Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Available online at www.sciencedirect.com

Respiratory Investigation

journal homepage: www.elsevier.com/locate/resinv

Original article

Clinical significance of chest CT for the exclusion of COVID-19 in pre-admission screening: Is it worthwhile using chest CT with reverse-transcription polymerase chain reaction test?

Kazuhiko Morikawa [a,*], *Shigeki Misumi* [a], *Takao Igarashi* [a], *Ayako Fujimori* [a], *Akira Ogihara* [a], *Ryo Akao* [a], *Jun Hasumi* [a], *Takashi Watanabe* [a], *Yuriko Fujii* [a], *Hiroya Ojiri* [a], *Shohei Mori* [b]

[a] *Department of Radiology, The Jikei University School of Medicine, Tokyo, Japan*
[b] *Division of Thoracic Surgery, Department of Surgery, The Jikei University School of Medicine, Tokyo, Japan*

ARTICLE INFO

Article history:
Received 1 February 2022
Received in revised form
4 April 2022
Accepted 19 April 2022
Available online 8 May 2022

Keywords:
Severe acute respiratory syndrome coronavirus-2
COVID-19
Chest computed tomography screening
Asymptomatic patient

ABSTRACT

Background: A single reverse-transcription polymerase chain reaction (RT-PCR) test is not sufficient to exclude COVID-19 in hospital pre-admission screening. However, repeated RT-PCR tests are time-consuming. This study investigates the utility of chest computed tomography (CT) for COVID-19 screening in asymptomatic patients.

Methods: Between April 2020 and March 2021, RT-PCR testing and chest CT were performed to screen COVID-19 in 10 823 asymptomatic patients prior to admission. Chest CT findings were retrospectively evaluated using the reporting system of the Radiological Society of North America. Using RT-PCR results as a reference, we assessed the diagnostic efficacy of chest CT during both the low- and high-prevalence periods of the COVID-19 pandemic.

Results: Following a positive RT-PCR test, 20 asymptomatic patients (0.18%) were diagnosed with COVID-19; in the low-prevalence period, 5 of 6556 patients (0.076%) were positive; and in the high-prevalence period, 15 of 4267 patients (0.35%) were positive. Of the 20 asymptomatic COVID-19 positive patients, chest CT results were positive for COVID-19 pneumonia in 8 patients. Chest CT results were false-positive in 185 patients (1.7% false-positive rate, and 60% false-negative rate). Pneumonia that was classified as a "typical appearance" of COVID-19 reported as false-positives in 36 of 39 patients (92.3%). Across the study period, the diagnostic efficacy of "typical appearance" on chest CT were characterized by a sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) of 15%, 99.7%, 99.7%, 7.7%, and 99.8%; 20%, 99.6%, 99.6%, 4%, and

Abbreviations: CKD, Chronic kidney disease; CT, Computed tomography; GGO, Ground-glass opacity; ICI, Immune checkpoint inhibitor; IP, Interstitial pneumonia; LC, Liver cirrhosis; LR+, Positive likelihood ratio; LR−, negative likelihood ratio; MTX, Methotrexate; NPV, Negative predictive value; NTM, Non-tuberculosis mycobacteria; PACS, Picture archiving and communication system; PPV, Positive predictive value; RSNA, Radiological Society of North America; RT-PCR, Reverse transcription polymerase chain reaction; VOC, Variant of concern; WHO, World Health Organization.

* Corresponding author. Department of Radiology, The Jikei University School of Medicine, 3-25-8, Nishi-Shimbashi, Minato-ku, Tokyo 105-8461, Japan.
E-mail address: k.morikawa@jikei.ac.jp (K. Morikawa).

https://doi.org/10.1016/j.resinv.2022.04.007

99.9%; and 13.3%, 99.7%, 99.7%, 14.3%, and 99.7%, in the entire study, low-, and high-prevalence periods, respectively.
Conclusions: Addition of chest CT to RT-PCR testing provides no benefit to the detection of COVID-19 in asymptomatic patients.

1. Introduction

On March 12, 2020, the World Health Organization declared a pandemic of a new coronavirus that had not been previously observed in humans, known as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), which causes COVID-19 [1]. The first wave of the COVID-19 pandemic in Japan was confirmed in February 2020, the fourth wave was confirmed in early 2021, and the fifth was confirmed in July 2021 [2].

The diagnosis of COVID-19 is confirmed through a positive reverse-transcription polymerase chain reaction (RT-PCR) test. However, this test has several shortcomings including limited availability, a long turnaround time, and an imperfect diagnostic performance, with a sensitivity of 89% and positive predictive value (PPV) of 95.4–99.8% according to a pooled meta-analysis [3,4]. The Radiological Society of North America (RSNA) introduced standardized COVID-19 reporting language [5], which led to publication of the COVID-19 Reporting and Data System (CO-RADS) [6]. Studies have demonstrated the significant diagnostic performance of these tools in terms of detecting COVID-19 pneumonia. Several studies suggested that the commonly used chest computed tomography (CT) evaluation methods proposed by the RSNA and CO-RADS could provide a faster triage of patients, and that the methods are highly predictive of RT-PCR results [7–9]. The high diagnostic performance of chest CT, which is not necessarily inferior to that of RT-PCR, may be important for COVID-19 diagnosis. Chest CT might complement RT-PCR testing.

