ORIGINAL ARTICLE

Diagnostic Performance of Computed Tomography Imaging for COVID-19 in a Region with Low Disease Prevalence

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Coronavirus disease 2019 (COVID-19) was first reported in Wuhan, China, in December 2019 as an outbreak of pneumonia of unknown origin. Previous studies have suggested the utility of chest computed tomography (CT) in the diagnosis of COVID-19 because of its high sensitivity (93%–97%), relatively simple procedure, and rapid test results. This study, performed in Japan early in the epidemic when COVID-19 prevalence was low, evaluated the diagnostic accuracy of chest CT in a population presenting with lung diseases having CT findings similar to those of COVID-19. We retrospectively included all consecutive patients (≥18 years old) presenting to the outpatient department of Keio University Hospital between March 1 and May 31, 2020, with fever and respiratory symptoms. We evaluated the performance of diagnostic CT for COVID-19 by using polymerase chain reaction (PCR) results as the reference standard. We determined the numbers of false-positive (FP) results and assessed the clinical utility using decision curve analysis. Of the 175 patients, 22 were PCR-positive. CT had a sensitivity of 68% and a specificity of 57%. Patients with FP results on CT diagnosis were mainly diagnosed with diseases mimicking COVID-19, e.g., interstitial lung disease. Decision curve analysis indicated that the clinical utility of CT imaging was limited. The diagnostic performance of CT for COVID-19 was inadequate in an area with low COVID-19 prevalence and a high prevalence of other lung diseases with chest CT findings similar to those of COVID-19. Considering this insufficient diagnostic performance, CT findings should be evaluated in the context of additional medical information to diagnose COVID-19. (DOI: 10.2302/kjm.2021-0012-OA)

Keywords: COVID-19, chest computed tomography, polymerase chain reaction, lung disease

Introduction

Coronavirus disease 2019 (COVID-19) was first reported in Wuhan, China, as an outbreak of pneumonia during December 2019.¹ The infection then spread rapidly from China to other countries around the world and resulted in many deaths.^{2,3} The management of highly contagious diseases mandates that suspected cases should be promptly confirmed and that infected patients should be

isolated and treated without delay; consequently, the development of adequate diagnostic methods is essential.

Although the polymerase chain reaction (PCR) method is used as the reference standard for the diagnosis of COVID-19, PCR usually takes several hours to produce results and requires specialized equipment and trained personnel. In contrast, chest computed tomography (CT) is quick to perform and is routinely used in a wide range of clinical settings. Because COVID-19 is a respiratory

Table 1. Chest CT protocols

CT equipment	Manufacturer	Rows	Tube voltage (kV)	Rotation time (s)	Pitch factor
Discovery 750 HD	GE Healthcare	64	120	0.4	0.984
Revolution	GE Healthcare	256	120	0.5	0.984
Aquilion One	Canon Medical Systems	320	120	0.5	0.813
Aquilion 64	Canon Medical Systems	64	120	0.5	0.844
Revolution Evo	GE Healthcare	64	120	0.5	1.375

Chest computed tomography (CT) images in our hospital were obtained with one of five CT systems: Discovery 750 HD (GE Healthcare, Chicago, IL, USA), Revolution (GE Healthcare), Revolution Evo (GE Healthcare), Aquilion One (CANON Medical Systems, Otawara, Japan), and Aquilion 64 (CANON Medical Systems). Patients were scanned in the supine position at the end of inhalation. The main scanning parameters were as follows: tube voltage, 120 kVp; rotation speed, 0.4 or 0.5 s; and tube current, auto-exposure control.

disease, it should be discernable on CT images. Indeed, previous studies have suggested that chest CT scans can be used as an alternative diagnostic tool for COVID-19 due to its high sensitivity (93%–97%), relatively simple procedure, and rapid results.^{4–6} However, most previous studies were conducted in regions with a high prevalence of COVID-19.^{4–6} Relatively few studies have been conducted in low-prevalence areas, such as Japan in Spring 2020. The peak number of new confirmed COVID-19 cases per million people between March 1 and May 31, 2020, was 4.2 in Japan; in contrast, there were 96.85, 93.6, 71.37, and 69.56 cases per million, respectively, in the United States, Italy, the United Kingdom, and Germany. Therefore, the prevalence of COVID-19 in Japan at that time was low compared to the United States and selected high-prevalence European countries.⁷

