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【 ORIGINAL ARTICLE 】

Efficacy of Chest Radiography as a Primary Care Triage Tool in Severe Coronavirus Disease

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Abstract:

Objective Severe acute respiratory syndrome coronavirus 2 has spread globally, and it is important to utilize medical resources properly, especially in critically ill patients. We investigated the validity of chest radiography as a tool for predicting aggravation in coronavirus disease (COVID-19) cases.

Methods A total of 104 laboratory-confirmed COVID-19 cases were referred from the cruise ship "Diamond Princess" to the Self-Defense Forces Central Hospital in Japan from February 11 to 25, 2020. Fifty-nine symptomatic patients were selected. Chest radiography was performed upon hospitalization; subsequently, patients were categorized into the positive radiograph (Group A) and negative radiograph (Group B) groups. Radiographic findings were analyzed with a six-point semiquantitative score. Group A was further classified into two additional subgroups: patients who required oxygen therapy during their clinical courses (Group C) and patients who did not (Group D). Clinical records, laboratory data, and radiological findings were collected for an analysis.

Results Among 59 patients, 34 were men with a median age of 60 years old. Groups A, B, C, and D consisted of 33, 26, 12, and 21 patients, respectively. The number of patients requiring oxygen administration was significantly larger in Group A than in Group B. The consolidation score on chest radiographs was significantly higher in Group C than in Group D. When chest radiographs showed consolidation in more than two lung fields, the positive likelihood ratio of deterioration was 10.6.

Conclusions Chest radiography is a simple and easy-to-use clinic-level triage tool for predicting the severity of COVID-19 and may contribute to the allocation of medical resources.

Key words: severe acute respiratory syndrome coronavirus 2, coronavirus disease, chest X-ray, severity

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Introduction

Coronavirus disease (COVID-19) is a global threat due to its high infectivity and transmissibility from human to human (1). As infections spread rapidly around the world, the World Health Organization (WHO) declared it a pandemic on March 11, 2020 (2). Underlying factors, such as hypertension, diabetes, an older age, and high levels of lactate dehydrogenase (LDH) and D-dimer, have been reported as risk factors of deterioration (3-5). According to a report from China, the mortality rate of COVID-19 is 2.3% (6). The same report also states that the majority of patients are asymptomatic. Therefore, it has become a pressing issue to be able to diagnose disease severity accurately in order to treat patients at appropriate medical institutions and to prevent medical collapse.

Although chest computed tomography (CT) may be useful in assessing the severity of COVID-19 (7, 8), the use of chest CT as a routine test for making a definitive diagnosis is still controversial because of its low negative predictive value (9) as well as from the perspective of high radiation exposure. Furthermore, chest CT is not always available, especially at primary care-level clinics. As the volume of pa-

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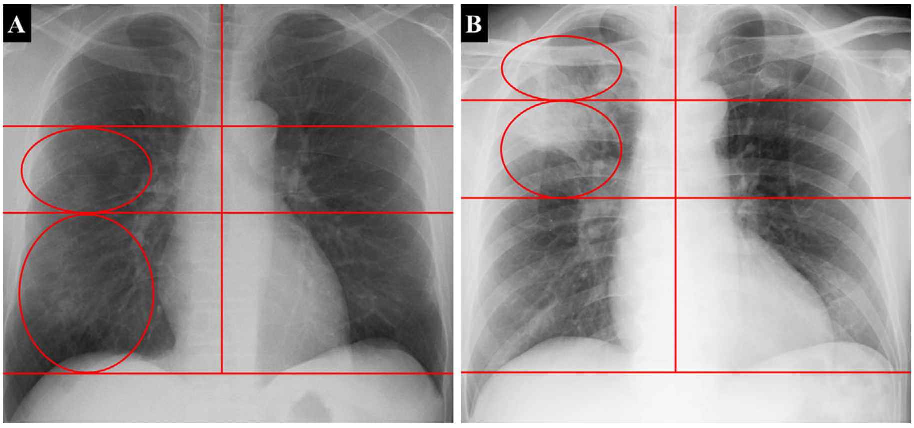

Figure 1. Method of calculating the six-point semiquantitative score. Lung fields are separated into six areas. GGA is in the right middle and lower lung fields; consequently, the GGA score is calculated as two points (A). Consolidation is in the upper and middle lung fields; consequently, the score is calculated as 2 points (B)

tients increases, the initial tool for assessment should be simpler and more convenient. Chest radiography is a simple and convenient tool generally used for assessing lung lesions and can be applied more readily than CT at the clinic level. However, its usefulness is not verified.

