


Semi-quantitative evaluation of chest computed tomography for coronavirus disease 2019 in a critical care unit

A case-control study

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Abstract

The spread of abnormal opacity on chest computed tomography (CT) has been reported as a predictor of coronavirus disease 2019 (COVID-19) severity; however, the relationship between CT findings and prognosis in patients with severe COVID-19 remains unclear. The objective of this study was to evaluate the extent of abnormal opacity on chest CT and its association with prognosis in patients with COVID-19 in a critical care medical center, using a simple semi-quantitative method. This single-center case-control study included patients diagnosed with severe COVID-19 pneumonia who were admitted to a critical care center. The diagnosis of COVID-19 was based on positive results of a reverse transcription polymerase chain reaction test. All patients underwent non-contrast whole-body CT upon admission. Six representative axial chest CT images were selected for each patient to evaluate the extent of lung lesions. The percentage of the area involved in the representative CT images was visually assessed by 2 radiologists and scored on 4-point scale to obtain the bedside CT score, which was compared between patients who survived and those who died using the Mann–Whitney *U* test. A total of 63 patients were included in this study: 51 survived and 12 died after intensive treatment. The inter-rater reliability of bedside scores between the 2 radiologists was acceptable. The median bedside CT score of the survival group was 12.5 and that of the mortality group was 16.5; the difference between the 2 groups was statistically significant. The degree of opacity can be easily scored using representative CT images in patients with severe COVID-19 pneumonia, without sophisticated software. A greater extent of abnormal opacity is associated with poorer prognosis. Predicting the prognosis of patients with severe COVID-19 could facilitate prompt and appropriate treatment.

Abbreviations: CI = confidence interval, COVID-19 = coronavirus disease 2019, CT = computed tomography, GGO = ground-glass opacity, HU = Hounsfield Unit, ICC = intraclass correlation, ICU = intensive care unit, IQR = interquartile range, LLL = left lower lobe, RLL = right lower lobe, RML = right middle lobe, ROC = receiver operating characteristic, RUL = right upper lobe, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Keywords: computed tomography, COVID-19, mortality, pneumonia, SARS-CoV-2

1. Introduction

Coronavirus disease 2019 (COVID-19) is a contagious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and is often associated with mild upper respiratory tract inflammation and pneumonia. However, severe pneumonia can lead to acute respiratory distress syndrome as well as

cardiovascular, thrombotic, and other complications, including death.^{1–31}

Chest computed tomography (CT) has a high diagnostic sensitivity for COVID-19 pneumonia,^{14,51} which may present with variable imaging features.^{16,71} In patients with COVID-19, chest CT generally shows diffuse ground-glass opacity (GGO), consolidation, or mixed GGO and consolidation in both lungs,

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

This study was approved by the National Hospital Organization Osaka National Hospital Institutional Review Board II (no. 20173). All procedures involving human participants were performed in accordance with the ethical standards of the institutional and/or national research committee and the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all participants in the form of opt-out on the website (https://osaka.hosp.go.jp/wp-content/themes/osaka-iryuu/doc/clinicalresearch/optout/20173_2.pdf). The requirement for written informed consent was waived because of the noninvasive, retrospective study design.

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mainly in the subpleural and lower lungs.^[7,8] Previous studies have investigated various predictors of COVID-19 severity.^[9,10] Although several recent reports have shown that the spread of abnormal opacity is a predictor of COVID-19 severity,^[11–16] the relationship between CT findings and prognosis in cases of severe COVID-19 remains unclear. This is pertinent because the practical quantitative evaluation of CT images obtained from patients with COVID-19 is a standard requirement in emergency settings.

This study aimed to evaluate a simple, semi-quantitative method for assessing the extent of opacity on CT in patients with severe COVID-19 and to analyze its association with prognosis in our emergency and critical care center. We hypothesized that a greater extent of abnormal opacity on chest CT would predict poorer prognosis.

2. Methods

2.1. Study design and data sources

This single-center retrospective case-control study was approved by the institutional review board of our medical center, and the requirement for written informed consent was waived because of the retrospective nature of the study. Patient confidentiality was maintained by anonymization of patient data. Patients with COVID-19 pneumonia who were admitted to our emergency and critical care center between December 25, 2020 and March 31, 2021 were included in this study. Clinical data were collected from the medical records up to June 2021.

