The Ichikado CT score as a prognostic tool for coronavirus disease 2019 pneumonia: a retrospective cohort study

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Abstract

Background: The relationship between computed tomography (CT) and prognosis of patients with COVID-19 pneumonia remains unclear. We hypothesized that the Ichikado CT score, obtained in the first 24 h of hospital admission, is an independent predictor for all-cause mortality during hospitalization in patients with COVID-19 pneumonia.

Methods: Single-center retrospective cohort study of patients with confirmed COVID-19 pneumonia admitted at our institution between March 20th, 2020 and October 31st, 2020. Patients were enrolled if, within 24 h of admission, a chest CT scan, an arterial blood gas, a complete blood count, and a basic metabolic panel were performed. Two independent radiologists, who were blinded to clinical data, retrospectively evaluated the chest CT scans following a previously described qualitative and quantitative CT scoring system. The primary outcome was all-cause in-hospital mortality or survival to hospital discharge. Secondary outcomes were new requirements for invasive mechanical ventilation and hospital length of stay. Cox regression models were used to test the association between potential independent predictors and all-cause mortality.

Results: Two hundred thirty-five patients, 197 survivors and 38 nonsurvivors, were studied. The median Ichikado CT score for nonsurvivors was significantly higher than survivors (P < 0.001). An Ichikado CT score of more than 172 enabled prediction of mortality, with a sensitivity of 84.2% and a specificity of 79.7%. Multivariate analysis identified Ichikado CT score (HR, 7.772; 95% CI, 3.164–19.095; P < 0.001), together with age (HR, 1.030; 95% CI, 1.030–1.060; P = 0.043), as independent predictors of all-cause in-hospital mortality.

Conclusions: Ichikado CT score is an independent predictor of both requiring invasive mechanical ventilation and all-cause mortality in patients hospitalized with COVID-19 pneumonia. Further prospective evaluation is necessary to confirm these findings.

Trial registration: The WCG institutional review board approved this retrospective study and patient consent was waived due to its non-interventional nature (Identifier: 20210799).

Keywords: Coronavirus disease 2019, COVID-19, CT score, Ichikado CT score, COVID-19 prognostic factor, Tomography

Background

In late December 2019, a cluster of pneumonia cases of unknown origin was reported in Wuhan, Hubei Province, China [1]. Days later, the Chinese health authorities confirmed that coronavirus disease 2019 (COVID-19) was caused by severe acute respiratory coronavirus 2...
incidence in mechanically ventilated patients [20]. A factor for survival, ventilator-free days, and barotrauma patients which proved to be an independent predictive system for acute respiratory distress syndrome (ARDS) Ichikado et al. proposed and validated a chest CT scoring system; rapid tests, plus clinical and imaging correlation. Antigen Fluorescent Immunoassay (SOFIA), or IgG/IgM transcription polymerase chain reaction (RT-PCR), SARS Coronavirus disease 2019 was initially thought to be a pulmonary-limited disease; however, we have learned that in moderate-to-severe cases it is accompanied by a systemic dysregulated inflammatory response and a hypercoagulable state [5–7]. The most common clinical presentation includes fever, cough, myalgias, fatigue and anosmia. While most patients will have mild symptoms and recover without medical management, some will develop dyspnea, requiring supplemental oxygen therapy, and eventually worsen to respiratory or multi-organ failure, requiring mechanical ventilation and intensive care unit (ICU) monitoring [8, 9]. As the number of people infected by SARS-CoV-2 continues to climb, early recognition of patients at risk of deterioration may aid in the triage and medical management of COVID-19 patients [10].

Most studies have focused on inflammatory biomarkers as predictive tools [11–13]. Data regarding prognostic value of chest computed tomography (CT) is scarce. To our knowledge, none of the chest CT scoring systems proposed for COVID-19 patients are quantitative and consider both the percentage of lung parenchyma affected and the type of infiltrate [10, 14–19]. In 2006, Ichikado et al. proposed and validated a chest CT scoring system for acute respiratory distress syndrome (ARDS) patients which proved to be an independent predictive factor for survival, ventilator-free days, and barotrauma incidence in mechanically ventilated patients [20].

The aim of this study was to determine the prognostic value of the Ichikado CT score upon admission for all-cause mortality in patients admitted to a COVID-19 ICU or intermediate care unit (IMU). We hypothesized that the Ichikado CT score is a useful predictive tool for hospital mortality.