We therefore investigated the correlation between disease severity and radiological findings in COVID-19 cases and tested the efficacy of chest radiography as a simple screening tool for predicting patient deterioration.

Materials and Methods

This is a retrospective review of 104 laboratory-confirmed COVID-19 cases referred from the cruise ship "Diamond Princess" to the Self Defense Forces Central Hospital in Japan. All cases were enrolled from February 11 to 25, 2020.

Symptomatic patients were categorized into two groups (A and B) depending on chest radiographic abnormalities. On the premise that people who visit primary care clinics generally have some symptoms, asymptomatic patients and patients who lacked chest radiographs were excluded from the analysis. Symptomatic patients with radiographic abnormalities (positive radiograph) that seemed to be caused by COVID-19 were allocated to Group A, and those without radiographic abnormalities (negative radiograph) were allocated to Group B. Group A was also further classified into two subgroups depending on oxygen administration: patients who required oxygen therapy during their clinical courses (Group C) and patients who did not (Group D). The symptoms were a fever (>37.5 °C), general malaise, headache, nasal discharge, sore throat, cough, muscle pain, joint pain, diarrhea, nausea and vomiting, abdominal pain, and dyspnea. Regardless of radiographic abnormalities, all cases were defined as severe or mild depending on oxygen administration.

Data collection

Patient information, including clinical records, laboratory findings, and radiographs, were collected and reviewed from the electronic medical records in our hospital.

Imaging analyses

Fifty-nine patients underwent chest radiography after admission. The examination protocol was standing position (post anterior) or supine position (anterior post). Two pulmonologists interpreted the chest radiographs of the 59 patients. Among the patients with positive findings on chest radiographs (Group A), radiological findings were classified according to their distribution and characteristics. A six-point semiquantitative score was used for the analysis. The distribution of chest radiographic abnormalities was sorted according to six affected lung fields (right upper field, right middle field, right lower field, left upper field, left middle field, and left lower field), and the abnormalities were classified into two common radiological manifestations [ground-glass attenuation (GGA) and consolidation]. GGA and consolidation of each lung field on chest radiographs were scored separately. If there were two localized consolidations in the same lung field, the score was one. If GGA straddled two lung fields, the score was two. GGA and consolidation were scored independently regardless of their size and number. Fig. 1 shows the scoring method and examples.

Statistical analyses

Data were statistically analyzed with the GraphPad Prism 8.4 software program (Graph Pad Software, San Diego, USA). Continuous variables were expressed as the mean± standard deviation (SD) or median with interquartile range (IQR), and groups were compared using Student's *t*-test and the Mann-Whitney U-test for parametric and non-parametric data, respectively, as well as using the chi-squared test. The sensitivity and specificity were calculated by a receiver op-