The typical CT features of COVID-19 mimic those of viral pneumonia and interstitial lung disease (ILD).⁸ Working at a university hospital, where we encounter many patients with lung diseases that mimic COVID-19, we doubted that CT findings were adequate to discriminate COVID-19 from other lung diseases. However, few studies have assessed the diagnostic accuracy of CT in hospitals with a patient spectrum different from those previously reported. Moreover, the final diagnoses of patients with initial false-positive (FP) COVID-19 diagnoses based on CT findings have been rarely documented. Consequently, studies filling these knowledge gaps are required.

This study aimed to evaluate the diagnostic accuracy of chest CT for COVID-19 in a hospital with numerous patients presenting lung disease findings on chest CT (many of which findings were similar to those associated with COVID-19) in a region with a relatively low prevalence of COVID-19 very early in the epidemic in Japan.

Methods

Study design and setting

To investigate the diagnostic accuracy of CT findings

for COVID-19, we conducted the current single-center, retrospective, observational study based on the methodology described by the Standards for Reporting of Diagnostic Accuracy Studies 2015 guidelines.⁹ The study was performed at Keio University Hospital, a 960-bed tertiary care center in an urban area of the Western Health Care District of Tokyo, Japan, with a population of 1.2 million. This study was approved by the Ethics Committee of Keio University School of Medicine (ID: 20200063), which waived the need for written informed consent based on the Ethical Guidelines for Medical and Health Research Involving Human Subjects in Japan. The study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Patients

This study included all consecutive patients aged 18 years or older who presented to the outpatient department of Keio University Hospital between March 1 and May 31, 2020, with new symptoms of fever, cough, sputum production, hemoptysis, or shortness of breath. The study period was defined based on the first wave of the COVID-19 epidemic in Japan, considering that the end of the state of emergency that was imposed because of the novel coronavirus disease occurred on May 25, 2020.¹⁰ During the study period, all patients with the symptoms mentioned above were isolated in the febrile outpatient room or in a private room of the COVID-19 inpatient ward. A physician using protective equipment took a specimen from each patients' nasopharynx, and the specimens were tested using PCR according to hospital's infection control policy. Moreover, based on the protocol in our hospital, all patients underwent CT imaging. **Table 1** details the chest CT protocols utilized. In principle, all patients suspected of having COVID-19 were admitted to the hospital. Even if the first PCR test results were negative, patients with CT images indicating pneumonia underwent a second PCR test after an interval of at least 3 days. Patients who did not undergo valid PCR tests within

Table 2. Chest CT classification system for COVID-19 pneumonia according to the Radiological Society of North America⁸

COVID-19 pneumonia imaging classification	Rationale	CT findings
Typical appearance	Commonly reported imaging features of greater specificity for COVID-19 pneumonia	Peripheral, bilateral GGO with or without consolidation or visible intralobular lines (“crazy-paving”) Multifocal GGO or rounded morphology with or without consolidation or visible intralobular lines (“crazy-paving”) Reverse halo sign or other findings of organizing pneumonia (observed later in the disease)
Indeterminate appearance	Nonspecific imaging features of COVID-19 pneumonia	Absence of typical features and presence of multifocal, diffuse, perihilar, or unilateral GGOs with or without consolidation lacking a specific distribution that are non-rounded or non-peripheral Few, very small GGOs with non-rounded and non-peripheral distribution
Atypical appearance	Uncommonly or not reported features of COVID-19 pneumonia	Absence of typical or indeterminate features and presence of isolated lobar or segmental consolidation without GGO Discrete small nodules (centrilobular, “tree-in-bud”)
Negative for pneumonia GGO, ground-glass opacity	No features of pneumonia	No CT features suggestive of pneumonia

5 days before or after the chest CT, patients without CT scan results, and patients with positive PCR results who had been treated before hospital admission were excluded from the study.