Methods
Study population and design
We performed a single-center retrospective cohort study of patients with COVID-19 pneumonia admitted between March 20th, 2020 and October 31st, 2020. Two hundred forty-one patients with confirmed SARS-CoV-2 infection were admitted at our institution's COVID-19 ICU and IMU. Infection was confirmed by reverse transcription polymerase chain reaction (RT-PCR), SARS Antigen Fluorescent Immunoassay (SOFIA), or IgG/IgM rapid tests, plus clinical and imaging correlation.

Patients were enrolled in our analysis if within 24 h from admission they underwent a chest CT, in supine or prone position, with or without intravenous contrast, and if within the same timeframe they had an arterial blood gas (ABG), a complete blood count, and a basic metabolic panel. Patients were excluded if they were younger than 18 years of age, they had a history of chronic interstitial lung disease or had missing demographic or outcome data. Considering the total patient population at our institution's COVID-19 units, we calculated requiring a sample size of 149 patients to achieve a 95% confidence level.

The WCG institutional review board approved this retrospective study and patient consent was waived due to its non-interventional nature (Identifier: 20210799). This study was conducted in accordance with the amended Declaration of Helsinki.

Data collection
Data were abstracted from both physical and digital hospital archives between February 24th, 2021 and February 25th, 2021. Two authors performed data entry to an electronic spreadsheet where information was double-checked. The demographic data included was age, gender, and race (African-American, Caucasian, Hispanic, Other). The clinical data included comorbidities like hypertension, diabetes mellitus, chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD) or end-stage renal disease (ESRD), the days since symptom onset until hospital admission, arterial partial pressure of oxygen (PaO2), arterial partial pressure of carbon dioxide (PaCO2), fraction of inspired oxygen (FiO2) at the time of ABG, arterial partial pressure of oxygen-to-fraction of inspired oxygen ratio (PaO2/FiO2), alveolar–arterial (A–a) gradient, Sequential Organ Failure Assessment (SOFA) score, absolute neutrophil count, absolute lymphocyte count, absolute neutrophil-to-lymphocyte ratio (NLR), Ichikado CT score, oxygen delivery device used at the time of CT scan and bloodwork obtention, medications utilized during hospitalization (corticosteroids, ascorbic acid, thiamine, anticoagulation, tocilizumab or remdesivir), prone positioning, renal replacement therapy (RRT), vasopressor use, acute kidney injury (AKI) during hospitalization, hospital length of stay (LoS) and new requirements for invasive mechanical ventilation. Fraction of inspired oxygen was estimated according to the oxygen delivery device used at the time of ABG. If patients had multiple laboratory measurements within the 24 h time frame, the worst clinical value was considered for this study.

Patients who underwent mechanical ventilation, before or after CT scan obtention, followed the low PEEP/high FiO2 ARDSnet protocol for lung protective ventilation,
with additional attention to maintain a plateau pressure below 27 cmH₂O and a driving pressure below 15 cmH₂O [21]. Prone positioning was done in both intubated and non-intubated patients, following the institutional protocol of 16 h of prone position and 8 h of supine position.

**CT scan examination**

Two independent radiologists with more than 10 years of experience of chest CT scan interpretation, who were blinded to clinical data, evaluated the chest CT scans included in our analysis. The observers followed a previously described qualitative and quantitative CT scoring system [20]. The visual scoring focused on the presence and extent of areas with normal lung parenchyma attenuation, ground-glass opacity (GGO), airspace consolidation, traction bronchiectasis or bronchiolectasis, and crazy-paving. Ground-glass attenuation was considered present if there was an area of opacification without obscuring the pulmonary vascular markings; airspace consolidation was defined as opacifications obscuring underlying vascular markings; traction bronchiectasis or bronchiolectasis were recognized as areas of irregularly dilated bronchi or bronchioles, respectively; presence of cystic air spaces with well-defined walls were defined as crazy-paving.