Patients diagnosed with severe COVID-19 were included based on the positive results of the SARS-CoV-2 reverse transcription polymerase chain reaction test, which was performed at other institutions. Admission for highly advanced medical treatment in our intensive care unit (ICU) was based on the respiratory and general condition of each patient. Patients who required ICU or ventilator management were classified as having severe COVID-19 in accordance with the guidelines of the Japanese Ministry of Health, Labour and Welfare.^[17] Analyses were performed on patients who died of COVID-19 and their complications (mortality group). The survival group included patients with COVID-19 who were admitted to our ICU and recovered by the time of discharge. The exclusion criteria were patients in whom chest CT scans were not performed on admission and patients whose outcomes were unknown at the time of collection of clinical data. Patient characteristics and information on comorbidities, including hypertension, diabetes, dyslipidemia, chronic pulmonary disease, chronic kidney disease, and cancer, were collected from electronic medical records (Table 1).

Table 1

Patient characteristics.

	Survival group (n = 51)	Mortality group (n = 12)	P-value
Sex			.48
Female	12 (23.5)	4 (33.3)	
Male	39 (76.5)	8 (66.7)	
Age	70 (59.5–76.5)	72.5 (66.75–81.25)	.20
BMI	23.9 (21.45–28.05)	22.9 (21.5–26.5)	.88
Smoking history			.009*
No	21 (41.2)	0 (0.0)	
Yes	22 (43.1)	8 (66.7)	
Unknown	8 (15.7)	4 (33.3)	
Comorbidity			>.99
No	14 (27.5)	3 (25)	
Yes	37 (72.5)	9 (75)	

Data are expressed as the number (%) or median (interquartile range).

BMI = body mass index.

* $P < .05$ was considered a significant difference.

2.2. Chest CT imaging

Non-contrast chest CT scans were performed for all patients at the point of arrival at our center using 64-multidetector raw CT (Revolution Maxima, GE Healthcare, Chicago, IL, USA). Patients were positioned supine during the scan; breath-holding after deep inhalation and free breathing were performed by non-intubated and intubated patients, respectively. The scanning parameters were as follows: tube voltage, 120 kVp; automatic tube current modulation; pitch factor, 1.531; matrix, 512 × 512; and slice thickness, 1.25 mm without an interslice gap. Lung images were reconstructed using a high-frequency enhancement filter.

2.3. Image selection

Whole lungs were divided into 6 lobes: the right upper lobe, right middle lobe, right lower lobe, left superior segment of the upper lobe, left lingual segment of the upper lobe, and left lower lobe. The left superior segment of the upper lobe was considered the left upper lobe, and the lingual segment was considered the left middle lobe (which corresponded to the right lung) because of its location and volume. The extent of abnormal opacity in each lobe was evaluated using axial CT images; 1 representative image of the 6 lobes was selected based on the bronchial tree landmarks. The bifurcation of the bronchus was used to select representative images of each lobe. Images of the right upper lobe, right middle lobe, right lower lobe, left superior segment of the upper lobe, left lingual segment of the upper lobe, and LLL were selected at the bifurcation points of the apical segmental bronchus, medial bronchus, posterior basal bronchus, apico-posterior bronchus, medial bronchus, and posterior basal bronchus. These bronchial bifurcations are located in the central area of the lung lobes (Fig. 1).

2.4. Image interpretation and scoring of opacity

Two board-certified radiologists (a chest radiologist with 29 years of experience and a general radiologist with 6 years of experience) independently reviewed the CT images.

The extent of abnormal opacity on chest CT images was evaluated without distinguishing between GGO and consolidation because it was sometimes difficult to distinguish between GGO and consolidation, which could decrease the inter-rater reliability of CT image assessments. The ratio of the area of abnormal opacity to the total lung area in each lobe was measured by visual estimation and scored on a 4-point scale (ratios of 0–25%, 26–50%, 51–75%, and 76–100% were assigned scores of 1, 2, 3, and 4, respectively) for selected representative CT images of the 6 lobes (Figs. 2 and 3). Several previous studies have used a simple method to assess lung lesions.^[18,19] The scores measured by the 2 radiologists were averaged, and the sum of the scores of all 6 lobes was considered as the bedside CT score of 6 axial images for each patient. Each patient's score was expressed as a consecutive number ranging from 6 to 24 (Table 2). The bedside CT score is a simple index that represents the extent of GGO and consolidation on chest CT.

