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Original Article

CT screening for COVID-19 in asymptomatic patients before hospital admission

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ABSTRACT

Introduction: In the novel coronavirus disease (COVID-19) pandemic era, it is essential to rule out COVID-19 effectively to prevent transmission in both communities and medical facilities. According to previous reports in high prevalence areas, CT screening may be useful in the diagnosis of COVID-19. However, the value of CT screening in low prevalence areas has scarcely been reported.
Methods: This report examines the diagnostic efficacy of CT screening before admission to a hospital in Tokyo. We conducted a retrospective analysis at Keio University Hospital from April 6, 2020, through May 29, 2020. We set up an outpatient screening clinic on April 6 for COVID-19, administering both PCR with nasopharyngeal swabs and chest CT for all patients scheduled for surgery under general anesthesia.
Results: A total of 292 asymptomatic patients were included in this study. There were three PCR-positive patients, and they all had negative CT findings, which revealed that both the sensitivity and positive predictive value of CT (PPV) were 0%. There were nine CT-positive patients; the specificity and the negative predictive value (NPV) were 96.9% and 98.9%, respectively.
Conclusion: CT screening was not useful in low prevalence areas at this time in Tokyo, even with the inclusion of the most prevalent phase. Given that the utility of CT screening depends on disease prevalence, the criteria for performing CT screening based on the prevalence of COVID-19 should be established.

1. Introduction

In the novel coronavirus disease (COVID-19) pandemic era, it is essential to rule out COVID-19 effectively to prevent transmission in both communities and medical facilities. Previous reports have indicated that the sensitivity of chest computed tomography (CT) in the diagnosis of COVID-19 may be greater than 90% [1,2]. Not only symptomatic patients but also asymptomatic patients often showed signs of COVID-19-like pneumonia on CT scans, and such findings could lead to the diagnosis of COVID-19 even when initial polymerase chain reaction (PCR) results were negative [3,4]. Previous studies have also revealed that approximately 40–45% of COVID-19 patients were asymptomatic [5] and that postoperative pulmonary complications associated with high mortality occurred in 43.5% of COVID-19 patients who were asymptomatic on admission [6]. According to these reports, performing CT screening before hospital admission may prevent nosocomial infections. However, most previous studies focused on high prevalence areas, and the value of CT screening in low prevalence areas has scarcely been reported. Although there may be no specific criteria for distinguishing between high and low prevalence, one previous meta-analysis defined low prevalence as less than 10% [7]. For example,

Abbreviations: COVID-19, (coronavirus disease 2019); CT, (computed tomography); SARS-CoV-2, (severe acute respiratory syndrome coronavirus-2); PPV, (positive predictive value); NPV, (negative predictive value).

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the prevalence of COVID-19 in Hubei, China, was 39.0% from January 2020 to February 2020 [7], whereas the prevalence in Tokyo, Japan, was 6.7% during our study period [8]. Herein, we report the results of CT screening in asymptomatic patients before admission to a hospital in Tokyo.

2. Methods

We conducted a retrospective analysis at Keio University Hospital, a tertiary care center with 960 beds located in Tokyo, Japan, from April 6, 2020, through May 29, 2020. We set up an outpatient screening clinic for COVID-19on April 6, 2020, performing both PCR with nasopharyngeal swabs and chest CT on the same day for all patients scheduled for surgery under general anesthesia. All asymptomatic outpatients who underwent COVID-19 screening at the clinic were included in this study. We obtained written informed consent from all participants for both PCR and chest CT for COVID-19 screening. We surveyed the diagnostic performance of chest CT along with the gold standard method, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) PCR. The diagnostic performance was evaluated by examining sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). Sensitivity was determined by the percentage of PCR-positive patients who had positive CT findings, and specificity was gauged by the percentage of PCR-negative patients who had negative CT findings. PPV was assessed by the percentage of CT-positive patients who had positive PCR results, and NPV was determined by the percentage of CT-negative patients who had negative PCR results. This study was reviewed and approved by the Keio University School of Medicine Ethics Committee (20200063).

We tested the patients using the BD MAX (Becton Dickinson, Franklin Lakes, NJ, USA) system for SARS-CoV-2. Real-time reverse transcription PCR was performed using BD MAX TNA MMK SPC and BD MAX ExK TNA. Two primer and probe sets were used to detect 2 regions in the SARS-CoV-2 nucleocapsid (N) gene (N1 and N2) [9]. Samples were considered positive in accordance with the latest standard operating procedures set by the Japanese Society for Clinical Microbiology at the time of testing [10].

