral regions. (C) The diffuse pattern reveals generalized pulmonary involvement, with regional inhomogeneity. (D, E, F) Semi-automated segmentation using Thoracic VCAR software (GE Healthcare, USA). Blue areas represent normal lung parenchyma in the -501, -900 HU interval; light blue areas represent hyperinflated lung in the -901, -1000 HU; yellow areas represent poorly aerated lung in the -500, -100 HU interval; and red areas represent non-aerated lung in the 100, -100 HU interval. COVID-19, coronavirus disease 2019; HU, Hounsfield unit; VCAR, Volume Computer-Assisted Reading
Figure 3

Violin plots for the three CT patterns and duration of intubation. There was a significant difference between the three CT patterns and duration of intubation (Kruskal–Wallis test, $p < 0.0001$). On the Mann-Whitney U test, there were significant differences between the peripheral and diffuse patterns and between the multifocal and diffuse patterns ($p = 0.003$ and $p = 0.001$, respectively). CT, computed tomography.
Figure 4

Violin plots for the three CT patterns and compromised lung (% CL) There was a significant difference between the three CT patterns and compromised lung (% CL) (Kruskal–Wallis test, p=0.003). On the Mann-Whitney U test, there were significant differences between the peripheral and diffuse patterns and between the multifocal and diffuse patterns (p=0.001 and p=0.002, respectively). CT, computed tomography
Figure 5

Results of the ROC curve analysis for the three patterns in predicting intubation. The three CT patterns predicted the tracheal intubation, with an area under the ROC curve of 0.77. CT, computed tomography; ROC, receiver operating characteristic.