However, the incidence of normal chest CT findings in asymptomatic patients with COVID-19 is considerably high (estimated 46%) [10], and chest CT findings are often normal in the early stage of the disease (i.e., the first 4–5 days after the onset of symptoms), even in symptomatic cases (13.9–33.3%) [3,11]. Based on these factors, chest CT is currently not recommended as a routine screening tool for COVID-19, especially in asymptomatic patients [3,12–14].

In a previous research report written in the early stages of the epidemic, the authors described that nearly half of their asymptomatic patients with COVID-19 had abnormal chest CT findings [10]. Therefore, we hypothesized that most asymptomatic patients with COVID-19 pneumonia could be detected using chest CT as a screening test during the high epidemic stage. Considering the sensitivity of the RT-PCR test, a single RT-PCR test could produce a false-negative result even if the patient already presents an abnormal chest CT finding that is highly suggestive of COVID-19 pneumonia. After experiencing domestic nosocomial clusters and COVID-19-related patient deaths in our hospital at the beginning of the epidemic in early 2020, as had other facilities in Japan [15,16], both RT-PCR testing and chest CT have been performed in our hospital to screen all the hospitalized patients, including asymptomatic patients, since the beginning of the epidemic in April 2020. Repeated RT-PCR tests are time-consuming, laborious, and burdensome for the patients. Therefore, we focused on chest CT as a screening tool for COVID-19 pneumonia, performed simultaneously with the RT-PCR test. We hypothesized that the high sensitivity of the chest CT would balance the limitations of the RT-PCR test and that we would be able to screen asymptomatic patients with COVID-19 who clear a single RT-PCR test. To the best of our knowledge, only a few studies had investigated the utility of chest CT as a screening method for the detection of COVID-19 in asymptomatic patients [13,14,17]; however, none have compared the utility of chest CT for COVID-19 screening in asymptomatic patients between the low-prevalence and high-prevalence periods at the same institution. Therefore, the objectives of this study were: (1) to investigate the utility of chest CT as a screening method for the detection of COVID-19 in asymptomatic patients; (2) to investigate whether the diagnostic performance of chest CT in detecting COVID-19 in asymptomatic patients changes according to the prevalence of COVID-19; and (3) to investigate the frequency of incidental chest CT findings that mimic COVID-19 pneumonia.

2. Materials and methods

2.1. Patients

Between April 2020 and March 2021, a total of 9117 scheduled inpatients visited the pre-admission COVID-19 testing center at our institution 1 or 2 days before their scheduled admission. We excluded all patients with symptoms that suggested COVID-19 (fever of 37.1 °C or higher, cough, dyspnea, or other respiratory symptoms that are not explained by the current disease) and all patients who had an apparent history of close contact with a patient with COVID-19, 2 weeks prior to admission (n = 96). After exclusion, 9021 asymptomatic patients who had traveled abroad within the 2 weeks prior to admission were enrolled in this retrospective study (Fig. 1). For all patients, RT-PCR testing and chest CT were performed on the same day at the pre-admission COVID-19 testing center. We then excluded patients without acute pneumonia on chest CT or with unchanged chest CT findings compared to previous

findings (Fig. 1). All of the patients were informed by their attending physicians that asymptomatic COVID-19 patients do exist, that pneumonia could be detected incidentally using chest CT, and that medical radiation exposure from chest CT has minimal impact on the individual. Attending physicians then obtained written informed consent for the RT-PCR screening tests and chest CT from all the patients scheduled for hospitalization. All the patients were exempted from medical fees for the RT-PCR tests and chest CT by hospital assistance. This study was approved by the Institutional Review Board of the Jikei University School of Medicine (approval number 33–333 (10 956); December 13, 2021 approved), and all procedures were in accordance with the ethical standards of the responsible committee on human experimentation and with the 1964 Declaration of Helsinki and later versions. Due to the retrospective nature of the research, we waived the requirement for informed consent.

2.2. *Image acquisition*

Chest CT scans were acquired using a multidetector CT scanner with 80 detector rows (Aquilion PRIME; Canon Medical Systems, Otawara, Japan). Patients were oriented in the supine position, and the entire chest (starting from the lung apices down to the posterior costophrenic sulci) was scanned using the following parameters: 1-mm collimation, 120 kV, and volume exposure control (standard deviation value: 17.0). Images were reconstructed with a slice thickness of 5 mm in the axial plane without an interval gap, where appropriate. No intravenous contrast medium was administered. Each chest CT examination was reviewed using chest images recorded on a picture archiving and communication system (PACS). Diagnostic imaging reports were prepared by radiologists with more than 6 years of experience, and who were blind to the results of the related RT-PCR tests. The presence of new pneumonia findings and the possibility of COVID-19 pneumonia were assessed for all CT images.

2.3. *Imaging evaluation*

Two experienced radiologists reviewed the CT images from eligible patients using a PACS workstation monitor. The two radiologists had 25 and 12 years of experience, respectively, were blind to the RT-PCR test results and associated clinical information, and evaluated the images independently of each other. Any differences in evaluation results were resolved via consensus. In this study, the RSNA reporting system was used for image evaluation because it is easy to understand and apply, and it facilitates communication with physicians in other fields [7]. Chest CT findings were categorized into four patterns: “typical,” “indeterminate,” “atypical,” and “negative” according to the reporting language proposed by the RSNA (Table 1) [5]. CT images that revealed preexisting lung lesions and no change in findings compared to previous images were categorized as “negative.”