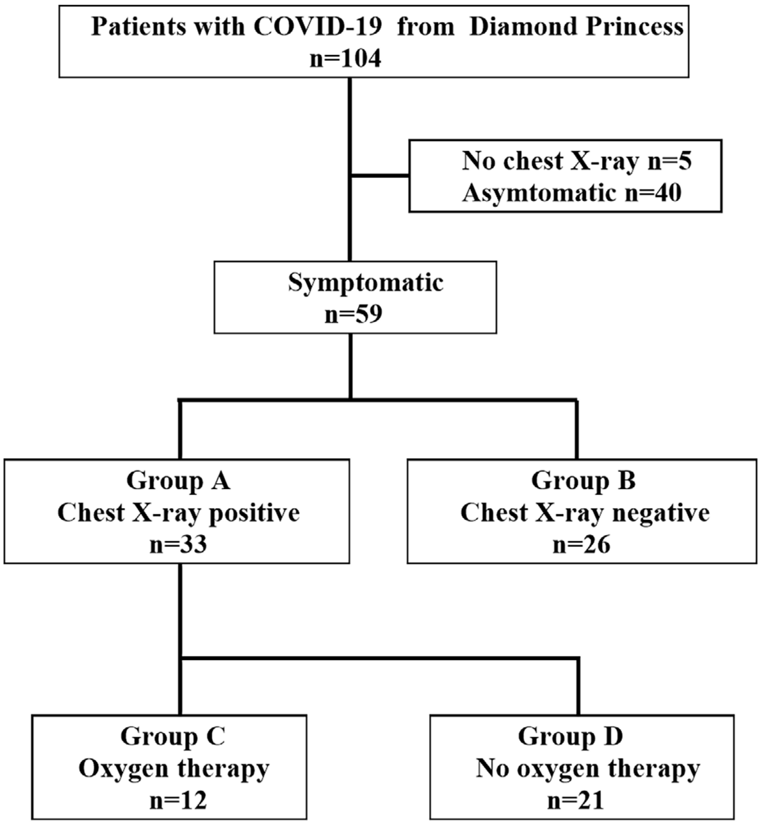

Figure 2. Flowchart of patient recruitment and patient breakdown in each group.

erating characteristic (ROC) curve to predict the severity of the disease based on the findings on chest radiographs. A two-sided p-value of less than 0.05 was considered statistically significant.

Ethical approval

The Institutional Review Board at the Self-Defense Forces Central Hospital approved this study (Approval number 01011), and all patients provided their written informed consent for the publication of their innominate data.

Results

Of the 59 patients, 34 (58%) were men with a median age of 60 years old. Fig. 2 shows the patient recruitment flowchart and breakdown. Thirty-three symptomatic patients (56%) had abnormal radiological findings (Group A) on their chest radiographs, and 26 symptomatic patients (44%) had no abnormal findings (Group B). Twelve patients from Group A (36%) required oxygen therapy during hospitalization (Group C), and the remaining 21 (Group D) (64%) did not require oxygen therapy.

Table 1 shows the characteristics of the symptomatic patients. There were significant differences in the age, fever incidence, and muscle pain between Group A and Group B. Table 2 shows the laboratory findings of symptomatic patients. Blood urea nitrogen (BUN), LDH, serum albumin, C-reactive-protein (CRP), white blood cell (WBC) counts, and lymphocyte counts showed statistically significant differences between Groups A and B. The 6-point semiquantitative score of consolidation was significantly higher in Group C than in Group D ($p<0.05$). In contrast, there were no significant differences in GGA scores between Groups C and D (Table 3). Twelve patients (36%) from Group A required oxygen administration through their clinical courses, whereas only 1 patient (3%) from Group B required oxygen therapy (Table 4). Of the 13 patients who required oxygen therapy, 8 (62%) were men, and the mean age was 70 years old. Five of the 13 patients received high-flow nasal oxygen therapy, and 1 patient was treated by mechanical ventilation with tracheal intubation. The area under the ROC curve was used to predict the disease severity based on chest radiography. Consolidation had an area under the curve of 0.816 [95% confidence interval (CI), 0.648-0.983; $p=0.002$] (Fig. 3). When chest radiographs showed consolidation in more than 2 lung fields, the sensitivity and specificity were 50% (95% CI, 25.4-74.6%) and 95% (95% CI, 77.3-99.7%), respectively. The positive likelihood ratio of severity was 10.6. Fig. 4 shows representative chest radiographs before and after treatment in a patient who required oxygen therapy.

Discussion

The present study investigated the correlation between radiographic findings and the severity of symptomatic COVID-19, which was considered the typical model for walk-in cases. The severity, age, underlying disease, inci-

Table 1. Characteristics of Symptomatic COVID-19 Patients.