The bedside CT score is obtained from 2-dimensional images. Volumetric analysis was performed to validate the application of the bedside CT score for the evaluation of 3-dimensional lung lesions using dedicated software (SYNAPSE VINCENT, Fujifilm Medical, Tokyo, Japan). After automatic whole lungs segmentation, segmentation errors were manually corrected by a radiologist. The volume and the ratio of GGO and consolidation were extracted by thresholding Hounsfield Unit (HU) values (–700 HU or more and 100 HU or less).

2.5. Statistical analyses

The sample size in this study was not pre-calculated based on the power or effect size but was defined by the inclusion period

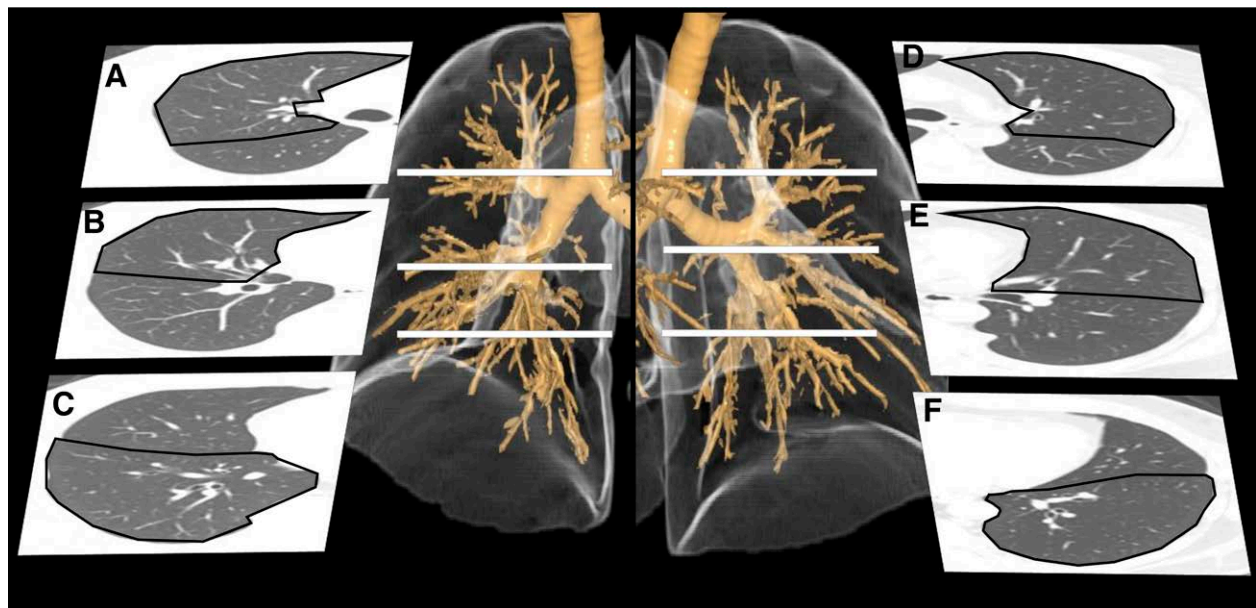


Figure 1. A schema of the selection of computed tomography levels in each lobe. A 3-dimensional image of the bronchial tree is shown in the center, which is flanked by the axial images (indicated by white lines). The area of each lobe is outlined in black. Representative images of the RUL (A), RML (B), RLL (C), left superior segment of the upper lobe (D), left lingual segment of the upper lobe (E), and LLL (F) are selected at the bifurcation points of the apical segmental bronchus, medial bronchus, posterior basal bronchus, apico-posterior bronchus, medial bronchus, and posterior basal bronchus, respectively. RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LLL, left lower lobe.