We divided the research period into two parts: low-prevalence of COVID-19 (April 2020 to November 2020 with a peak prevalence of 17.41/100 000 people in Tokyo) and high-prevalence of COVID-19 (December 2020 to March 2021 with a peak prevalence of 88.94/100 000 people in Tokyo) [18,19]. The frequency of chest CT findings was evaluated for each period.

2.4. *Statistical analyses*

Using RT-PCR test results as the reference, the diagnostic efficacy of chest CT was evaluated for each prevalence period by calculating the sensitivity, specificity, accuracy, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+), and negative likelihood ratio (LR−). The statistical analysis was performed using SPSS version 25 (IBM Corp., Armonk, NY, USA). Dichotomous variables were analyzed using Fisher's exact test. For all statistical tests, a P-value of <0.05 was considered statistically significant.

3. Results

3.1. *Patient characteristics*

A total of 9021 asymptomatic patients were included in the study, of which 5191 were men and 3830 were women (mean age: 62 years; range: 12–103 years). Of the total patient pool, 5581 patients (3247 men and 2334 women; mean age: 60 years; range: 14–102 years) were included in the low-prevalence period, and 3440 patients (1944 men and 1496 women; mean age: 62 years; range: 12–103 years) were included in the high-prevalence period. A total of 384 patients were admitted several times (range: 2–13 times). RT-PCR testing and chest CT were performed 10 823 times throughout the study period (6556 times in the low-prevalence period and 4267 times in the high-prevalence period). Of the 10 823 tests, 193 (1.8%) unexpected chest CT findings suggesting acute pneumonia (and possible COVID-19) were extracted from the PACS database (Fig. 1). To rule out COVID-19 from these 193 unexpected findings, more than one RT-PCR test was performed in 90 of those patients who received negative initial RT-PCR result (twice in 86 patients and thrice in 4 patients). Table 2 summarizes the demographic characteristics and comorbid diseases in those patients with chest CT findings that suggested acute pneumonia (including COVID-19).

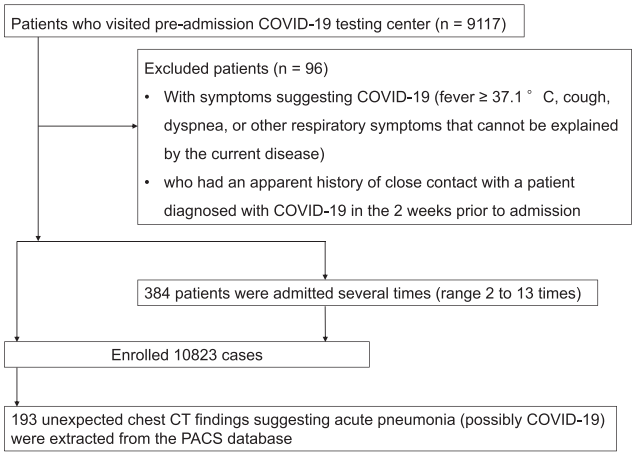

Fig. 1 – Criteria for the enrollment and exclusion of patients from the current study.

Table 1 – Standardized reporting language for findings of COVID-19 by computed tomography (CT), as defined by the Radiological Society of North America (RSNA) [5].

Imaging pattern	Chest CT findings
Typical appearance	Peripheral, bilateral, ground-glass opacity (GGO) with or without consolidation or visible intralobular lines ("crazy-paving") Multifocal GGO of rounded morphology with or without consolidation or visible intralobular lines ("crazy-paving") Reverse halo sign or other findings of organizing pneumonia (seen later in the disease)
Indeterminate appearance	*Absence of typical features AND presence of*: Multifocal, diffuse, perihilar, or unilateral GGO with or without consolidation lacking a specific distribution and are nonrounded or non-peripheral Few very small GGO with a nonrounded and non-peripheral distribution
Atypical appearance	*Absence of typical or indeterminate features AND presence of*: Isolated lobar or segmental consolidation without GGO Discrete small nodules (centrilobular, "tree-in-bud") Lung cavitation Smooth interlobular septal thickening with pleural effusion
Negative for pneumonia	No CT features to suggest pneumonia

Table 2 – Abnormal chest computed tomography (CT) findings leading to suspicion of COVID-19 as asymptomatic cases.

Sex (n = 193)	Number	Count Percent (%)
Male	125	64.8
Female	68	35.2
Age (years)	68 (range 22–93)	
Number of RT-PCR tests (n = 193)		
1 test	103	53.4
2 tests	86	44.6
3 tests	4	2.1
Comorbid disease		
Cardiovascular disease including post-therapeutic or undertreatment	21	10.9
Diabetes mellitus	33	17.1
Bronchial asthma	14	7.3
Lung disease (emphysema, IP, NTM)	34 (24, 8, 2)	17.6 (12.4, 4.1, 1)
Malignancies including post-therapeutic or undertreatment state (lung cancer, hematologic malignancies, others)	85 (12, 2, 71)	44 (6.2, 1, 36.8)
Renal disease (more than CKD stage IV or nephrosis syndrome)	27	14
Other disease	LC (5), Collagen disease (5)	2.6, 2.6
Drugs that may affect patient's immunocompetence		
Corticosteroid (median 10 mg; range 2–30 mg)	10	5.2
Immunosuppressive agents	Ciclosporin:1, MTX:1	0.5, 0.5
Anticancer drug (conventional, ICI)	28 (21, 7)	14.5 (10.9, 3.6)

IP, interstitial pneumonia; NTM, non-tuberculosis mycobacteria; CKD, chronic kidney disease; LC, liver cirrhosis; MTX, methotrexate; ICI, immune checkpoint inhibitor.