		No. (%)		
		Group A (n=33)	**Group B (n=26)**	**p value**
Age (mean±SD) , y		65±16	53±18	**<0.05**
Sex				
	Male	17 (52)	17 (65)	0.284
Comorbidities	Hypertension	9 (27)	6 (30)	0.713
	Cardiovascular disease	4 (14)	1 (4)	0.257
	Diabetes mellitus	2 (6)	2 (8)	0.805
	Hyperlipemia	6 (18)	3 (12)	0.481
Smoking status	Current	2 (6)	2 (8)	0.805
	Ex	4 (12)	2 (8)	0.576
	Never	27 (82)	22 (84)	0.776
Symptoms	Fever (>37·5°C)	10 (30)	2 (8)	**<0.05**
	General malaise	4 (12)	1 (4)	0.257
	Headache	5 (15)	5 (19)	0.678
	Nasal discharge	8 (24)	7 (27)	0.814
	Sore throat	3 (9)	4 (15)	0.458
	Cough	12 (36)	10 (38)	0.869
	Muscle pain	1 (3)	5 (19)	**<0.05**
	Joint pain	5 (15)	1 (4)	0.154
	Diarrhea	4 (12)	1 (4)	0.257
	Nausea and vomiting	2 (6)	1 (4)	0.701
	Abdominal pain	2 (6)	0 (0)	0.202
	Dyspnea	2 (6)	3 (12)	0.453
Duration from symptom onset to radiography (mean±SD), days		4±2.4	6±2.7	**<0.05**

Symptomatic patients with chest X-ray abnormalities are categorized into Group A. Symptomatic patients without chest X-ray abnormalities are into Group B. Continuous variables were expressed as mean±SD. p values indicate differences between patients in Groups A and B. Groups were compared using unpaired *t*-tests and chi-squared tests. p<0.05 was considered statistically significant.

Table 2. Laboratory Findings of Symptomatic COVID-19 Patients.

	No. (%)		
Laboratory findings (mean±SD)	**Group A (n=33)**	**Group B (n=26)**	**p value**
BUN (mg/dL)	16±6	12±3	**<0.05**
Creatinine (mg/dL)	0.86±0.33	0.77±0.14	0.171
AST (U/L)	31±11	29±13	0.547
ALT (U/L)	29±15	36±28	0.266
Total bilirubin (mg/dL)	0.5±0.2	0.6±0.2	0.431
γ-GTP (IU/L)	38±29	39±24	0.938
Amylase (U/L)	90±51	77±24	0.228
LDH (U/L)	224±51	192±31	**<0.05**
Serum albumin (g/dL)	3.9±0.4	4.3±0.4	**<0.05**
CRP (mg/dL)	2.12±2.29	0.43±0.50	**<0.05**
WBC counts(/μL)	4,970±1,360	5,921±1,809	**<0.05**
Neutrophil counts (μ/L)	3,284±1,088	3,671±1,691	0.290
Lymphocyte counts (μ/L)	1,205±560	1,711±614	**<0.05**
Monocyte counts (μ/L)	414±120	420±136	0.080
Platelet (/μL×10^4)	21±6	23±5	0.155
APTT (s)	33±3	31±4	0.860

The p values indicate differences between patients in Groups A and B patients. Continuous variables were expressed as mean±SD. Groups were compared using unpaired t-tests. p<0.05 was considered statistically significant.

SD: standard deviation, BUN: blood urea nitrogen, AST: aspartate aminotransferase, ALT: alanine aminotransferase, γ-GTP: γ-glutamyltransferase, LDH: lactate dehydrogenase, CRP: C-reacted-protein, WBC: white blood cells, APTT: activated partial thromboplastin time

Table 3. Comparative Results of Six-point Semiquantitative Score in Symptomatic Patients with Abnormal X-ray Findings.

		Group C (n=12)	Group D (n=21)	p value
Number of GGA in the six lung fields (mean±SD)		1.3 (±1.7)	1.4 (±2.9)	0.845
Number of Consolidation in the six lung fields (mean±SD)		1.9 (±1.9)	0.2 (±0.5)	**<0.05**
Number of GGA in each fields (%)				
Right lung	**upper field**	3 (25)	4 (19)	0.687
	middle field	1 (8)	5 (23)	0.268
	lower field	3 (25)	11 (52)	0.126
Left lung	**upper field**	2 (17)	2 (9)	0.545
	middle field	1 (8)	2 (9)	0.909
	lower field	5 (42)	6 (28)	0.443
Number of Consolidation in each fields (%)				
Right lung	**upper field**	4 (33)	1 (4)	**<0.05**
	middle field	5 (42)	0 (0)	**<0.05**
	lower field	4 (33)	1 (4)	**<0.05**
Left lung	**upper field**	2 (17)	0 (0)	0.054
	middle field	4 (33)	0 (0)	**<0.05**
	lower field	4 (33)	2 (9)	0.088

Comparison of six-point semiquantitative score between patients who required oxygen during their clinical courses (group C) and patients who did not (group D) with abnormal chest X-ray findings.
Continuous variables were expressed as mean standard deviation (SD). Groups were compared using the Mann Whitney U-test or chi-squared tests. p value <0.05 was considered statistically significant.
GGA: ground glass attenuation

Table 4. Patients in Need of Oxygen Administration during Hospitalization.