(December 25, 2020–March 31, 2021). Continuous variables are presented as median and interquartile range (IQR), and categorical variables are presented as number (percentage) of occurrences. The intraclass correlation coefficient (ICC) of the sum of the scores of all 6 lobes for each patient was calculated to validate the inter-rater reliability between the 2 radiologists. The squared weighted kappa coefficient for the opacity score of each lung lobe was used to measure agreement between the 2 radiologists. We used the following criteria proposed by Landis and Koch for the interpretation of ICC and kappa: < 0.20 (poor-to-slight agreement), 0.21 to 0.40 (fair agreement), 0.41 to 0.60 (moderate agreement), 0.61 to 0.80 (substantial agreement), and > 0.81 (almost perfect agreement).^[20,21] The Spearman's rank correlation coefficient was calculated between the bedside CT score and the ratio of GGO and consolidation to whole lungs in volumetric analysis. The Mann–Whitney *U* test was used to compare continuous variables, and the chi-square or Fisher exact test was used to compare categorical variables. Receiver operating characteristic (ROC) analysis was performed to determine the cutoff value of the bedside CT score for mortality and its sensitivity, specificity, and accuracy. Statistical significance was defined as a 2-sided *P*-value < 0.05. All statistical analyses were performed using free statistical software (EZRv1.54, Saitama Medical Center, Jichi Medical University, Saitama, Japan),^[22] which is a modified version of R commander with additional statistical functions.

3. Results

This study included 63 patients admitted to our emergency and critical care center with severe COVID-19 pneumonia. None of the patients were excluded from the study. The patient characteristics are shown in Table 1. Of the 63 patients, 47 were men and 16 were women, with a median age of 70 years (IQR, 61.5–77) years. Twelve patients died during intensive care, and 51 showed improvements in respiratory status after intensive care at our emergency and critical care center. They were subsequently discharged from the ICU and transferred to other hospitals for continued care.

Images and bedside CT scores of representative cases in the survival and mortality groups are shown in Figs. 2 and 3, respectively. The extent of GGO and consolidation in each lung lobe varied widely between groups. Patients in the mortality group had higher bedside CT scores than those in the survival group. The ICC (2, 1) between the 2 radiologists for the sum of the scores of all 6 lobes for each patient was 0.848 (95% confidence interval [CI], 0.761–0.905), and the weighted kappa coefficient between the 2 radiologists for the opacity score of each lung lobe was 0.829 (95% CI, 0.794–0.865). The inter-rater reliability of the bedside CT score was within the acceptable range, and agreement between the 2 radiologists was adequate for daily practice. The Spearman's rank correlation coefficient was 0.625 between the bedside CT score and the ratio of GGO and consolidation to whole lungs in volumetric analysis. There was a positive correlation between them.

The median bedside CT score of the survival group was 12.5 (IQR, 10.75–16), and that of the mortality group was 16.5 (IQR, 15.25–19.625); the difference between the 2 groups was statistically significant (Fig. 4). The results of the ROC analysis for bedside CT scores are shown in Fig. 5. The area under the ROC curve was 0.749 (95% CI, 0.617–0.882); at a cutoff value of 16, the sensitivity, specificity, and accuracy for predicting patient death were 0.750, 0.706, and 0.714, respectively.

4. Discussion

The results of this study showed that patients with severe COVID-19 pneumonia who exhibit a greater extent of abnormal opacity on chest CT have an increased risk of mortality. Predicting the prognosis of patients with severe COVID-19 could facilitate prompt and appropriate treatment. The method used to obtain the bedside CT score in this study is simple and suitable for daily practice, as it requires only visual evaluation of 6 representative axial CT images without sophisticated software.