Data collection

The following patient data were obtained from medical records or the COVID-19 database: age, sex, interval between CT and PCR, clinical symptoms, pulmonary comorbidities, CT findings, PCR test results, final diagnosis, and disease severity (intensive/high care unit entry, use of invasive mechanical ventilation, and survival status). Missing data were noted as “unknown.”

CT image analysis

One respiratory physician (H.L.) and one radiologist (T.S.), who were blinded to the clinical information, independently evaluated the CT images. If their assessments differed, they discussed the case and decided by agreement. If there was still no consensus, another senior respiratory physician (M.I.) made the final evaluation. The CT images were grouped into four categories according to the chest CT classification system for reporting COVID-19 of the Radiological Society of North America: typical, indeterminate, atypical, and negative.⁸ The details of this classification system are described in **Table 2**. CT findings were defined as positive for typical or indeterminate images and negative for images atypical or negative for pneumonia.

PCR

Patients were tested for the SARS-CoV-2 virus using the BD MAX (Becton Dickinson, Franklin Lakes, NJ, USA) system. Real-time reverse transcription PCR was performed using BD MAX ExK TNA and BD MAX TNA MMK SPC. Tests were defined as positive according to the latest standard operating procedures established by the Japanese Society for Clinical Microbiology.¹¹

Analysis

Using PCR results as the reference standard, we evaluated the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (PLR), and negative likelihood ratio (NLR) of CT for the diagnosis of COVID-19 with 95% confidence intervals (95% CIs). A sensitivity analysis was performed to examine the impact on diagnostic performance of changing the cutoff for the assessment of CT findings (i.e., positive: typical; negative: indeterminate, atypical, or negative for pneumonia). We also performed subgroup analyses for the following patient groups in a post-hoc analysis to explore the impact of heterogeneity of the patient population on the diagnostic test performance: pre-existing lung diseases (i.e., diseases with CT findings similar to those of COVID-19), age (>60 years vs. <60 years), and symptoms (fever and respiratory symptoms). Forest plots of sensitivity, specificity, and 95% CIs of each result were generated to visually evaluate the heterogeneity of diagnostic performance. Additionally, we

evaluated the usefulness of CT using decision curve analysis (DCA), which evaluated the clinical usefulness (net benefit) of CT for the diagnosis of COVID-19.¹²

Net-benefit and DCA

DCA is a method that helps clinical staff to decide whether to perform a test by evaluating its clinical usefulness.^{12,13} The x-axis of the graph is defined as the threshold probability, and the y-axis as the net benefit. The threshold probability represents the relative value of receiving treatment in the presence of a disease or avoiding treatment in its absence. This value varies according to disease and setting.¹ The net benefit represents the difference between the benefit gained by identifying true-positive (TP) patients and the loss or harm caused by identifying FP patients undergoing testing or treatment. Specifically, the formula for the DCA is as follows¹⁴:

$$\text{Net benefit} = \text{TP}/n - (\text{Pt}/\{1-\text{Pt}\})\text{FP}/n$$

where Pt is the threshold probability.

For example, if $\text{Pt} = 0.2$, $(\text{Pt}/\{1-\text{Pt}\}) = 0.2/(1 - 0.2) = 1/4$, FP is equivalent to 1 TP. In other words, if 20% of patients are TP (4 FP and 1 TP), all positive patients should be treated. In this study, the usefulness of CT imaging in the diagnosis of COVID-19 was evaluated by DCA.

Statistics

Statistical analysis was performed using Easy R version 1.51¹⁵ and Review Manager version 5.4.1. The alpha error was set at 5%. To assess the patient background, the median and interquartile range were presented for continuous variables, and numbers and percentages for categorical variables. The influence of the patient background was examined by assessing the entire patient population or subgrouping by PCR result.