3.2. *Imaging evaluation*

Of the 10 823 patients, 20 asymptomatic patients (0.18%) were diagnosed with COVID-19 due to a positive RT-PCR test. COVID-19 was ruled out in the remaining 10 803 patients (99.82%), and none of these patients were diagnosed with COVID-19 after hospitalization. Table 3 summarizes the chest CT findings during the study period.

During the low-prevalence period, 5 of 6556 patients (0.076%) were diagnosed with COVID-19. Of the 25 patients with abnormal chest CT findings corresponding to a "typical appearance" of COVID-19 pneumonia, only 1 (4%) was diagnosed with COVID-19. Of the 69 patients with "indeterminate appearance" on chest CT, only 1 (1.4%) was diagnosed with COVID-19. In all 16 patients with "atypical appearance" on chest CT, COVID-19 was ruled out. For the remaining 6446 patients, chest CT findings were "negative"; however, following a positive RT-PCR test, 3 of these patients (0.047%) were diagnosed with COVID-19.

During the high-prevalence period, 15 of 4267 patients (0.35%) were diagnosed with COVID-19. Of the 14 patients with abnormal chest CT findings corresponding to a "typical appearance" of COVID-19 pneumonia, only 2 (14.3%) were diagnosed with COVID-19. Of the 61 patients with "indeterminate appearance" on chest CT, only 4 (6.6%) were diagnosed with COVID-19. In all 8 patients with "atypical appearance" on

Table 3 – Summary of computed tomography (CT) findings in asymptomatic patients during low-prevalence and high-prevalence periods of the COVID-19 pandemic.

	Low-prevalence period		High-prevalence period		Entire period	
	COVID-19 (–) (n = 6551)	COVID-19 (+) (n = 5)	COVID-19 (–) (n = 4252)	COVID-19 (+) (n = 15)	COVID-19 (–) (n = 10803)	COVID-19 (+) (n = 20)
Typical (n = 39)	24 (96%)	1 (4%)	12 (85.7%)	2 (14.3%)	36 (92.3%)	3 (7.7%)
Bilateral, peripheral, GGO (with or without consolidation)	21 (84%)	1 (4%)	10 (71.4%)	1 (7.1%)	31 (79.5%)	2 (5,1%)
Multifocal GGO of rounded morphology (with or without consolidation)	1 (4%)	0	1 (7.1%)	1 (7.1%)	2 (5.1%)	1 (2.6%)
Reverse halo sign or other findings of organizing pneumonia (seen later in the disease)	2 (8%)	0	1 (7.1%)	0	3 (7.7%)	0
Indeterminate (n = 130)	68 (98.6%)	1 (1.4%)	57 (93.4%)	4 (6.6%)	125 (96.2%)	5 (3.8%)
Few very small GGO with a non-rounded and non-peripheral distribution	3 (4.3%)	0	0	0	3 (2.3%)	0
Diffuse, multifocal, perihilar or unilateral GGO lacking a specific distribution and are non-rounded or non-peripheral (with or without consolidation)	65 (94.3%)	1 (1.4%)	57 (93.4%)	4 (3.3%)	122 (93.8%)	5 (3.8%)
Atypical (n = 24)	16 (100%)	0	8 (100%)	0	24 (100%)	0
Isolated segmental or lobar consolidation without GGO	4 (25%)	0	4 (50%)	0	8 (33.3%)	0
Centrilobular small nodules ("tree in bud" appearance)	12 (75%)	0	3 (37.5%)	0	15 (62.5%)	0
Lung cavitation	0	0	0	0	0	0
Smooth interlobular septal thickening with pleural effusion	0	0	1 (12.5%)	0	1 (4.2%)	0
Negative (n = 10630)	6443 (99.9%)	3 (0.047%)	4175 (99.9%)	9 (0.22%)	10618 (99.9%)	12 (0.11%)

Table 4 – Diagnostic efficacy of chest appearance by computed tomography (CT) images in asymptomatic patients during low-prevalence and high-prevalence periods of the COVID-19 pandemic.

Chest CT appearance	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)	LR +	LR –	P value
Typical appearance								
Low-prevalence period	20	99.6	99.6	4	99.9	54.6	0.8	0.019
High-prevalence period	13.3	99.7	99.7	14.3	99.7	47.2	0.87	0.001
Entire period	15	99.7	99.7	7.7	99.8	45	0.85	<0.001
Typical and indeterminate appearance								
Low-prevalence period	40	98.6	98.6	2.1	100	28.4	0.61	0.002
High-prevalence period	40	98.4	98.4	8	99.8	24.3	0.61	<0.001
Entire period	40	98.5	98.5	4.7	99.9	26.8	0.61	<0.001

Fisher's exact test used to analyze the dichotomous variables.
PPV, positive predictive value; NPV, negative predictive value; LR+, positive likelihood ratio; LR–, negative likelihood ratio.

chest CT, COVID-19 was ruled out. The remaining 4184 patients were classified as "negative" based on chest CT; however, following a positive RT-PCR test, 9 of these patients (0.22%) were diagnosed with COVID-19.