All unenhanced chest CT examinations were performed on the Aquilion 64 scanner (CANON Medical Systems, Otawara, Japan). All the patients were scanned craniocaudally during a single breath-hold while in the supine position. The scanning parameter was a tube voltage of 120 kV, a rotation speed of 0.5 s, slice collimation of 0.5 mm, pitch factor of 0.844, and tube current set using an automatic volume exposure control with a noise index of 15 (5 mm slice). Axial images of 1 mm slice thickness and 5 mm slice thickness without overlap were reconstructed with Adaptive iterative dose reduction three-dimensional (AIDR 3D) using a standard lung reconstruction kernel (FC 05; lung images). Two radiologists blinded to the clinical data evaluated CT findings by consensus. The chest CT findings were classified into four categories; typical, indeterminate, atypical, and negative (Table 1) [11]. Typical and indeterminate CT findings were considered positive, whereas atypical and negative chest CT findings were considered negative for COVID-19.

3. Results

A total of 292 patients were included in this study. The most common medical specialties admitting these patients were general surgery (98 patients), orthopedics (48 patients), and gynecology (42 patients). There were three PCR-positive patients, and they all had negative CT findings, indicating that both sensitivity and PPV were 0% (Tables 2 and 3). All three patients postponed surgery and remained asymptomatic for 2 weeks after diagnosis. There were nine CT-positive patients, and they all tested negative on initial PCR, indicating that the specificity and NPV were 96.9% and 98.9%, respectively. Seven out of nine patients underwent a second PCR more than 48 h after initial PCR, and they were all negative. All nine patients did not develop COVID-19 symptoms for more than two weeks following the initial CT, indicating that the possibility of them having COVID-19 was low. The profiles of these nine patients were heterogeneous in terms of age, sex, and underlying diseases (Table 4). Their CT findings were all categorized as indeterminate. The ultimate cause of positive CT findings was unknown in five of the nine. Six patients postponed surgery, and their CT findings improved or remained unchanged on a second CT performed 7–24 days later. Three cases with the most prominent CT findings are shown in Figs. 1–3. Of the 283 CT-negative patients, 29 had atypical CT findings; these included bronchitis and bronchiolitis with granular and nodular shadows of trans-pneumatic distribution, which are rarely shown in CT images of COVID-19 patients. Chronic interstitial pneumonia and pulmonary edema were also classified as atypical. Some examples of atypical CT findings are shown in Fig. 4.

4. Discussion

In Tokyo, the number of COVID-19 patients began to increase at the end of March (Fig. 5), and our hospital experienced a

Table 1
Radiological Society of North America chest CT classification system for reporting COVID-19 pneumonia (adapted from Simpson S et al., 2020).

Pneumonia Imaging Classification	Rationale	CT Findings
Typical appearance	Commonly reported imaging features of greater specificity for COVID-19 pneumonia	Peripheral, bilateral, GGO[a] 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	Nonspecific imaging features of COVID-19 pneumonia	Absence of typical features and presence of: Multifocal, diffuse, perihilar, or unilateral GGO with or without consolidation lacking a specific distribution and are non-rounded or non-peripheral Few very small GGO with a 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") Lung cavitation Smooth interlobular septal thickening with pleural effusion
Negative for pneumonia	No features of pneumonia	No CT features to suggest pneumonia.

[a] GGO: ground glass opacity.

Table 2
CT findings and PCR results.

		PCR result		Total
		Positive	Negative	
CT findings[a]	Positive	0	9	9
	Negative	3	280	283
	Total	3	289	292

[a] Chest CT findings were categorized according to the Radiological Society of North America chest CT classification system for reporting COVID-19 pneumonia [11]—i.e., typical, indeterminate, atypical, and negative. Typical and intermediate were considered positive, whereas atypical and negative were considered negative.

Table 3
Profiles of PCR-positive patients.

No.	Age	Sex	Department	Category of CT findings[a]	Operation	Development of COVID-19 symptoms[b]
1	70s	F	Surgery	Negative	Postponed	None
2	40s	F	Gynecology	Negative	Postponed	None
3	40s	F	Orthopedics	Negative	Postponed	None

[a] Chest CT findings were categorized according to the Radiological Society of North America chest CT classification system for reporting COVID-19 pneumonia [11]—i.e., typical, indeterminate, atypical, and negative.
[b] Over two weeks following PCR.

Table 4
Profiles of CT-positive patients.