The previously described findings were graded on a scale of 1–6: 1, normal attenuation; 2, GGO; 3, airspace consolidation; 4, GGO with traction bronchiectasis or bronchiolectasis; 5, airspace consolidation with traction bronchiectasis or bronchiolectasis; 6, crazy-paving. Each attenuation was assessed in three (upper, middle, and lower) zones of each lung. The upper zone was defined as the lung parenchyma above the carina, the middle zone as the area between the carina and the pulmonary vein, and the lower zone as the infrapulmonary vein area (Fig. 1). The extent of each aberration was visually estimated to the nearest 10% of the lung parenchyma affected in each zone. The score for each zone was calculated by multiplying the percentage area by its respective point value (the score of 1 to 6). The six zones scores were averaged to determine an overall CT score for each patient (Fig. 2). The visual scoring of both radiologists was averaged, yielding a final score which was utilized in our analysis.

**Outcomes**

The primary endpoint was all-cause mortality during hospitalization or survival to hospital discharge. Additionally, secondary endpoints were duration of hospital LoS, and new requirements for invasive mechanical ventilation after the time of CT examination.

**Statistical analysis**

Continuous variables were expressed as mean ± standard deviation (SD) or median with interquartile range (IQR), depending on normality of distribution, and analyzed using a non-paired Student’s t test or Mann–Whitney U test, as appropriate. Categorical variables were expressed as frequencies and percentages, and compared using a Chi-squared test. Interobserver variability among radiologists, in chest CT scoring, was assessed with intraclass correlation coefficient. Correlations between Ichikado CT score and clinical data were determined using Spearman’s rank correlation coefficient.

Univariable and multivariable Cox regression models were used to test the association between potential independent predictive factors and all-cause mortality during COVID-19 hospitalization.

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**Fig. 1** Ichikado pulmonary zones. The upper zone is defined as the lung parenchyma above the carina, the middle zone as the area between the carina and the pulmonary vein, and the lower zone as the infrapulmonary vein area. **A** Coronal lung window of CT chest showing all 6 Ichikado pulmonary zones. **B** Sagittal lung window of CT chest showing right lung Ichikado areas. **C** Axial lung window of CT chest showing right and left middle zones. This example shows images of a 34-year-old lady with coronavirus disease 2019.
in multivariable approach were those that have been reported with higher risk of adverse events; to avoid overfitting, we excluded factors for which \( P \geq 0.1 \) in univariate analysis, as well as those that significantly correlated with Ichikado CT score in Spearman’s analysis.

The Kaplan–Meier method was utilized to evaluate the relationship between CT score and all-cause mortality. Receiver operator characteristic (ROC) curve analysis was used to determine the optimal cutoff value of Ichikado CT score that yielded the highest sensitivity and specificity. The area under the ROC curve (AUC) was used to assess the performance of the discrimination models based on Ichikado CT score.

Statistical analysis was performed based on non-missing data using IBM SPSS, version 26.0, and missing data were not imputed. All tests were two-sided and a \( P \)-value < 0.05 was considered statistically significant. The authors assume responsibility for the accuracy and completeness of the data and analysis, as well as the fidelity of the study.

Results

A total of 241 patients were admitted at our institution’s COVID-19 units, of which 235 were included in our analysis. Five patients were excluded due to missing chest CT scan within 24 h of admission, and one patient due to missing demographic or clinical data; none of the patients excluded died during hospitalization (Fig. 3). Demographic characteristics and clinical variables on the first 24 h from hospitalization for all 235 patients are reported in Table 1.

One hundred twenty-nine (54.9%) patients were male and 106 (45.1%) were female, with a mean age of 56.0 ± 15.6. The most common races were Hispanics (44.2%) and African Americans (31.1%), followed by Caucasians (18.3%). Hypertension (50.3%) and diabetes mellitus (37.9%) were the most common comorbidities, followed by COPD (34.0%), CKD (26.8%) and ESRD (6.0%). At the time of CT scan and bloodwork obtention, 110 (46.8%) patients were on nasal cannula, 81 (34.5%) on high-flow nasal cannula (HFNC), and 8 (3.4%) were endotracheally intubated. During hospitalization, 59 (25.1%) developed AKI. Forty-two (17.9%) patients had new requirements for invasive mechanical ventilation. One hundred ninety-seven (83.8%) patients survived to hospital discharge, while 38 (16.2%) died during their hospital stay. When compared to nonsurvivors, survivors were younger (\( P < 0.001 \)), more likely to be women (\( P = 0.011 \)) and had less days since onset of symptoms until hospitalization (\( P = 0.003 \)). The median Ichikado CT score for nonsurvivors was 215.8 (179.6–240.0), which was significantly higher compared to survivors who had a median score of 138.3 (119.2–165.8) (\( P < 0.001 \)). The interobserver variability among radiologists in calculating Ichikado CT score was excellent.