Similar to our results, previous studies have reported that the volume of abnormal opacity on chest CT (measured using a

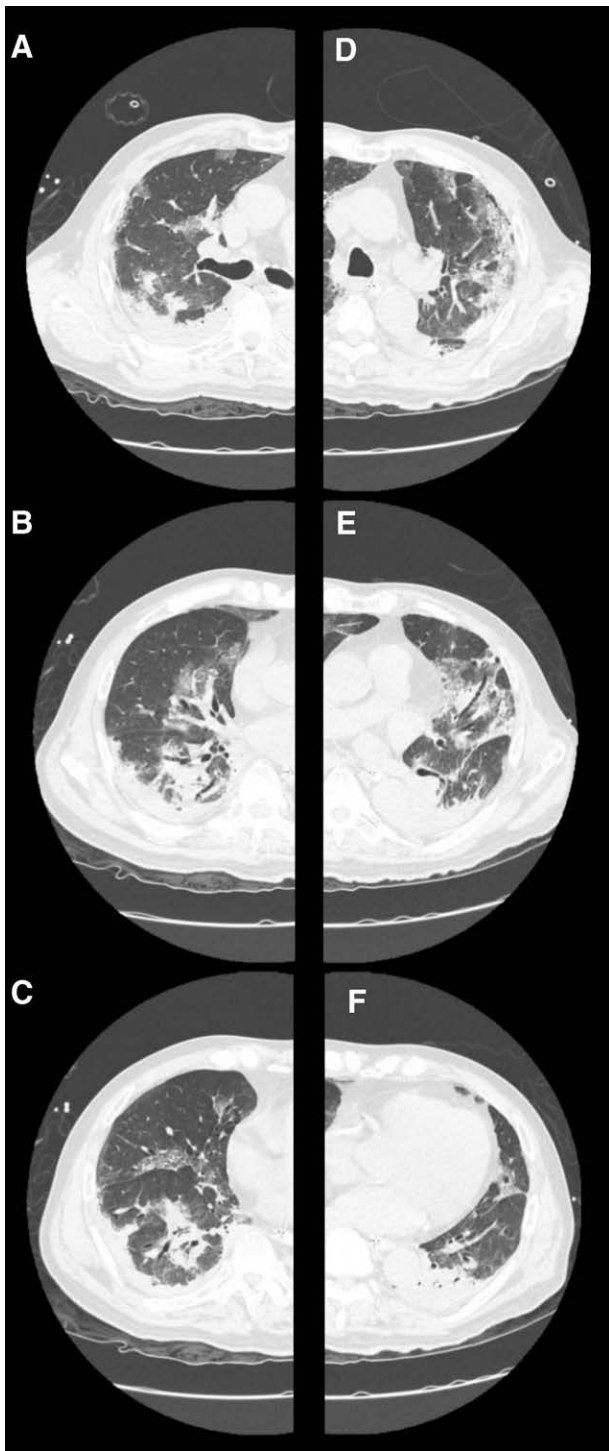


Figure 2. Representative images of each lobe in a surviving patient. Chest CT images showing ground-glass opacity and consolidation in 6 lobes. The bedside CT score was 12.5. The images of the RUL (A), RML (B), RLL (C), left superior segment of the upper lobe (D), left lingual segment of the upper lobe (E), and LLL (F) are shown. RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LLL, left lower lobe; CT, computed tomography.

machine learning-based workstation) is a predictor of COVID-19 severity and mortality.^[12,14] In those studies, multivariate analyses of the relationship between mortality and volume of abnormal opacity or of residual normal lung were performed, and the areas under the ROC curves for multivariate models were 0.762 or 0.79. Furthermore, the cutoff value of residual lung volume was 64%, and the sensitivity and specificity were 85.3% and 50%,