	No. (%)		
	Group A (n=33)	Group B (n=26)	p value
Oxygen (+)	12 (36)	1 (3)	<0.05
Oxygen (-)	21 (64)	25 (97)	

Groups were compared using chi-squared tests. p<0.05 was considered statistically significant.

dence of a fever (>37.5 °C), levels of LDH and CRP, and leukocyte and lymphocyte counts have been reported as risk factors (3-5). These factors are consistent with those in previous reports.

Our results imply that the GGA score at the initial chest radiographic examination has a limited effect on the need for oxygen administration. In contrast, the consolidation score was significantly associated with the presence or absence of oxygen administration. Specifically, our study suggests that there may be a risk of aggravation if chest radiographs show consolidation in two or more lung fields. Patients diagnosed with COVID-19 may be less likely to progress to a severe disease state if their initial chest radiograph findings are normal or show only GGA. The typical CT finding in COVID-19 is patchy GGA in the peripheral area, and when it deteriorates, consolidations are found and increase in number (10, 11). Consolidations are easily detectable, unlike GGA, on chest radiographs, even for doctors who are not familiar with chest radiography. In other words, patients at potential risk for deterioration may have chest radiographs that show easily identifiable abnormalities compared to those in mild cases. Chest radiography is simpler to administer and has a lower radiation exposure than CT. Furthermore, primary care physicians can perform radiography easily at clinics, unlike CT (12).

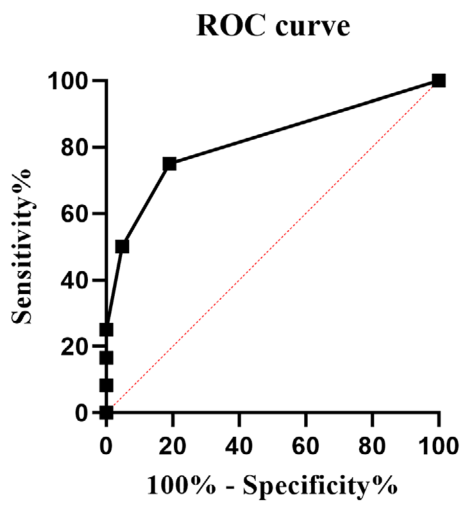

Figure 3. The ROC curve corresponding to the consolidation score to predict disease severity based on chest radiography. A two-sided p value of less than 0.05 was considered statistically significant. The vertical axis represents sensitivity, and the horizontal axis represents specificity. When chest radiographs showed consolidation in more than 2 lung field, the sensitivity and specificity were 50% [95% confidence interval (CI), 25.4-74.6%] and 95% (95% CI, 77.3-99.7%), respectively. The positive likelihood ratio of severity was 10.6.