No.	Age	Sex	Department	Category of CT findings[a]	Cause of CT findings	Operation	Development of COVID-19 symptoms[b]
1	60s	M	Urology	Indeterminate	Unknown	Postponed	None
2	40s	M	Thoracic surgery	Indeterminate	Unknown	On schedule	None
3	70s	M	Neurosurgery	Indeterminate	Hypersensitivity pneumonitis	Postponed	None
4	60s	M	Otolaryngology	Indeterminate	Unknown	Postponed	None
5	90s	F	Urology	indeterminate	Unknown	Postponed	None
6	50s	F	Gynecology	indeterminate	Unknown	Postponed	None
7	20s	F	Otolaryngology	indeterminate	GVHD[c]	Postponed	None
8	70s	F	Cardiovascular surgery	indeterminate	Interstitial pneumonia	On schedule	None
9	80s	M	Surgery	indeterminate	Renal failure	On schedule	None

[a] Chest CT findings were categorized according to the Radiological Society of North America chest CT classification system for reporting COVID-19 pneumonia [11]—i.e., typical, indeterminate, atypical, and negative.
[b] Over two weeks following CT.
[c] GVHD; graft versus host disease.

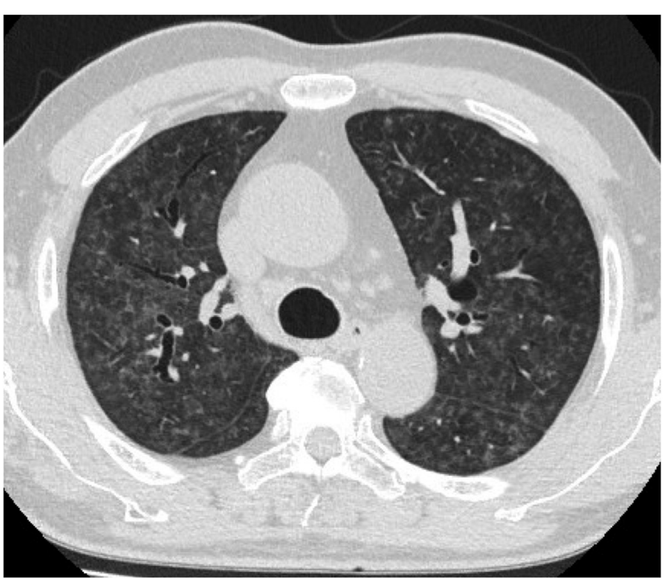

Fig. 1. CT image of Patient 3. Axial CT image demonstrating extensive ground-glass opacity with a centrilobular concentration.

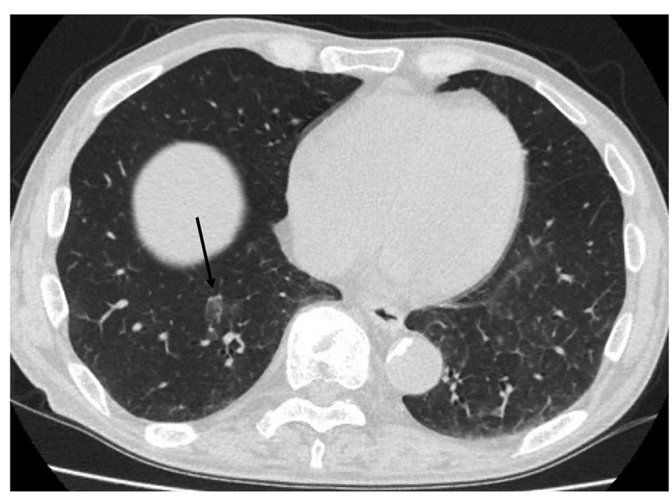

Fig. 2. CT image of Patient 4. Axial CT image demonstrating inhomogeneous ground-glass opacity in the left lower lobe and round ground-glass opacity in the right lower lobe (→).

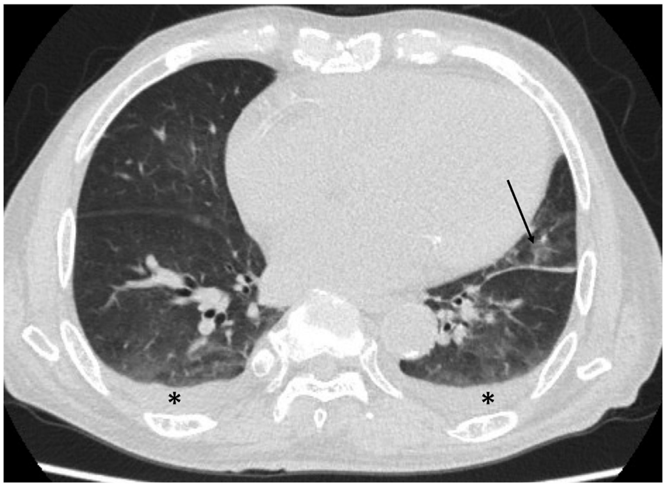

Fig. 3. CT image of Patient 9. Axial CT image showing dorsal dominant ground-glass opacity, bilateral pleural effusions (*), and left interlobular effusion (→).