Table 4 shows the diagnostic efficacy of chest CT based on the appearance of each image, with RT-PCR results used as the reference. In the low-prevalence period, the efficacy values of the "typical appearance" on chest CT were: 20% sensitivity, 99.6% specificity, 99.6% accuracy, 4% PPV, 99.9% NPV, 54.6 LR+, and 0.8 LR–. In the high-prevalence period, the efficacy values of the "typical appearance" on chest CT were: 13.3% sensitivity, 99.7% specificity, 99.7% accuracy, 14.3% PPV, 99.7% NPV, 47.2 LR+, and 0.87 LR–. Across the entire study period, the efficacy values of the "typical appearance" on chest CT were: 15% sensitivity, 99.7% specificity, 99.7% accuracy, 7.7% PPV, 99.8% NPV, 45 LR+, and 0.85 LR–.

When the combination of "typical appearance" and "indeterminate appearance" was considered in the low-prevalence period, the efficacy values were: 40% sensitivity, 98.6% specificity, 98.6% accuracy, 2.1% PPV, 100% NPV, 28.4 LR+, and 0.61 LR–. In the high-prevalence period, the efficacy values for this combination were: 40% sensitivity, 98.4% specificity, 98.4% accuracy, 8% PPV, 99.8% NPV, 24.3 LR+, and 0.61 LR–. Across the entire study period, the efficacy values for this combination were: 40% sensitivity, 98.5% specificity, 98.5% accuracy, 4.7% PPV, 99.9% NPV, 26.8 LR+, and 0.61 LR–.

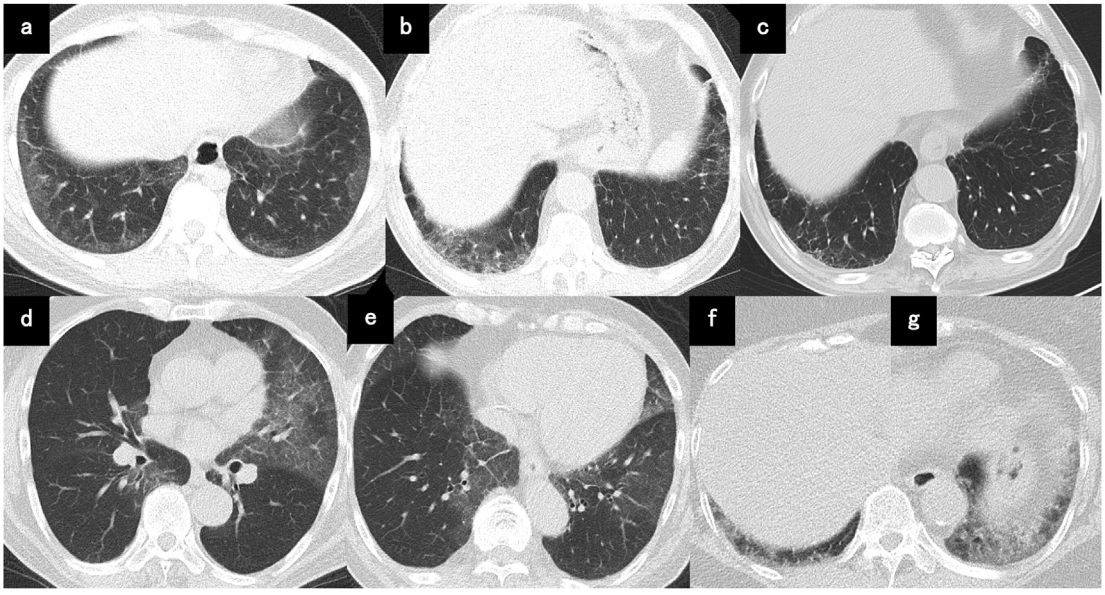

Fig. 2 – Computed tomography (CT) images depicting different lung diseases that mimic COVID-19 pneumonia. (a) Non-specific interstitial pneumonia classified as "typical appearance" of COVID-19 pneumonia in a 31-year old woman with systemic scleroderma. The axial chest CT image shows an area of a ground-glass opacity (GGO) with peripheral distribution in the posterior basal segment of the bilateral lower lobe. (b) Exacerbation of interstitial pneumonia classified as the "typical appearance" of COVID-19 pneumonia in an 84-year old man before transurethral lithotripsy. (c) Axial chest CT image showing new lesions with areas of GGO (arrow) with peripheral distribution in the posterior basal segment of the bilateral lower lobe, which were not detected 6 months earlier. (d, e) Drug-induced pneumonia classified as "typical appearance" of COVID-19 pneumonia in a 70-year old man before percutaneous coronary intervention. The axial chest CT image shows an area of small GGO with peripheral distribution in the middle and bilateral lower lobe. (f, g) Lung collapse classified as "typical appearance" of COVID-19 pneumonia in a 74-year old woman before total knee arthroplasty. The axial chest CT image shows an area of GGO with peripheral distribution in the bilateral lower lobe.

We diagnosed COVID-19 using chest CT in 8 patients. However, there were 185 patients who were diagnosed as false-positive for COVID-19 pneumonia during the entire study period (1.7% false-positive rate; 60% false-negative rate). From 36 of the false-positive patients with a "typical appearance" on chest CT, COVID-19 pneumonia was suspected in 13 patients due to lack of comparative images; these 13 patients were later diagnosed as having interstitial pneumonia (either non-specific interstitial pneumonia, desquamative interstitial pneumonia, or smoking-related interstitial lung disease). Outcomes of the remaining false-positive patients with a "typical appearance" on chest CT were as follows: diagnosis of and treatment for drug-induced lung injury (n = 6 patients), exacerbation of interstitial pneumonia (n = 4 patients), collapse of the dorsal lung induced by poor air intake (n = 4 patients), infectious pneumonia unrelated to COVID-19 (n = 2 patients), unknown cause with improvement during follow-up (n = 1 case), and no follow-up (n = 6 patients). Fig. 2 shows CT images of the different lung diseases mimicking COVID-19 pneumonia.

