Descriptive Analysis of Chest Computed Tomography Scan in Coronavirus Disease 2019 Pneumonia: Correlation with Reverse Transcription-polymerase Chain Reaction and Clinical Features

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Abstract

BACKGROUND: Reverse transcriptase-polymerase chain reaction (RT-PCR) is the primary diagnostic tool to confirm coronavirus disease 2019 (COVID-2019) due to its high specificity. However, it has relatively low sensitivity and time consuming. In contrast, chest computed tomography (CT) has high sensitivity and achieves quick results. It may, therefore, play a critical role in screening and diagnosing COVID-19. A cross-sectional study was done in 212 patients with confirmed cases and patients under surveillance for COVID-19 tested for RT-PCR and chest CT scan. Statistical analysis was performed using SPSS Version 23 (Statistical Package for the Social Sciences, IBM Corp., Armonk, NY, USA).

AIM: We aim to investigate the diagnostic value of chest CT in correlation to RT-PCR in Indonesia.

METHODS: A cross-sectional study was done in 212 patients with confirmed cases and patients under surveillance for COVID-19 tested for RT-PCR and chest CT scan. Statistical analysis was performed using SPSS Version 23 (Statistical Package for the Social Sciences, IBM Corp., Armonk, NY, USA).

RESULTS: From a total of 212 patients, 92% of them were diagnosed as confirmed cases of COVID-19. It was found that the sensitivity of CT scan for COVID-19 patients was 72.3% (65.5% and 78.5%) with positive predictive value (PPV) of 93.9% (90.9% and 96.0%) and the sensitivity and PPV improve in symptomatic patients. Typical chest CT scan lesions were 8.0 times which were more likely (3.9–16.4; p <0.001) to be detected in symptomatic patients while patients with severe CT scan findings were 4.4 times more likely (3.0–6.5; p <0.001) to be admitted to the intensive care unit.

CONCLUSION: A high PPV suggests that a chest CT scan can detect COVID-19 lesions, but the absence of the lesions would not exclude the disease's presence.

Introduction

A cluster of pneumonia cases of unknown etiology in Wuhan, China, was reported to the World Health Organization (WHO) in December 2019 [1]. The infectious agent responsible for this outbreak was identified to be a new type of coronavirus, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and the disease caused by this new virus was officially named coronavirus disease 2019 (COVID-19) [2]. Human-to-human transmission was confirmed shortly after [3], primarily through respiratory droplets [4]. As a result, COVID-19 was able to rapidly spread throughout China and eventually to other countries worldwide. Subsequently, it was declared a pandemic by the WHO in March 2020 [5]. As of July 26, 2020; there have been 15,785,641 confirmed COVID-19 cases globally, including 640,016 deaths, while Indonesia had 97,286 confirmed cases, including 4714 deaths [6].

Clinical features of COVID-19 can range from asymptomatic or mildly symptomatic to critical illness or even death. Signs and symptoms include fever, respiratory symptoms such as cough and shortness of breath, and non-respiratory symptoms, including anosmia, gastrointestinal and neurological symptoms, and cardiovascular events [7], [8]. Mild-to-moderate illness constitutes about 81% of cases, while severe and critical illness makes up 14% and 5% of cases, respectively [9].

Diagnosis of COVID-19 is confirmed by reverse transcription-polymerase chain reaction (RT-PCR), which amplifies the genetic material of SARS-CoV2 obtained from naso-oropharyngeal samples [10], and is considered the gold standard for COVID-19 detection [4].

However, it typically takes hours to complete, and with a sensitivity ranging from 30% to 90%, it has a high false-negative rate [11]. Chest computed tomography (CT) is the imaging modality of choice in COVID-19 due to its high sensitivity and ability to achieve quick results [10]. Its sensitivity of 98% is significantly higher than that of the RT-PCR [12]. Furthermore, with 3.9%, chest CT was found to have a low rate of missed diagnosis of COVID-19 [13]. As a consequence, chest CT enables a quick diagnosis of COVID-19 pneumonia and may play a role in screening for COVID-19, particularly in RT-PCR-negative patients [12], [14], [15].