Results

Patient characteristics and CT results

Of the 218 patients who met the inclusion criteria, we excluded 32 patients who did not undergo chest CT and 11 patients who did not undergo PCR within 5 days before or after the chest CT. As a result, 175 patients were included in the analysis (**Fig. 1**). The characteristics of the patients and their CT results are shown in **Table 3**. The median age was 71 years (range, 20–96 years). There were 22 (12.6%) PCR-positive patients; all repeat PCR tests were negative in patients with an initially negative PCR who had CT findings of pneumonia. Fever was the most common symptom (136/175 patients, 78%), and all PCR-positive patients had a fever (22/22 patients, 100%). The median

time between PCR and chest CT was 1 day (range, 0–5 days). Forty-four patients had a history of ILD. Patients admitted to the intensive/high care unit accounted for 9% (16/175) of all patients and 18% (4/22) of PCR-positive patients. CT findings were evaluated in 23% (41/175) as typical, in 23% (40/175) as indeterminate, in 10% (17/175) as atypical, and in 44% (77/175) as negative for pneumonia. **Figure 2** shows examples of CT findings corresponding to each of these groups. Among PCR-positive patients, most were classified as typical (64%, 14/22). CT shadows consisted mainly of ground-glass opacities (GGOs) and consolidation, which were observed in 46% (81/175) and 31% (54/175) of all patients, respectively.

Diagnostic performance of chest CT

Using the PCR results as the reference standard, the diagnostic performance of chest CT was as follows: sensitivity, 68% (95% CI: 45–86); specificity, 57% (95% CI: 49–65); PPV, 19% (95% CI: 11–29); NPV, 93% (95% CI: 85–97); PLR, 1.58 (95% CI: 1.13–2.22); and NLR, 0.56 (95% CI: 0.30–1.05) (**Table 4**). Bacterial pneumonia was the most common final diagnosis among FP patients (32%, 21/66), followed by ILD (30%, 20/66), and all final diagnoses were diseases that could present with GGO on CT (**Table 5**). The sensitivity analysis revealed a nearly unchanged sensitivity of 64% (95% CI: 41–83) and an increase in specificity to 82% (95% CI: 0.41–0.83) if the cutoff value was changed to: positive – typical; negative – indeterminate, atypical, or negative for pneumonia.

The results of the subgroup analyses are shown in **Fig. 3**. The sensitivity values did not differ significantly among conditions, but there was a difference in specificity between patients with and without a history of diseases presenting with GGO on CT. The specificity was higher in the group that excluded patients with diseases characterized by GGO.

DCA

Figure 4 demonstrates the decision curve for the value of chest CT in the diagnosis of COVID-19. The blue curve shows the net benefit of CT imaging for the diagnosis of COVID-19. The orange line shows the net benefit when all patients are considered positive and PCR is performed regardless of the CT results, and the red line shows the net benefit when all patients are considered negative regardless of the results of CT imaging for the diagnosis of COVID-19. As a result, chest CT was determined to be useful for threshold probabilities in the range 0.07–0.19.

Discussion

In this single-center, retrospective study, we determined the diagnostic accuracy of CT for COVID-19 diagnosis in

Fig. 1 Flowchart describing patient selection.

All consecutive patients aged 18 years or older who presented to the outpatient department at Keio University hospital between March 1 and May 31, 2020, with new fever or respiratory symptoms (cough, sputum production, hemoptysis, or shortness of breath) were included. After the exclusion of 43 patients, 175 patients who underwent a valid polymerase chain reaction (PCR) test within 5 days before or after chest computed tomography (CT) were enrolled in this study.

a university hospital with a population presenting various lung diseases that may lead to FP COVID-19 diagnoses based on CT findings. Using PCR as the reference standard, the sensitivity and specificity of CT were 68% (95% CI: 45–86) and 57% (95% CI: 49–65), respectively. According to these results, it would be inappropriate to use CT imaging alone for the diagnosis of COVID-19.