![Ichikado chest CT score](image)
with an intraclass correlation coefficient of 0.992 (95% CI, 0.989–0.994; \( P < 0.001 \)).

Analysis by Spearman’s correlation coefficient (\( R \)) indicated that Ichikado CT score was significantly associated with age (\( R = 0.243; \ P < 0.001 \)), days from onset of symptoms to hospitalization (\( R = 0.270; \ P < 0.001 \)), hospital length of stay (\( R = 0.414; \ P < 0.001 \)), FiO2 (\( R = 0.425; \ P < 0.001 \)), PaO2:FiO2 (\( R = 0.530; \ P < 0.001 \)), A-a gradient (\( R = 0.481; \ P < 0.001 \)), SOFA score (\( R = 0.260; \ P < 0.001 \)), absolute neutrophil count (\( R = 0.361; \ P < 0.001 \)), absolute lymphocyte count (\( R = -0.366; \ P < 0.001 \)) and NLR (\( R = 0.493; \ P < 0.001 \)).

Receiver operator characteristic curve analysis yielded an optimal cutoff value of an Ichikado CT score of 172 for prediction of mortality, with a sensitivity of 84.2% and a specificity of 79.7% (AUC = 0.873); optimal cutoff value of CT score for prediction of new requirement of invasive mechanical ventilation was 170, with a sensitivity of 82.4% and a specificity of 79.3% (AUC = 0.870) (Fig. 4). A Kaplan–Meier survival curve was performed utilizing the ROC curve cutoff value for Ichikado CT score. By this method, a CT score \( \geq 172 \) was predictive of all-cause hospital mortality (Fig. 5).