Typical CT findings of COVID-19 include ground-glass opacities (GGO) and consolidation with or without vascular enlargement, interlobular septal thickening, and air bronchogram [13]. Other, less common findings include the "reverse halo" sign and pulmonary nodules with a halo sign [13]. Lesions are located predominantly in the peripheral and subpleural and are most commonly found multilocally rather than unilocally [13]. The Radiological Society of North America (RSNA) released a consensus statement that classifies CT features of COVID-19 patients into four categories: Typical, atypical, indeterminate, and negative for pneumonia [16]. In a study conducted by Fang *et al*., 72% of COVID-19 patients had typical CT findings, with the remaining 28% showing atypical CT manifestations [12], [17]. The British Society of Thoracic Imaging (BSTI) further classifies chest CT scans of COVID-19 based on severity: Mild (up to three focal abnormalities, maximum 3 cm in diameter) and moderate/severe (more than 3 abnormalities or larger than 3 cm in diameter), where the differentiation between moderate and severe is assessed clinically [18].

Considering the high sensitivity of chest CT and its ability to achieve a prompt diagnosis, combined with the fact that RT-PCR has a relatively low sensitivity and is rather time-consuming, it is, therefore, argued that chest CT plays a critical role along with RT-PCR in diagnosing COVID-19, especially in epidemic areas where rapid and accurate identification of COVID-19 patients is needed [15], [19]. However, studies supporting chest CT use as a primary tool to screen, identify, and diagnose COVID-19 are still lacking in Indonesia. We aim to investigate the diagnostic value of chest CT in correlation to RT-PCR in Indonesia.

Materials and Methods

A cross-sectional study was done where the data were obtained from medical records. This study includes patients who tested positive for RT-PCR and included patients referred to our hospital for RT-PCR testing due to positive rapid tests results in which the results of RT-PCR were negative. Still, the CT scan results initially showed lesions suggestive of COVID-19. Patients with positive testing were then traced back for chest CT scan data and other descriptive data such as age, sex, comorbidities, and presence of symptoms, and whether they were admitted to the intensive care unit (ICU). Flowchart of the inclusion criteria is shown in Figure 1.
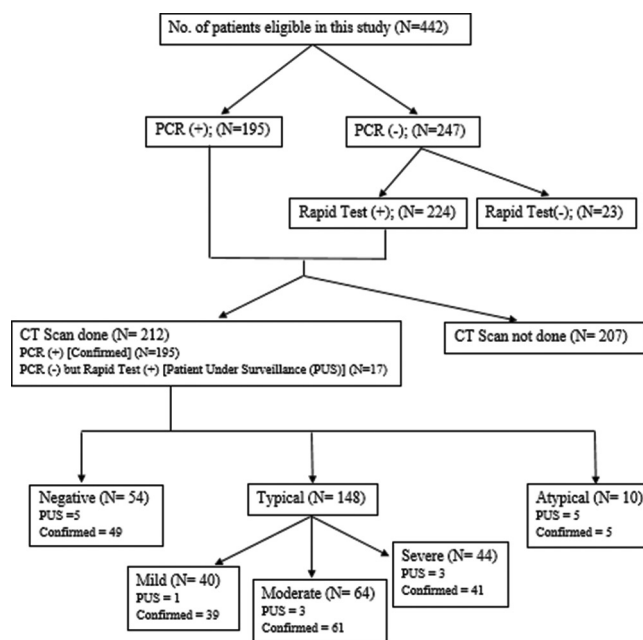

Figure 1: Flowchart of the study

Patients who were positive for COVID-19 were defined as patients who tested positive SARS-CoV-2 by RT-PCR from March 2020 to June 2020 in Siloam Hospitals Lippo Village. The classification of COVID-19 diagnosis referred to the 4th edition guidelines that were released by Minister of Health of Indonesia on March 27, 2020 [20]. Conversion of PCR was defined as the number of days taken from the first positive RT-PCR results to two consecutive negative results of RT-PCR and conversion was only measured in those who tested positive for RT-PCR. Traveling was defined as any visits outside the countries or nation from December 2019 up to RT-PCR testing while contact with COVID-19 patients was defined as any gatherings or close contacts with patients known positive for COVID-19. The number of days taken from the onset of symptoms to CT scan was defined as the 1st day of onset of COVID-19 manifested by signs and symptoms suggestive of COVID-19. If the patients were asymptomatic, this value would be 0 days. Geriatric was defined as age ≥65 years old.