Of the 149 false-positive patients with "indeterminate appearance" and "atypical appearance" on chest CT, incidental findings suggestive of COVID-19 pneumonia were as follows: diagnosis and treatment for infectious pneumonia (n = 14 patients), old interstitial pneumonia (n = 5 patients), suspected drug-induced pneumonia (n = 3 patients), non-tuberculosis mycobacterium infection (n = 3 patients).

Of the 185 false-positive patients, delay in admission or treatment occurred in 56 patients (30%), with a median delay of 28 days, and a range of delay of 1–180 days. Suspension of hospitalization occurred in 6 patients (3.2%). Among the 56 false-positive patients, 10 patients were treated for bacterial pneumonia, 3 were treated for drug-induced lung injury, and 2 were treated for acute exacerbation of interstitial pneumonia.

4. Discussion

In this study, the incidence of chest CT findings leading to suspected COVID-19 pneumonia in asymptomatic pre-hospital patients was 1.8%. These results were much lower than those reported in similar studies that targeted pre-operative asymptomatic patients (7–9.6%) [13,14,17].

Using the RSNA reporting system, our results suggest that chest CT findings that are consistent with "typical appearance" were more likely to be COVID-19 pneumonia than those consistent with the other two patterns. This finding is consistent with the results of previous studies [3,5,7,8]; however, most of the cases were false-positive. Some studies have demonstrated the usefulness of chest CT even in a low-prevalence region [21,22]. These studies reported that chest CT may be useful for early diagnosis of COVID-19 in symptomatic patients in the early stages of disease with false-negative RT-PCR results [20,21]; however, one meta-analysis indicated that screening patients with suspected disease using chest CT was associated with low PPV (range: 1.5–8.3%) in a low-prevalence region and low-to-moderate PPV (range: 24.3–44.8%) even in a high-prevalence region [4]. In this study, we compared the diagnostic efficacy of chest CT for screening in asymptomatic patients between the low-prevalence and high-prevalence periods of the pandemic. Our findings indicated that the PPV was 4% in the low-prevalence period and 14.3% in the high-prevalence period, in accordance with values reported in previous studies [4,13].

One explanation for the high false-positive rate of chest CT in asymptomatic patients is that many diseases can radiologically mimic COVID-19 pneumonia, including other forms of viral pneumonia [22,23], atypical pneumonia [24], interstitial pneumonia [3,8,12,21,22], drug-induced pneumonia [21,25,26], and traumatic changes such as rib fractures [27]. Our results suggested that unknown early or mild interstitial pneumonia and bilateral lower lobe dorsal lung collapse due to poor inspiration were difficult to differentiate from mild COVID-19 pneumonia, which supports the findings of previous reports [3,8,12,21,22]. Based on these results, chest CT used as an adjunct to RT-PCR testing for COVID-19 screening in asymptomatic patients did not contribute to the exclusion of COVID-19, even in the high-prevalence period.

At the end of the study period, the Alpha strain as a variant of concern (VOC) was the dominant origin of COVID-19 infections across Japan [28–30]. A shift to the Delta strain had been reported, following a trend that was also developing in other countries [28,31,32]. Several studies (including preprints) reported that the time taken from viral exposure to the result of a positive RT-PCR test result may be shorter in patients with the Delta strain than in those without VOCs, that the Delta strain may multiply faster and be more infectious in the initial stages, and that the Delta strain may prove to be more virulent than non-VOCs [33,34]. Several studies have reported that COVID-19 vaccinations remain highly effective against COVID-19 hospitalization and death, including those caused by the Delta variant [35]; however, breakthrough infection in vaccinated patients remains the focus of attention [36] and newer VOCs have been defined in early 2022 that have contributed to a global re-epidemic [18,28,37,38]. We did not find chest CT to be an effective pre-admission screening tool for asymptomatic patients because it was not effective even during the high-prevalence period when the vaccine was not widely available. Moreover, considering the increased medical costs associated with chest CT compared with those of RT-PCR, we do not recommend using chest CT as an effective tool to screen for COVID-19.

This study has several limitations. First, it had a single-center retrospective design with a heterogenous pre-admission patient group. Second, we cannot exclude the possibility that some asymptomatic and infected patients passed all pre-admission examinations. Third, we did not investigate vaccination status as a potential confounder in this study. Lastly, since the Omicron strain is currently at the center of the epidemic [18,28,37,38], the results of this study obtained from April 2020 to March 2021 were based on the data at a time when other mutants, such as the Delta variant,

were endemic. The current situation in which the Omicron variant is prevalent is different to the circumstances in which this study was conducted with previous COVID-19 variants.

5. Conclusions

In conclusion, chest CT is not adequately sensitive for COVID-19 screening in asymptomatic patients compared with RT-PCR, even in high-prevalence periods. Moreover, 1.7% of patients in our study had false-positive results, even with the use of the RSNA reporting system, which deterred them from treatment and hospitalization. Our findings indicate that addition of chest CT to RT-PCR testing does not provide additional benefit for COVID-19 screening in asymptomatic patients.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of Interest

The authors have no conflicts of interest.