Table 2 summarizes univariable and multivariable Cox regression analysis results for all-cause mortality. On univariable analysis, an Ichikado CT score \( \geq 172 \) was a statistically significant predictor for mortality with a hazard ratio (HR) of 6.864 (95% CI, 2.843–16.572; \( P < 0.001 \)).
| Characteristic                                      | All (N = 235) | Survivors (N = 197) | Nonsurvivors (N = 38) | P-value |
|---------------------------------------------------|---------------|---------------------|-----------------------|---------|
| Age (y)†                                          | 56.0 ± 15.6   | 53.9 ± 15.2         | 67.1 ± 13.1           | 0.000   |
| Gender                                            |               |                     |                       | 0.011   |
| Male                                              | 129 (54.9%)   | 101 (51.3%)         | 28 (73.7%)            |         |
| Female                                            | 106 (45.1%)   | 96 (48.7%)          | 10 (26.3%)            |         |
| Race                                              |               |                     |                       | 0.804   |
| African-American                                  | 73 (31.1%)    | 60 (30.5%)          | 13 (34.2%)            |         |
| Caucasian                                         | 43 (18.3%)    | 38 (19.3%)          | 5 (13.1%)             |         |
| Hispanic                                          | 104 (44.2%)   | 86 (43.6%)          | 18 (47.4%)            |         |
| Other                                              | 15 (6.4%)     | 13 (6.6%)           | 2 (5.3%)              |         |
| Comorbidities                                     |               |                     |                       |         |
| Hypertension                                      | 119 (50.3%)   | 85 (43.1%)          | 34 (89.5%)            | 0.000   |
| Diabetes mellitus                                 | 89 (37.9%)    | 62 (31.5%)          | 27 (71.1%)            | 0.000   |
| COPD                                             | 80 (34.0%)    | 56 (28.4%)          | 24 (63.2%)            | 0.000   |
| CKD                                              | 63 (26.8%)    | 38 (19.3%)          | 25 (65.8%)            | 0.000   |
| ESRD                                             | 14 (6.0%)     | 11 (5.6%)           | 3 (7.9%)              | 0.582   |
| PaO2 (Torr)‡                                      | 76.0 (64.0–88.0) | 77.0 (65.0–88.0) | 70.5 (62.2–86.0)     | 0.216   |
| PaCO2 (Torr)‡                                      | 38.0 (35.0–41.0) | 38.0 (35.0–41.0) | 35.5 (33.0–40.2)     | 0.131   |
| FiO2 (%)‡                                         | 33.0 (28.0–40.0) | 32.0 (28.0–40.0) | 50.0 (40.0–100.0)    | 0.000   |
| PaO2:FiO2‡                                        | 217.8 (157.5–275.0) | 230.3 (171.1–285.7) | 140.1 (70.2–215.6) | 0.000   |
| Mild (≥ 200)                                       | 132 (56.2%)   | 121 (61.4%)         | 11 (29.0%)            |         |
| Moderate (100–200)                                 | 67 (28.5%)    | 57 (28.9%)          | 10 (26.3%)            |         |
| Severe (< 100)                                     | 36 (15.3%)    | 19 (9.7%)           | 17 (44.7%)            |         |
| Oxygen delivery device                             |               |                     |                       | 0.000   |
| Room air                                          | 19 (8.1%)     | 19 (9.6%)           | 0 (0%)                |         |
| Nasal cannula                                      | 110 (46.8%)   | 101 (51.3%)         | 9 (23.7%)             |         |
| HFNC                                             | 81 (34.5%)    | 62 (31.5%)          | 19 (50%)              |         |
| BiPAP/CPAP                                        | 13 (5.5%)     | 9 (4.6%)            | 4 (10.5%)             |         |
| Non-rebreather mask                                | 4 (1.7%)      | 3 (1.5%)            | 1 (2.6%)              |         |
| Endotracheal tube                                 | 8.3 (4.3%)    | 3 (1.5%)            | 5 (13.2%)             |         |
| Onset of symptoms to hospitalization (days)‡      | 7.0 (5.0–10.0) | 7.0 (5.0–10.0) | 10.0 (6.5–14.0)     | 0.003   |
| Hospital length of stay (days)‡                   | 10.0 (7.0–15.0) | 9.0 (6.5–14.0) | 12.0 (7.0–19.0)     | 0.045   |
| AKI during hospitalization                         | 59 (25.1%)    | 27 (13.7%)          | 32 (84.2%)            | 0.000   |
| Ichikado CT score‡                                 | 146.7 (121.7–188.3) | 138.3 (119.2–165.8) | 215.8 (179.6–240.0) | 0.000   |
| A–a gradient (Torr)‡                               | 119.7 (81.1–181.2) | 109.3 (73.6–161.1) | 235.7 (134.3–562.6) | 0.000   |
| SOFA score‡                                       | 3.0 (2.0–4.0) | 3.0 (2.0–4.0)       | 4.0 (3.0–5.0)         | 0.000   |
| Absolute neutrophil count × 10⁹/L‡                | 4.8 (3.4–7.4) | 4.7 (3.3–6.5)       | 6.7 (3.6–10.7)        | 0.005   |
| Absolute lymphocyte count × 10⁹/L‡                | 1.1 (0.7–1.7) | 1.2 (0.8–1.7)       | 0.7 (0.6–1.0)         | 0.000   |
| NLR‡                                              | 4.3 (2.7–8.3) | 3.7 (2.5–6.9)       | 9.4 (5.9–13.3)        | 0.000   |
| Treatment modalities                              |               |                     |                       |         |
| Corticosteroids                                   | 235 (100%)    | 197 (100%)          | 38 (100%)             | –       |
| Ascorbic acid                                     | 235 (100%)    | 197 (100%)          | 38 (100%)             | –       |
| Thiamine                                          | 235 (100%)    | 189 (95.9%)         | 38 (100%)             | –       |
| Anticoagulation                                   | 227 (96.6%)   | 7 (3.6%)            | 38 (100%)             | 0.206   |
| Tocilizumab                                       | 17 (7.2%)     | 7 (3.6%)            | 10 (26.3%)            | 0.000   |
| Remdesivir                                       | 10 (4.3%)     | 197 (100%)          | 3 (7.9%)              | 0.225   |
| Prone positioning                                 | 142 (60.4%)   | 109 (55.3%)         | 33 (86.8%)            | 0.000   |
| RRT                                              | 31 (13.2%)    | 24 (12.2%)          | 7 (18.4%)             | 0.298   |
| Vasopressor use                                   | 53 (22.6%)    | 17 (8.6%)           | 36 (94.7%)            | 0.000   |