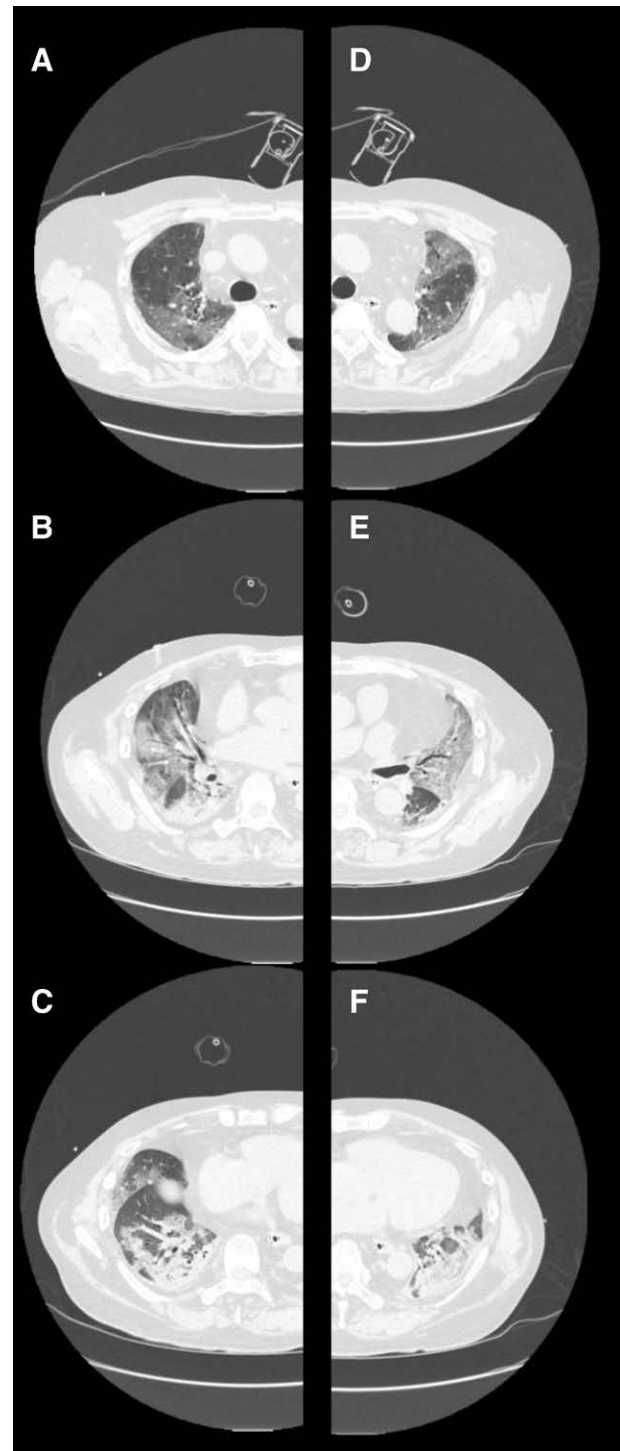


Figure 3. Representative images of each lobe in a patient who died from coronavirus 2019. Chest CT images showing extensive ground-glass opacity and consolidation in the 6 lobes. The bedside CT score was 19.5. The images of the RUL (A), RML (B), RLL (C), left superior segment of the upper lobe (D), left lingual segment of the upper lobe (E), and LLL (F) are shown. RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LLL, left lower lobe; CT, computed tomography.

respectively.^[14] In addition, others have reported that a mean CT value of -704 HU in the lungs of patients with COVID-19 had a sensitivity and specificity of 82% and 65%, respectively, for predicting COVID-19 severity.^[15] Our results indicate that the association between the extent of abnormal opacity and mortality risk also applies to cases of severe COVID-19. Patients with a

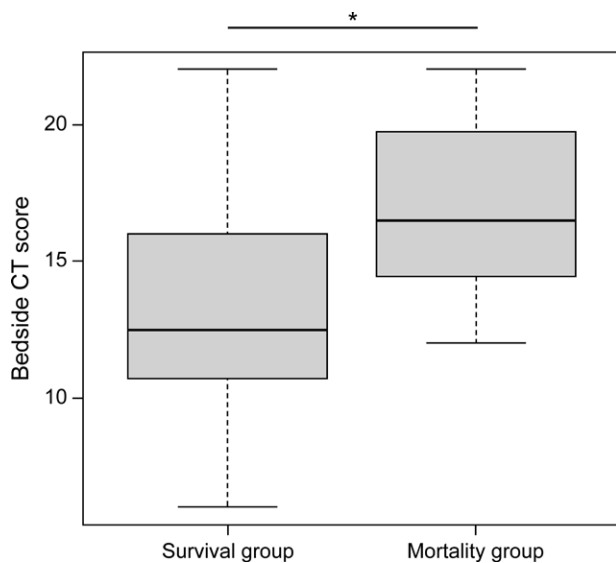
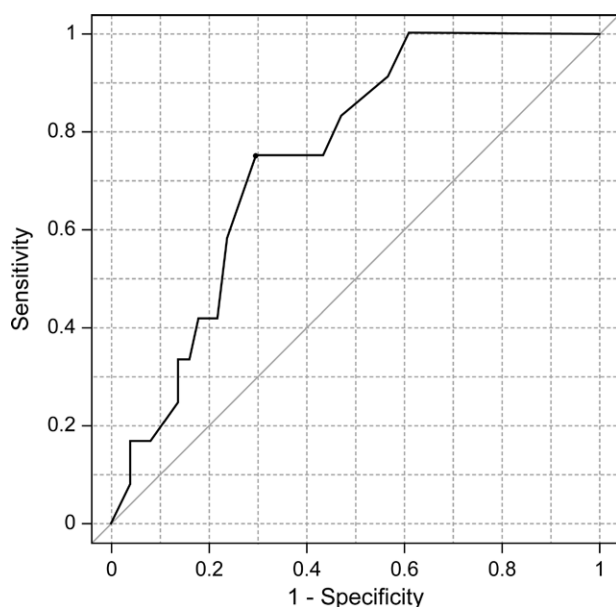
Table 2**Comparison of bedside computed tomography scores between the survival and mortality groups.**