Acknowledgments

We would like to thank Editage (http://www.editage.com) for editing and reviewing this manuscript for English language.

REFERENCES

[1] WHO, director. General's opening remarks at the media briefing on COVID-19 [Internet], https://www.who.int/director-general/speeches/detail/who-director-general-sopening-remarks-at-the-media-briefing-on-covid-19e-11-march-2020. [accessed October 8, 2021].
[2] Ministry of Health, Labour and Welfare current situation in Japan. Situation report. Current situation in Japan [Internet], https://www.mhlw.go.jp/stf/covid-19/kokunainohasseijoukyou_00006.html. [accessed October 8, 2021].
[3] Kwee TC, Kwee RM. Chest CT in COVID-19: what the radiologist needs to know. Radiographics 2020;40:1848–65. https://doi.org/10.1148/rg.2020200159.
[4] Kim H, Hong H, Yoon SH. Diagnostic performance of CT and reverse transcriptase polymerase chain reaction for coronavirus disease 2019: a meta-analysis. Radiology 2020;296:E145–55. https://doi.org/10.1148/radiol.2020201343.
[5] Simpson S, Kay FU, Abbara S, Bhalla S, Chung JH, Chung M, et al. Radiological society of North America expert consensus document on reporting chest CT findings related to COVID-19: endorsed by the society of thoracic radiology, the American college of radiology, and RSNA. Radiol Cardiothorac Imaging 2020;2:e200152. https://doi.org/10.1148/ryct.2020200152.
[6] Prokop M, van Everdingen W, van Rees Vellinga T, Quarles van Ufford H, Stöger L, Beenen L, et al. CO-RADS: a categorical CT assessment scheme for patients suspected of having COVID-19-definition and evaluation. Radiology 2020;296:E97–104. https://doi.org/10.1148/radiol.2020201473.
[7] Inui S, Kurokawa R, Nakai Y, Watanabe Y, Kurokawa M, Sakurai K, et al. Comparison of chest CT grading systems in coronavirus disease 2019 (COVID-19) pneumonia. Radiol Cardiothorac Imaging 2020;2:e200492. https://doi.org/10.1148/ryct.2020200492.
[8] Machnicki S, Patel D, Singh A, Talwar A, Mina B, Oks M, et al. The usefulness of chest CT imaging in patients with suspected or diagnosed COVID-19: a review of literature. Chest 2021;160:652–70. https://doi.org/10.1016/j.chest.2021.04.004.
[9] Ciccarese F, Coppola F, Spinelli D, Galletta GL, Lucidi V, Paccapelo A, et al. Diagnostic accuracy of North America expert consensus statement on reporting CT findings in patients suspected of having COVID-19 infection: an Italian single-center experience. Radiol Cardiothorac Imaging 2020;2:e200312. https://doi.org/10.1148/ryct.2020200312.
[10] Inui S, Fujikawa A, Jitsu M, Kunishima N, Watanabe S, Suzuki Y, et al. Chest CT findings in cases from the cruise ship "diamond princess" with coronavirus disease 2019 (COVID-19). Radiol Cardiothorac Imaging 2020;2:e200110.
[11] Wang Y, Dong C, Hu Y, Li C, Ren Q, Zhang X, et al. Temporal changes of CT findings in 90 patients with COVID-19 pneumonia: a longitudinal study. Radiology 2020;296:E55–64. https://doi.org/10.1148/radiol.2020200843.
[12] Kanne JP, Bai H, Bernheim A, Chung M, Haramati LB, Kallmes DF, et al. COVID-19 imaging: what we know now and what remains unknown. Radiology 2021;299:E262–79. https://doi.org/10.1148/radiol.2021204522.
[13] Gümüs T, Kabaoglu ZU, Coskun B, Kartal F, Artukoglu F, Atasoy KC. Preoperative computerized tomography screening for COVID-19 pneumonia in asymptomatic patients: experiences from two centers. Jpn J Radiol 2021;39:240–5. https://doi.org/10.1007/s11604-020-01061-w.
[14] Knol WG, Thuijs DJFM, Odink AE, Maurovich-Horvat P, de Jong PA, Krestin GP, et al. Preoperative chest computed tomography screening for coronavirus disease 2019 in asymptomatic patients undergoing cardiac surgery. Semin Thorac Cardiovasc Surg 2021;33:417–24. https://doi.org/10.1053/j.semtcvs.2020.09.027.
[15] Tani Y, Sawano T, Kawamoto A, Ozaki A, Tanimoto T. Nosocomial SARS-CoV-2 infections in Japan: a cross-sectional newspaper database survey. Int J Health Pol Manag 2020;9:461–3. https://doi.org/10.34172/ijhpm.2020.75.
[16] Iritani O, Okuno T, Hama D, Kane A, Kodera K, Morigaki K, et al. Clusters of COVID-19 in long-term care hospitals and facilities in Japan from 16 January to 9 May 2020. Geriatr Gerontol Int 2020;20:715–9. https://doi.org/10.1111/ggi.13973.
[17] Chetan MR, Tsakok MT, Shaw R, Xie C, Watson RA, Wing L, et al. Chest CT screening for COVID-19 in elective and emergency surgical patients: experience from a UK tertiary centre. Clin Radiol 2020;75:599–605. https://doi.org/10.1016/j.crad.2020.06.006.
[18] Tokyo Metropolitan Government. Updates on COVID-19 in Tokyo [Internet], https://stopcovid19.metro.tokyo.lg.jp/en. [accessed October 8, 2021].
[19] The National Institute of Infectious Diseases. Current situation of infection [Internet], https://www.niid.go.jp/niid/en/2019-ncov-e.html. [last accessed March 16, 2022].
[20] Himoto Y, Sakata A, Kirita M, Hiroi T, Kobayashi KI, Kubo K, et al. Diagnostic performance of chest CT to differentiate COVID-19 pneumonia in non-high-epidemic area in Japan. Jpn J Radiol 2020;38:400–6. https://doi.org/10.1007/s11604-020-00958-w.
[21] Hani C, Trieu NH, Saab I, Dangeard S, Bennani S, Chassagnon G, et al. COVID-19 pneumonia: a review of typical CT findings and differential diagnosis. Diagn Interv Imaging 2020;101:263–8. https://doi.org/10.1016/j.diii.2020.03.014.