This study has several strengths compared to previous studies. First, unlike previous studies, it was conducted in a setting that included many patients with comorbidities of respiratory disease. To the best of our knowledge, no previous cohort study has explicitly included patients with respiratory diseases mimicking the CT findings of COVID-19 pneumonia. If patients with these diseases were not included, specificity would be overestimated; however, few studies have considered this point. In contrast, this study was performed in a setting where many patients had respiratory diseases, such as ILD, with imaging findings similar to those of COVID-19. Furthermore, this study also indicated that these patient characteristics resulted in FP results. Compared with previous studies, these findings may provide new and meaningful information for clinicians.

Second, this study focused on a geographic region in which the epidemic was relatively mild compared to the regions examined in previous studies. Previous studies

have mainly been conducted in highly endemic regions such as China and Italy.^{4,16–18} Both of these countries had a large number of infected people at the time of the studies, and the clinical application of the study findings to areas with low COVID-19 incidence was unclear. In contrast, the current study focused on an area where the incidence of COVID-19 was relatively low compared to the abovementioned countries. The generalizability of the current results is expected to be high in countries such as Japan, South Korea, Australia, and Taiwan, where the impact of the epidemic has been relatively mild.⁶

Third, our study results may be more reliable than previous study findings. In previous studies, CT has shown high sensitivity for COVID-19; however, the majority of the literature covered in a Cochrane review (71/84 studies) were case–control studies (two-gate type) in patients who had already been diagnosed.⁵ Case–control diagnostic accuracy studies (two-gate type) are known to have a high risk of bias and often do not allow for accurate assessment.¹⁹ Moreover, although some studies did not follow the case–control approach, their patient populations were not clearly defined. Therefore, the validity of the results was limited.^{4,20} In contrast, our study design was a cohort type (single-gate), and the target population, as well as the criteria for CT imaging, were clearly defined. Therefore, the results of the current study may be more

Table 3. Patient characteristics and CT results

	All patients n =175	PCR negative n =153	PCR positive n =22
Median age, years	71 (56,79)	73 (58,79)	58 (42,70)
	Range 20–96		
Sex			
Male	97 (55%)	84 (55%)	13 (59%)
Female	78 (45%)	69 (45%)	9 (41%)
Symptom			
Fever	136 (78%)	114 (75%)	22 (100%)
Cough	38 (22%)	29 (19%)	9 (41%)
Sputum/hemoptysis	19 (11%)	18 (12%)	1 (5%)
Shortness of breath	60 (34%)	55 (36%)	5 (23%)
Median time between chest CT scan and RT-PCR assay (days)	1 (1,2)	1 (1,2)	1 (0,1)
	Range 0–5		
Underlying respiratory disease			
Diseases with CT findings similar to those of COVID-19	52 (30%)	50 (33%)	2 (9%)
Interstitial lung disease	44 (25%)	43 (28%)	1 (5%)
Pulmonary veno-occlusive disease	1 (1%)	1 (1%)	0 (0%)
Heart failure with ground-glass opacities	1 (1%)	1 (1%)	0 (0%)
Lymphangitic carcinomatosis	1 (1%)	1 (1%)	0 (0%)
Unknown ground-glass opacities	5 (3%)	4 (3%)	1 (5%)
Chronic obstructive pulmonary disease	25 (14%)	23 (15%)	2 (9%)
Cancer (lung cancer, lung metastasis)	9 (5%)	8 (5%)	1 (5%)
After lobectomy	5 (3%)	5 (3%)	0 (0%)
Non-tuberculous mycobacteria	4 (2%)	4 (3%)	0 (0%)
Aspergillosis	2 (1%)	2 (1%)	0 (0%)
Bronchiectasis	2 (1%)	2 (1%)	0 (0%)
Sinobronchial syndrome	1 (1%)	1 (1%)	0 (0%)
Severity			
Intensive/high care unit entry	16 (9%)	12 (7%)	4 (18%)
Invasive mechanical ventilation	6 (3%)	3 (2%)	3 (14%)
Death	11 (6%)	9 (6%)	2 (9%)
CT imaging classification			
Typical	41 (23%)	27 (18%)	14 (64%)
Indeterminate	40 (23%)	39 (25%)	1 (4%)
Atypical	17 (10%)	17 (11%)	0 (0%)
Negative for pneumonia	77 (44%)	70 (46%)	7 (32%)
CT features			
Ground-glass opacities	81 (46%)	66 (43%)	15 (68%)
Consolidation	54 (31%)	47 (31%)	7 (32%)
Reticulation/thickened interlobular septa	37 (21%)	33 (22%)	4 (18%)
Nodules/tree-in-bud opacities	9 (11%)	19 (12%)	0 (0%)
Pleural effusion	34 (19%)	29 (19%)	5 (23%)
Number of affected lobes			
0	71 (41%)	64 (42%)	7 (32%)
1	16 (9%)	15 (10%)	1 (5%)
2	24 (14%)	22 (14%)	2 (9%)
3	13 (7%)	11 (7%)	2 (9%)
4	15 (9%)	14 (9%)	1 (5%)
5	36 (20%)	27 (18%)	9 (41%)