Two expert radiologists interpreted the CT scan results and classification of the CT scan was according to the RSNA classification [16]. Severity of the CT scan referred to BSTI consensus [18]. Any conflicts in interpretation were resolved internally according to the consensus. Both radiologists were consultants in thoracic imaging, and they were both blinded for the diagnosis and test results of RT-PCR. Signs and

symptoms were revealed to allow interpretation of radiological findings according to clinical symptoms. Chest CT scan was done in Siemens SOMATOM Drive Straton MX Sigma (Siemens AG, Germany). Simultaneously, the RT-PCR samples were obtained through nasopharyngeal swab and analyzed with QIAGEN Rotor-Gene Q (Roche Molecular Systems, USA).

The primary objective was to analyze whether the CT scan was sensitive and specific enough to detect lesions of COVID-19. Other analyses were done to analyze whether the CT scan will detect typical lesions in symptomatic and asymptomatic patients and look at the severity of CT scan and their association with admission to the ICU. Descriptive statistics were used for representing the demographic and clinical variables. Association between variables is assessed with χ^2. Statistical analysis was performed using SPSS Version 23 (Statistical Package for the Social Sciences, IBM Corp., Armonk, NY, USA).

The committee approved this study protocol on Ethics at University of Pelita Harapan, Tangerang, Indonesia, with approval number of 153/K-LKJ/ETIK/VIII/2020 with protocol number 01082020.

Results

A summary of descriptive data on the correspondents studied is shown in Table 1. A total of 212 correspondents' data were collected where 92% of them were diagnosed as confirmed cases of COVID-19. The high patient number who did not undergo CT scan among negative PCR cases could be explained by the fact that since insurances do not cover CT scan for patients who were not positive by PCR testing even though their rapid testing is positive, most patients were reluctant to make out-of-pocket payment for CT scan. The mean age was 45.5 years old (±15.2), predominant toward males (54.7%). In this study, the mean days taken for conversion of RT-PCR were 13.2 days (±16.7). The number of days taken from the onset of symptoms to the CT scan was 4.1 days (±4.8 days).

Out of all the lesions, GGOs were the most frequent lesion detected (59.4%) followed by crazy paving (33%) and consolidation (22.6%). In comparison, the parenchymal band (3.8%) and halo sign (0.9%) were the least detected lesions. Other lesions were found, such as tuberculosis fibrosis, mosaic patterns, sub-solid nodules, and acute respiratory distress syndrome, which made up 8.5% of the lesions.

According to RSNA classification, 69.8% CT scan findings were typical, 4.7% were atypical, while 25.5% was negative for COVID-19. With BRTI consensus, 27% of the lesions were mild, 43.2%

Table 1: Descriptive analysis of correspondents

Characteristics	Results
Age (years)	45.5 (±15.2)
COVID-19 diagnosis classification (%)	
Confirmed	195 (92)
Patients under surveillance	17 (8)
Sex (%)	
Male	116 (54.7)
Female	96 (45.3)
Conversion of RT-PCR (days)	13.2 days (±16.7)
Ground-glass opacity (%)	
Yes	126 (59.4)
No	86 (40.6)
Crazy paving (%)	
Yes	70 (33.0)
No	142 (67.0)
Consolidation (%)	
Yes	48 (22.6)
No	164 (77.4)
Curvilinear band (%)	
Yes	34 (16.0)
No	178 (84.0)
Traction bronchiolectasis (%)	
Yes	25 (11.8)
No	187 (88.2)
Atoll sign (%)	
Yes	12 (5.7)
No	200 (94.3)
Halo sign (%)	
Yes	2 (0.9)
No	210 (99.1)
Parenchymal band (%)	
Yes	8 (3.8)
No	204 (96.2)
Fibrosis (%)	
Yes	13 (6.1)
No	199 (93.9)
Others (%)	
Yes	18 (8.5)
No	194 (91.5)
Classification (%)	
Atypical	10 (4.7)
Negative	54 (25.5)
Typical	148 (69.8)
Grading of CT (%)	
Mild	40 (27.0)
Moderate	64 (43.2)
Severe	44 (29.7)
Outcome (%)	
Alive	203 (95.8)
Dead	9 (4.2)
Days from onset of symptoms to CT scan	4.1 (±4.8)
Traveling (%)	
Yes	11 (5.2)
No	201 (94.8)
Contact with positive cases (%)	
Yes	56 (26.4)
No	156 (73.6)
Admission into ICU (%)	
Yes	15 (7.1)
No	197 (92.9)
Presentation (%)	
Symptomatic	135 (63.7)
Asymptomatic	77 (36.3)
Comorbidities	
Asthma	3
Previous tuberculosis	4
Geriatric	50
Hypertension	4
Diabetes mellitus type 2	4
Pregnancy	1
Dyslipidemia	2
Coronary artery disease	2
Chronic obstructive pulmonary disease	1