[22] Bai HX, Hsieh B, Xiong Z, Halsey K, Choi JW, Tran TML, et al. Performance of radiologists in differentiating COVID-19 from non-COVID-19 viral pneumonia at chest CT. Radiology 2020;296:E46–54. https://doi.org/10.1148/radiol.2020200823.
[23] Lin L, Fu G, Chen S, Tao J, Qian A, Yang Y, et al. CT manifestations of coronavirus Disease (COVID-19) pneumonia and influenza virus pneumonia: a comparative study. AJR Am J Roentgenol 2021;216:71–9. https://doi.org/10.2214/AJR.20.23304.
[24] Chrzan R, Bociąga-Jasik M, Bryll A, Grochowska A, Popiela T. Differences among COVID-19, bronchopneumonia and atypical pneumonia in chest high resolution computed tomography assessed by artificial intelligence technology. J Personalized Med 2021;11:391. https://doi.org/10.3390/jpm11050391.
[25] Rossi SE, Erasmus JJ, McAdams HP, Sporn TA, Goodman PC. Pulmonary drug toxicity: radiologic and pathologic manifestations. Radiographics 2000;20:1245–59. https://doi.org/10.1148/radiographics.20.5.g00se081245.
[26] Dumoulin DW, Gietema HA, Paats MS, Hendriks LEL, Cornelissen R. Differentiation of COVID-19 pneumonitis and ICI induced pneumonitis. Front Oncol 2020;10:577696. https://doi.org/10.3389/fonc.2020.577696.
[27] Abdolrahimzadeh Fard HA, Mahmudi-Azer S, Sefidbakht S, Iranpour P, Bolandparvaz S, Abbasi HR, et al. Evaluation of chest CT scan as a screening and diagnostic tool in trauma patients with coronavirus disease 2019 (COVID-19): a cross-sectional study. Emerg Med Int 2021;2021:4188178. https://doi.org/10.1155/2021/4188178.
[28] Ministry of Health, Labour and welfare current situation in Japan. Variant of concern cases [Internet], https://www.mhlw.go.jp/stf/covid-19/kokunainohasseijoukyou_00006.html. [last accessed March 16, 2022].
[29] National Institute of Infectious Diseases. Current situation of infection. Internet, https://www.niid.go.jp/niid/en/2019-ncov-e/10398-covid19-ab35th-en.html. [Accessed 8 October 2021].
[30] Ito K, Piantham C, Nishiura H. Predicted dominance of variant delta of SARS-CoV-2 before Tokyo olympic games, Japan, july 2021. Euro Surveill 2021;26:2100570. https://doi.org/10.2807/1560-7917.ES.2021.26.27.2100570.
[31] World Health Organization. COVID-19 weekly epidemiological update. 49th ed 2021.
[32] World Health Organization. COVID-19 weekly epidemiological update. 50th ed 2021.
[33] Li B, Deng A, Li K, Hu Y, Li Z, Shi Y, et al. Viral infection and transmission in a large, well-traced outbreak caused by the SARS-CoV-2 delta variant. Nat Commun 2022;460:13. https://doi.org/10.1038/s41467-022-28089-y.
[34] Ong SWX, Chiew CJ, Ang LW, Mak T, Cui L, Toh MPH, et al. Clinical and virological features of SARS-CoV-2 variants of concern: a retrospective cohort study comparing B.1.1.7 (alpha), B.1.315 (beta), and B.1.617.2 (delta). SSRN Journal 2021. https://doi.org/10.2139/ssrn.3861566.
[35] Centers for Disease Control and Prevention. Science brief: COVID-19 vaccines and vaccination, updated September. 15, 2021 [Internet], https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/fully-vaccinated-people.html. [accessed October 8, 2021].
[36] Centers for Disease Control and Prevention. Reporting breakthrough cases. Internet Possibility of COVID-19 Illness after Vaccination, Updated December 2021;17. https://www.cdc.gov/coronavirus/2019-ncov/vaccines/effectiveness/why-measure-effectiveness/breakthrough-cases.html. [Accessed 29 December 2021].
[37] Centers for Disease Control and Prevention.SARS-CoV-2 Variant Classifications and Definitions [Internet]. https://www.cdc.gov/coronavirus/2019-ncov/variants/variant-classifications.html [accessed March 16, 2022].
[38] World Health Organization. Tracking SARS-CoV-2 variants [Internet]. https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/[accessed March 16, 2022].