Several limitations associated with the present study war-

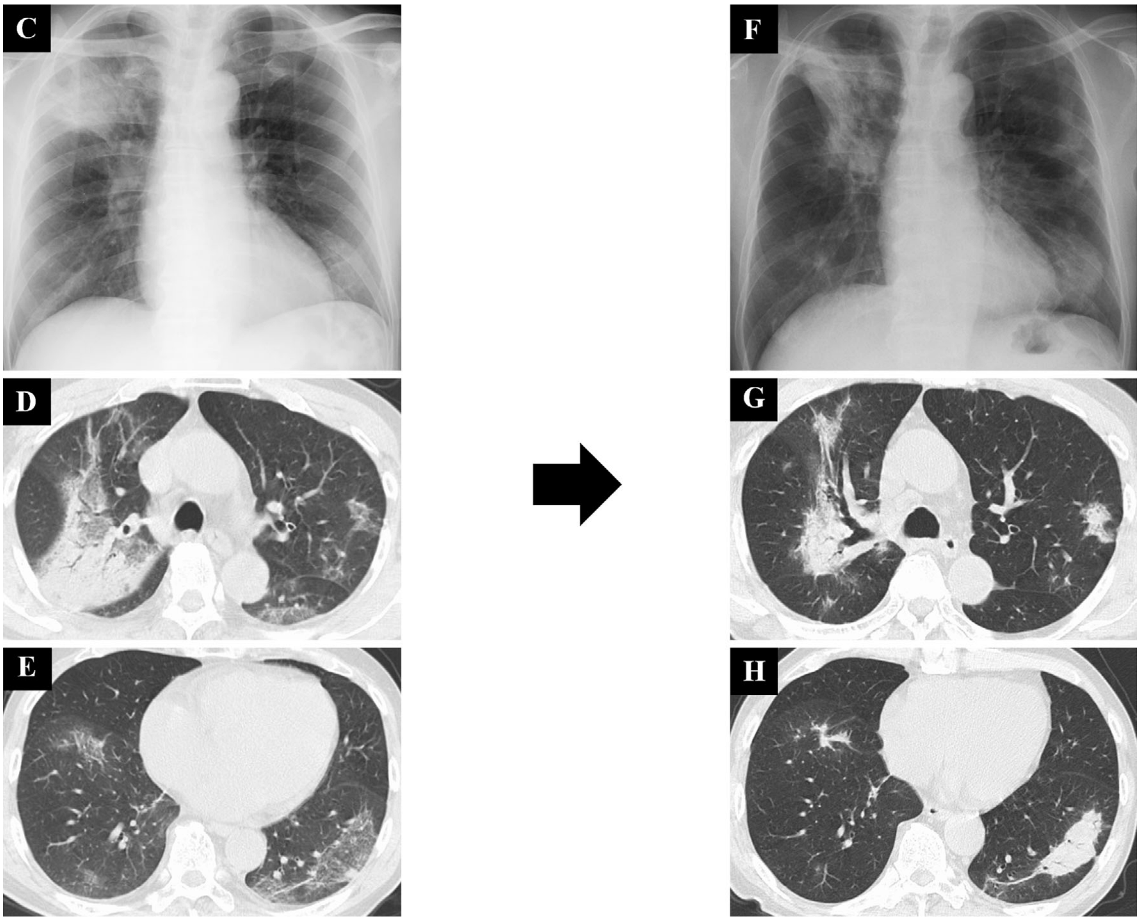

Figure 4. **A 76-year-old man with symptoms of a fever, cough, and sore throat. A chest radiograph at 10 days from the onset showed GGA and consolidation in the right upper and middle fields (C). Chest computed tomography at seven days from onset showed consolidation and GGA with an air bronchogram in the right upper lobe and the left lower lobe (D, E). Both the GGA and consolidation scores in this case were two. This patient required oxygen with a maximum 2-L cannula during hospitalization. At 17 days from the onset, the consolidation and GGA improved with lung volume loss (F-H).**

rant mention. First, this was a retrospective review, and the number of patients analyzed was small. Second, the enrolled patients were mostly elderly people, and the data of young people are not shown. However, given the evidence that being elderly is an important risk factor of disease progression, the disproportional age distribution in the sample may be acceptable. Third, we were unable to strictly distinguish similar respiratory diseases, such as interstitial lung diseases, microbial superinvasion with influenza, mycoplasma, and other types of bacterial pneumonia, from COVID-19. Some of the patients with a positive polymerase chain reaction (PCR) test and an abnormal chest radiograph may not have had true lung lesions due to COVID-19. Finally, the radiographic results may not reflect the exact clinical status of patients due to variations in the timing of chest radiography in each patient. It is important to avoid overlooking the timing of aggravation by comprehensively considering risk factors for aggravation, such as underlying diseases, other than chest radiographic findings.

Conclusion

Chest radiography can be an easy-to-use primary care triage tool for COVID-19 patients, which can lead to the appropriate consumption of medical resources and may prevent medical disruption. We hope that our results will be of use to all healthcare providers who are currently struggling around the world with the management of COVID-19.

The authors state that they have no Conflict of Interest (COI).

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