Data are presented as the median (interquartile range) or n (%).

Fig. 2 Representative CT imaging classification.

CT images of 175 patients were classified into four groups: typical, intermediate, atypical, and negative.⁸ Examples of axial unenhanced thin-section CT images for each group are shown. (A) Typical: multifocal, peripheral, bilateral, and rounded ground-glass opacities. (B) Indeterminate: multifocal, unilateral, and non-rounded ground-glass opacities. (C) Atypical: segmental consolidation without ground-glass opacities. (D) Negative: no CT features to suggest pneumonia.

reliable and applicable than those of previous studies.

We discussed potential reasons for the inadequacy of CT performance for COVID-19 diagnosis. Regarding the low sensitivity, about one-third of the PCR-positive patients had no pneumonia imaging findings at the time that CT was performed. This may be because the study was conducted in an area with low COVID-19 prevalence compared to other regions, and abnormal findings on chest CT may not be observed in mild cases.²¹ Regarding the low specificity, the high prevalence of respiratory diseases with COVID-19-like imaging findings may have decreased the specificity of CT. Our subgroup analysis suggested that there may be heterogeneity in specificity depending on the presence or absence of diseases with imaging findings reminiscent of COVID-19. This suggests that, compared to the general population, many patients with respiratory diseases that present CT findings similar to those for COVID-19 tend to be misdiagnosed as FPs. Based on these findings, we suggest that CT imag-

ing should be carefully interpreted in patient populations frequently presenting with the aforementioned diseases. Many factors may reduce the diagnostic sensitivity and specificity of CT, including the frequency of pre-existing lung disease, the severity of COVID-19, the interval between the onset of disease and the CT scan, and the presence of asymptomatic cases.

We also discussed the interpretation of the DCA results, which suggested that using CT imaging may be beneficial if hospital policy can accept one FP in 5–13 TP patients. However, this policy may not be acceptable in the current social situation. Therefore, a diagnosis based on CT imaging alone may not be indicated under the current circumstances.

We offer some recommendations for the clinical application of the current results. Our findings indicate that CT has low sensitivity and poor NLR for COVID-19 diagnosis, limiting its use as the sole screening test before PCR testing. Furthermore, there are disadvantages to screen-

Table 4. Diagnostic performance of chest CT for COVID-19 diagnosis

Results	CT findings†	PCR findings		
		Positive	Negative	Total
	Positive	15	66	81
	Negative	7	87	94
	Total	22	153	175
CT diagnostic performance‡				
	Sensitivity	68% (45–86%)		
	Specificity	57% (49–65%)		
	PPV	19% (11–29%)		
	NPV	93% (85–97%)		
	PLR	1.58 (1.13–2.22)		
	NLR	0.56 (0.30–1.05)		

†Data represent patient numbers. Chest CT findings were classified into four groups⁷: typical, indeterminate, atypical, and negative. Typical or indeterminate findings were considered COVID-19 positive, and atypical or negative findings were considered COVID-19 negative.