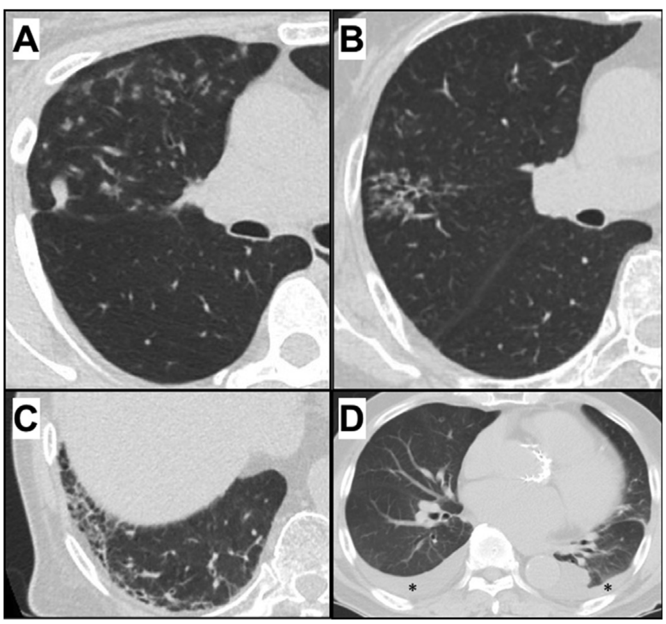

Fig. 4. CT images of patients with atypical CT findings. CT images of patients whose CT findings were classified as atypical according to the Radiological Society of North America chest CT classification system for reporting COVID-19 pneumonia [11]. Axial CT image showing bronchiolitis (A, B), chronic interstitial pneumonia (C), and pulmonary edema and pulmonary effusion (*) (D).

nosocomial outbreak of COVID-19 from the end of March to the middle of April. During this time, we set up the outpatient screening clinic for COVID-19 to prevent further nosocomial infections. We performed both PCR and CT screening because we did not know which had a higher sensitivity at that time. However, as the epidemic in Tokyo peaked after we set up the clinic, the number of PCR-positive patients in this study was lower than expected. As a result, we performed CT screening in a low prevalence population and obtained a PPV of 0%.

While the sensitivity of CT was 0%, the specificity we found was higher than that reported in previous reports [1,2], which is possibly because our study included asymptomatic patients, who may be less likely to have any significant CT findings. Except for cases with high urgency or surgical needs, we postponed surgery in cases with positive CT findings because COVID-19 patients are at high risk of developing fatal complications post surgery [6]. However, none of the six patients who postponed surgery developed any symptoms suggestive of COVID-19 during the two weeks following the initial positive CT results, which implied that the postponement of surgery due to false-positive CT findings was unnecessary. In addition, the cost of performing universal CT could also be a problem.

Hyungjin Kim et al. reported a meta-analysis on the relationship between the prevalence and predictive value of CT [7]. They defined the prevalence as the proportion of patients diagnosed with COVID-19 by PCR among those tested. According to their definition and analysis, the prevalence in Tokyo from April 6, 2020, through May 29, 2020, was 6.7% based on published data [8], indicating that the PPV and NPV of CT were expected to be 8.3% and 99.0%, respectively, which is substantially different from our results. One reason for this discrepancy may be that our subjects were asymptomatic, as mentioned above. Meanwhile, a total of 4175 cases were confirmed in Tokyo from April 6, 2020, through May 29, 2020, corresponding to only 0.03% of the city's population [8]. As PCR tests were reserved for patients with severe symptoms or patients who have been symptomatic for more than 4 days at that time in Tokyo [12], there could be many undiagnosed cases, leading to an underestimation of prevalence. Conversely, the strict control of PCR tests to only those likely to have the disease could then overestimate prevalence. Thus, even if CT screening is useful in epidemic areas, it is currently difficult to decide whether CT screening should be performed in Japan without reliable prevalence rate data. In this respect, the significance of the current study is that it was conducted during a highly prevalent phase, including the peak of the reported number of new cases in the Tokyo metropolitan area, the epicenter of COVID-19 in Japan, despite the absence of accurate prevalence rate.