	Survival group (n = 51)	Mortality group (n = 12)	P-value
Bedside CT score	12.5 (10.75–16)	16.5 (15.25–19.625)	.008*

Data are expressed as medians (interquartile ranges).

CT = computed tomography.

*P < .05 was considered a significant difference.

**Figure 4.** Box plot comparing the median bedside CT score between the survival and mortality groups. The bedside CT score was significantly higher in the mortality group than in the survival group (*P = .008). CT, computed tomography.**Figure 5.** Diagnostic performance of the receiver operating characteristic curve for the bedside computed tomography score.

bedside CT score ≥ 16 , which indicated that GGO and consolidation occupied more than half of the total lung area, had a poorer prognosis, and the precision of this result was similar to that of

previous studies. Thus, the use of bedside CT scores is warranted to predict mortality risk in patients with severe COVID-19 pneumonia in critical care centers.

Previous studies that investigated the association between the extent of abnormal opacity in the lungs and subsequent mortality analyzed all obtained CT images. This resulted in a relatively large workload and required the use of special workstations for machine learning analysis. To address this problem, we used a semi-quantitative evaluation of representative axial CT images, which has been used in other diseases.^[18,19] This facilitated easy measurement of abnormal opacity and achieved a high rate of inter-radiologist agreement. Our method would also enable non-radiologists to rapidly calculate bedside CT scores and estimate prognosis, thereby guiding the provision of appropriate medical care to patients with severe COVID-19.

This study had some limitations. First, the use of selected representative axial CT images may not provide an accurate evaluation of lung opacity if the lesion distribution in each lung lobe is unbalanced. Secondly, the selection of representative images for evaluation was determined in advance; therefore, both radiologists evaluated the same images. The true concordance rate between the 2 radiologists is expected to be lower in clinical practice, as different representative images may be selected by each radiologist. The variability of bedside CT scores may be higher in radiologists with fewer years of experience and may affect the prediction accuracy of mortality. Third, it is important to note that long-term mortality and sequelae after hospital discharge were not considered. Recent long-term follow-up studies have shown that some patients may exhibit prolonged lung dysfunction^[23–25] Additional studies are required to determine whether bedside CT scores obtained from representative CT images can predict the long-term prognosis of patients after hospital discharge. Finally, during the study period, B.1.1.214, B.1.1.284, R.1, and B.1.1.7 were the predominant SARS-CoV-2 variants in Japan.^[26] However, the patients included in this study were not tested to determine the SARS-CoV-2 variants they were infected with. Thus, further investigation is warranted to determine whether the severity and mortality of pneumonia is influenced by specific SARS-CoV-2 variants.

5. Conclusion

This study demonstrated that the degree of lung opacity in patients with severe COVID-19 can be easily scored using 6 axial CT images. This novel method does not require sophisticated software to estimate the prognosis of patients with severe COVID-19 in the ICU and is simple and suitable for daily practice, even in an emergency setting. A greater extent of abnormal opacity, as indicated by a bedside CT cutoff score of 16, was associated with a poorer prognosis. Predicting the prognosis of patients with severe COVID-19 could facilitate prompt and appropriate treatment.

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