For continuous variables, comparison of groups (survivors and nonsurvivors) was determined using the Student’s t test or Mann–Whitney U test, as appropriate. Chi-squared test was utilized for categorical variables. Statistically significant values (P < 0.05) are in bold. A–a gradient alveolar–arterial gradient, NLR absolute neutrophil-to-lymphocyte ratio, AKI acute kidney injury, PaCO2 arterial partial pressure of carbon dioxide, PaO2 arterial partial pressure of oxygen, PaO2/FiO2 arterial partial pressure of oxygen to fraction of inspired oxygen ratio.
Other significant variables for prediction of mortality were age (HR, 1.033; 95% CI, 1.010–1.058; \( P = 0.005 \)), hypertension (HR, 4.621; 95% CI, 1.627–13.121; \( P = 0.004 \)), diabetes mellitus (HR, 2.533; 95% CI, 1.248–5.139; \( P = 0.010 \)), COPD (HR, 2.205; 95% CI, 1.135–4.285; \( P = 0.020 \)), CKD (HR, 3.348; 95% CI, 1.698–6.602; \( P < 0.001 \)), days from onset of symptoms to hospitalization (HR, 1.056; 95% CI, 1.005–1.109; \( P = 0.032 \)), AKI during hospitalization (HR, 9.169; 95% CI, 3.806–22.085; \( P < 0.001 \)), A-a gradient (HR, 1.003; 95% CI, 1.001–1.004; \( P < 0.001 \)), SOFA score (HR, 1.189; 95% CI, 1.054–1.341; \( P = 0.005 \)), absolute neutrophil count (HR, 1.123; 95% CI, 1.060–1.190; \( P < 0.001 \)), absolute lymphocyte count (HR, 0.442; 95% CI, 0.220–0.891; \( P = 0.022 \)), NLR (HR, 1.039; 95% CI, 1.021–1.058; \( P < 0.001 \)), vasopressor use during hospitalization (HR, 33.935; 95% CI, 8.113–141.942; \( P < 0.001 \)).

Multivariate analysis showed that Ichikado CT score (HR, 7.772; 95% CI, 3.164–19.095; \( P < 0.001 \)), together with age (HR, 1.030; 95% CI, 1.030–1.060; \( P = 0.043 \)), were independent predictors of all-cause in-hospital mortality. Additionally, an Ichikado CT score \( \geq 172 \) (HR, 22.480; 95% CI, 8.161–61.921; \( P < 0.001 \)) was an independent predictor of new requirement of invasive mechanical ventilation during hospitalization.

**Discussion**

Ichikado et al. previously validated a CT score in patients with ARDS, identifying a score above 230 as an independent predictor of mortality [20]. In our single-center retrospective cohort study, we recognized the Ichikado CT score as an independent predictor of both requiring mechanical ventilation and all-cause mortality in patients hospitalized with COVID-19 pneumonia. However, our cutoff value with highest sensitivity and specificity for prediction of mortality was 172. We believe this difference is explained mainly by the time to obtention of the CT scans. In contrast with their study, which analyzed scans up to 7 days from the onset of ARDS, we only included CT scans taken in the first 24 h of hospital...
admission. It has previously been described that COVID-19 CT imaging features will vary drastically according to the stage of disease. Early on, patients will have predominantly small areas of GGOs, compared to the late phase of disease (12–17 days after onset of symptoms), during which patients will have bilateral consolidations mixed with GGOs, and even crazy-paving pattern [22, 23]. The presence of fibroproliferative attenuations in chest CT scans obtained in later stages of the disease, could potentially explain the discrepancies between their study and ours. In addition, the CT findings of “typical” ARDS differ considerably from that of COVID-19 organizing pneumonia [24].

Multiple CT scoring models have been proposed in COVID-19 for quantifying severity of disease, and predicting prognosis. Regardless of the CT scoring system analyzed, all prior studies have identified a CT score as an independent predictor of adverse outcome in patients with COVID-19 pneumonia [10, 15, 17, 18]. Moreover, CT scores had significant associations with various inflammatory biomarkers known to be predictors of mortality [14, 16]. However, to our knowledge, no other study has followed the Ichikado scoring method, which we believe might be superior to previously described methods due to its reproducibility and having both a quantitative and qualitative approach.

Our multivariate regression results showed that an Ichikado CT score ≥ 172 was the highest independent predictor of all-cause in-hospital mortality. Furthermore, a higher absolute lymphocyte count at the time of hospital admission was associated with significantly decreased odds of mortality. These findings are consistent with prior reports [25–27].