‡Test performances are given as percentages and 95% CIs.

NLR, negative likelihood ratio; NPV, negative predictive value; PLR, positive likelihood ratio; PPV, positive predictive value.

Table 5. Final diagnosis of the 66 false-positive CT-diagnosed COVID-19 cases

Diagnosis	n
Pneumonia	21
Interstitial lung disease	20
Congestive heart failure	6
Pneumocystis pneumonia	2
Chronic hypersensitivity pneumonitis	2
Atypical pneumonia	2
Viral pneumonia	1
Lymphangitic carcinomatosis	1
Hemoptysis	1
Human T lymphotropic virus 1 infection associated with bronchioloalveolar disorder	1
Unknown	9

Data represent patient numbers.

ing with CT, such as the problem of spreading the infection in the radiology department, unnecessary exposure of patients to X-rays, and cost. Considering these factors, we do not recommend a hospital policy of performing CT as screening for all patients, as per the recommendation of the American College of Radiology.²² Furthermore, based on the specificity and PLR results, CT may have limited use as a PCR substitute to confirm a diagnosis of COVID-19. Therefore, it is considered inappropriate to determine the necessity of infection control measures (e.g., the cessation of patient isolation and the use of personal protective equipment by medical personnel) based on CT results alone because of the likelihood of false-negative results. However, we do not argue against the use of CT. This imaging modality provides valuable diagnostic information and enables us to exclude other similar respiratory diseases. We believe that CT imaging

findings should be considered as one piece of information contributing to a comprehensive diagnosis based on the current history, physical examination, and other tests.

This study has the following limitations. First, there could be bias in patient selection. During the study period, the hospital sometimes performed telephone triage to decrease the number of face-to-face consultations if the patient was in a stable condition. Therefore, some patients with new minor symptoms were triaged by telephone interview and might not have been included in this study. In contrast, patients with respiratory comorbidities might have been advised to go to the hospital when their symptoms reappeared. There might have been a tendency for this population to be treated as suspected COVID-19 cases and PCR tests might have been performed more often. Furthermore, pediatric patients were not included in the study. Second, the number of patients who participat-

Fig. 3 Forest plot of subgroup analysis.

Subgroup analysis was performed for the sensitivity and specificity of CT for COVID-19 diagnosis in each of the following patient groups: those with or without pre-existing lung diseases (i.e., diseases with CT findings similar to those in COVID-19 presented in **Table 3**), those over or under 60 years old, and those with fever or respiratory symptoms (cough, sputum production, hemoptysis, or shortness of breath). FN, false negative; FP, false positive; TN, true negative; TP, true positive.

Fig. 4 Decision curve analysis for the clinical usefulness of CT for COVID-19 diagnosis.

Decision curves for the value of diagnosing COVID-19 using chest CT. The blue line represents the net benefit of chest CT in the diagnosis of COVID-19. The orange line is the net benefit when all patients are considered positive, and a PCR test is performed regardless of the CT results. The red line is the net benefit if all patients are considered negative regardless of the CT results.

ed in this study was relatively small. However, because we have discontinued routine CT imaging of all patients with suspected COVID-19, there will be no further cases to add to the analysis. Third, the use of PCR as the reference includes some risk of bias because the sensitivity

of PCR is not 100%, as has been confirmed in various previous reports.^{4,6,18,23} Furthermore, there may be a risk of false-negative COVID-19 diagnoses by PCR. Fourth, the applicability of the current results to other settings is unclear. Therefore, further research is needed to address these limitations.

Collectively, the results of this study demonstrated that the accuracy of chest CT for COVID-19 diagnosis was inadequate in an area with low COVID-19 prevalence and a high prevalence of diseases with CT findings similar to those of COVID-19. CT imaging should be evaluated comprehensively in each clinical setting along with other medical information to determine a diagnosis of COVID-19, and the diagnostic performance of CT imaging should be taken into consideration.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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