While most radiology professional organizations and societies have recommended against performing CT screening for the identification of COVID-19 [13,14], there is little evidence to support these recommendations, as COVID-19 is an emerging infectious disease. Specifically, there have been no studies on CT screening in asymptomatic patients before admission in low prevalence areas. Considering that nearly half of COVID-19 patients are asymptomatic [5] and they are at high risk of developing fatal complications post surgery [6], screening asymptomatic patients before surgery could be significant in and of itself. In this regard, the current study could be part of the evidence for determining the criteria for CT screening of asymptomatic patients.

This study was limited by the sample size and the small number of PCR-positive patients. If there had been a patient who had been both PCR and CT positive, the sensitivity and PPV of CT would have been 25% and 10%, respectively. This could have led to a different conclusion. Therefore, it is difficult to evaluate the utility of CT screening with this small number of PCR positive patients. However, we think that we can show the likely results if CT screening is performed on asymptomatic patients before hospital admission in low prevalence areas. Consequently, the present study could be part of the evidence for determining the criteria for CT screening of asymptomatic patients.

In addition, patients' radiation exposure could be an issue even when using a low dose. However, it should be noted that not all patients received additional radiation exposure, as many required a CT scan for preoperative evaluation independent of this screening. Further studies with larger patient sample sizes and reliable epidemiological data are needed to clarify the relationship between the usefulness of CT screening and the prevalence of COVID-19.

Another limitation is the diagnostic criteria of COVID-19 in asymptomatic patients. It is unclear whether PCR results of SARS-CoV-2 alone is sufficient to make a diagnosis or not. However, as

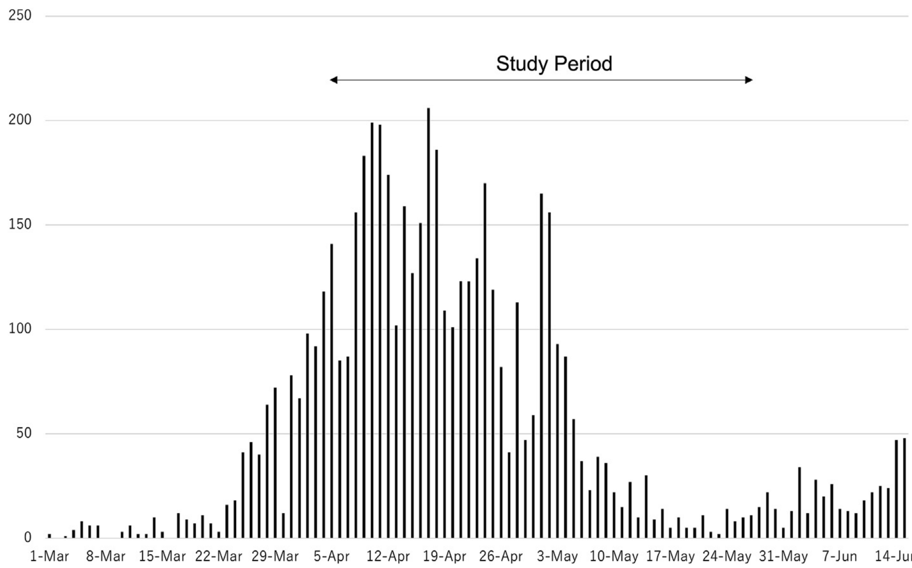

Fig. 5. Number of novel coronavirus disease (COVID-19) confirmed cases in Tokyo. The current study was conducted over a period that includes both before and after the peak of daily reported new cases.

long as PCR is the gold standard for diagnosis, it is probably acceptable to make a diagnosis based on a positive PCR result, although the diagnostic criteria may be revised in the future to include symptoms and other laboratory findings.

5. Conclusion

In conclusion, CT screening was not useful in a low prevalence area currently in Tokyo. Given that the utility of CT screening depends on disease prevalence, the criteria for performing CT screening based on the prevalence of COVID-19 should be established.

Authorship statement

Sho Uchida designed the study, analyzed, and drafted the manuscript. Shunsuke Uno, Yoshifumi Uwamino, and Naoki Hasegawa designed the study and edited the manuscript. Masahiro Hashimoto, Shunsuke Matsumoto, and Masahiro Jinzaki were responsible for the methodology of CT scan and edited the manuscript. Hideaki Obara and Yuko Kitagawa conceptualized the study and revised the article for intellectual content. All authors contributed to the writing of the final manuscript.

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Declaration of competing interest

None.

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