The role of chest CT scan in the diagnosis and management of COVID-19 remains controversial. While some authors and radiological societies recommend against routine use of CT scan in patients with COVID-19, our analysis seems to suggest a benefit by allowing early recognition of patients at high risk of decompensation [28, 29]. Additionally, the high diagnostic sensitivity may prove to be an asset as CT scans may show characteristic findings of the disease even when RT-PCR is negative (false-negative), or in hospitals with a relatively long turn-around time for RT-PCR results [16, 30].

There were limitations in our analysis. Due to the single-center retrospective observational nature of the study, we cannot exclude the possibility of unmeasured confounders. Furthermore, despite including laboratory
| Variable | Univariable analysis | Multivariable analysis |
|----------|----------------------|------------------------|
|          | Hazard ratio | 95% confidence interval | P-value | Hazard ratio | 95% confidence interval | P-value |
| Age (y)  | 1.033       | 1.010–1.058             | 0.005   | 1.030       | 1.001–1.060             | 0.043   |
| Gender   |             |                        |         |             |                        |         |
| Male     | 1.425       | 0.682–2.979             | 0.346   | –           | –                      | –       |
| Female   | 1 (ref)     |                        |         | –           | –                      | –       |
| Race     |             |                        |         |             |                        |         |
| African-American | 1 (ref) |          |         | –           | –                      | –       |
| Caucasian | 0.652      | 0.232–1.832             | 0.417   | –           | –                      | –       |
| Hispanic | 0.808       | 0.394–1.654             | 0.559   | –           | –                      | –       |
| Other    | 0.916       | 0.206–4.072             | 0.908   | –           | –                      | –       |
| Comorbidities |          |                        |         |             |                        |         |
| Hypertension | 4.621    | 1.627–13.121            | 0.004   | 2.056       | 0.665–6.359             | 0.211   |
| Diabetes mellitus | 2.533  | 1.248–5.139             | 0.010   | 2.004       | 0.940–4.273             | 0.072   |
| COPD     | 2.205       | 1.135–4.285             | 0.020   | –           | –                      | –       |
| CKD      | 3.484       | 1.698–6.602             | 0.000   | –           | –                      | –       |
| ESRD     | 0.788       | 0.241–2.574             | 0.693   | –           | –                      | –       |
| PaO2 (Torr) | 0.991    | 0.975–1.007             | 0.284   | –           | –                      | –       |
| PaCO2 (Torr) | 1.005  | 0.971–1.040             | 0.789   | –           | –                      | –       |
| FiO2 (%) | 1.020       | 1.009–1.031             | 0.000   | –           | –                      | –       |
| PaO2:FiO2 | 0.993      | 0.988–0.997             | 0.001   | –           | –                      | –       |
| Oxygen delivery device |          |                        |         |             |                        |         |
| Room air | –           | –                      | –       | –           | –                      | –       |
| Nasal cannula | 0.194   | 0.064–0.587             | 0.004   | –           | –                      | –       |
| HFNC     | 0.459       | 0.169–1.242             | 0.125   | –           | –                      | –       |
| BiPaP/CPAP | 0.383   | 0.102–1.441             | 0.156   | –           | –                      | –       |
| Non-rebreather mask | 0.882   | 0.101–7.730             | 0.910   | –           | –                      | –       |
| Endotracheal tube | 1 (ref) |          |         | –           | –                      | –       |
| Onset of symptoms to hospitalization (days) | 1.056 | 1.005–1.109 | 0.032 | – | – | – |
| AKI during hospitalization | 9.169 | 3.806–22.085 | 0.000 | – | – | – |
| Ichikado CT score | 1.010 | 1.005–1.014 | 0.000 | – | – | – |
| ≥172     | 6.864       | 2.843–16.572            | 0.000   | 3.164–19.095 | 0.000 | – |
| <172     | 1 (ref)     |                        | 7.772   |             | –                      | –       |
| A–a gradient (Torr) | 1.003 | 1.001–1.004 | 0.000 | – | – | – |
| SOFA score | 1.189    | 1.054–1.341             | 0.005   | –           | –                      | –       |
| Absolute neutrophil count x 10⁹/L | 1.123 | 1.060–1.190 | 0.000 | – | – | – |
| Absolute lymphocyte count x 10⁹/L | 0.442 | 0.220–0.891 | 0.022 | – | – | – |
| NLR      | 1.039       | 1.021–1.058             | 0.000   | –           | –                      | –       |
| Treatment modalities |          |                        |         |             |                        |         |
| Steroids | –           | –                      | –       | –           | –                      | –       |
| Ascorbic acid | –     | –                      | –       | –           | –                      | –       |
| Thiamine | –           | –                      | –       | –           | –                      | –       |
| Anticoagulation | –   | –                      | –       | –           | –                      | –       |
| Tocilizumab | 1.743    | 0.822–3.693             | 0.147   | –           | –                      | –       |
| Remdesivir | 1.162    | 0.354–3.811             | 0.805   | –           | –                      | –       |
| Prone positioning | 1.674  | 0.643–4.359             | 0.291   | –           | –                      | –       |
| RRT      | 0.812       | 0.354–1.860             | 0.622   | –           | –                      | –       |
| Vasopressor use | 33.935 | 8.113–141.942          | 0.000   | –           | –                      | –       |
data obtained on the same day as the chest CT, we did not provide correlation analysis with biomarkers (e.g., interleukin-6, C-reactive protein, D-dimer, ferritin, etc.) known to be predictors of mortality in COVID-19. External validation of our analysis is required as most of the studied patients, unless medically contraindicated, received the MATH+ protocol (methylprednisolone, IV ascorbic acid, thiamine, heparin, etc.) which is not the standard of care in most institutions, and could potentially be a confounder in our study [31, 32].

Conclusions
Further prospective evaluation of the Ichikado CT score in patients with COVID-19 will be necessary not only to clarify its prognostic value, but also to assess its potential application in stratifying severity of disease, guiding treatment, and monitoring disease progression. Ideally, such investigations would help identify the patients at high risk of deterioration who require prompt initiation of treatment and ICU monitoring.

In summary, this study provided evidence that Ichikado CT score obtained in the first 24 h of hospital admission, is an independent predictor of requiring invasive mechanical ventilation and all-cause in-hospital mortality in patients with COVID-19 pneumonia. Since COVID-19 is a potentially fatal disease, utilizing the Ichikado CT score may aid in appropriately triaging patients, so that those with severe disease can timely initiate more aggressive treatment under closer monitoring.

Abbreviations
95% CI: 95% Confidence interval; A–a: gradient; Alveolar–arterial gradient; ABG: Arterial blood gas; AKI: Acute kidney injury; ARDS: Acute respiratory distress syndrome; AUC: Area under roc curve; CKD: Chronic kidney disease; COPD: Chronic obstructive pulmonary disease; COVID-19: Coronavirus disease 2019; CT: Computed tomography; ESRD: End-stage renal disease; FiO2: Fraction of inspired oxygen; GGO: Ground-glass opacity; HFNC: High-flow nasal cannula; HR: Hazard ratio; ICU: Intensive care unit; IMU: Intermediate care unit; IQR: Interquartile range; LoS: Length of stay; MATH+ protocol: Methylprednisolone, IV ascorbic acid, thiamine, heparin, etc.; NLR: Absolute neutrophil-to-lymphocyte ratio; PaCO2: Partial pressure of arterial carbon dioxide; PaO2: Partial pressure of arterial oxygen; PaO2/FiO2: Arterial partial pressure of oxygen-to-fraction of inspired oxygen ratio; R: Spearman’s correlation coefficient; RRT: Renal replacement therapy; ROC curve: Receiver operator characteristic curve; RT-PCR: Reverse transcription polymerase chain reaction; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; SD: Standard deviation; SOFA Score: Sequential Organ Failure Assessment Score; SARS: Severe Acute Respiratory Syndrome; SOFIA: SARS-CoV-2 influenza antigen immunoassay.

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Guarantor
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Authors’ contributions
All authors were responsible for the study design, study data integrity, data analysis, data interpretation, and preparation of the manuscript. AA, MD and CP were responsible for data acquisition. AA, CP and PM did the statistical analysis. All authors reviewed the manuscript and approved the final submitted version. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The WCG institutional review board approved this retrospective study and patient consent was waived due to its non-interventional nature (Identifier: 20210799).

Consent for publication
Not applicable.

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

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