One patient can have more than 1 lesion on their CT scan findings. CT: Computed tomography, COVID-19: Coronavirus disease 2019; RT-PCR: Reverse transcription-polymerase chain reaction, ICU: Intensive care unit.

were moderate, while 29.7% were severe lesions (Figures 2-4). The outcome found in this study was 95.8% of patients were alive, while 4.2% were dead. Meanwhile, 7.1% of patients were admitted to the ICU (Table 1).

Table 2 describes the association between the usefulness of chest CT scan in detecting lesions in COVID-19 patients. It was found that the sensitivity of CT scan for COVID-19 patients was 72.3% (65.5% and
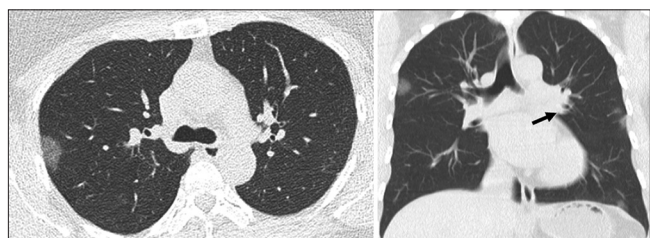
Figure 2: Mild coronavirus disease 2019 chest computed tomography scan axial view (left) and coronal view (right), indicating multifocal ground-glass opacities (black arrows)

78.5%) with positive predictive value (PPV) of 93.9% (90.9% and 96.0%). However, with 18.8% (12.0% and 28.3%) negative predictive value (NPV), it means that normal or atypical CT scans could not exclude the diagnosis of COVID-19.
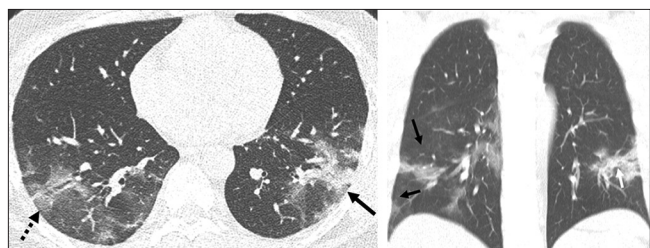

Figure 3: Moderate coronavirus disease 2019 chest computed tomography scan axial view (left) and coronal view (right), indicating multifocal ground-glass opacities (black arrows), crazy paving (dotted black arrow), and atoll sign (white arrow)

Table 3 shows the usefulness of chest CT scan in detecting lesions in symptomatic COVID-19 patients, and it found that the sensitivity was 88.1% with PPV value of 97.4%. This means that the sensitivity and PPV of the CT scan will increase in symptomatic patients.

Typical chest CT scan lesions were 8.0 times which were more likely (3.9–16.4; p <0.001) to be detected in symptomatic patients (Table 4) while patients with severe CT scan findings were 4.4 times more likely (3.0–6.5; p <0.001) to be admitted to the ICU (Table 5).

Discussion

In this study, we found that the mean age was 45.5 years old (±15.2) whereas one study conducted in Wuhan by Zhou et al. where they found that the mean age was 52.3 years old (±13.1) from a total of 272 CT scans. This might be explained by the fact that patients who came into our clinic were 36.3% asymptomatic. It was found that people with younger age without any comorbidities tend to be asymptomatic, and hence, these patients might skew the mean age [21]. The mean days taken for conversion of RT-PCR were 13.2 days (±16.7 days), longer than another study conducted by Ai et al. where the conversion to after negative was 6.9 days (±2.3) [15]. In our study, one possibility that could explain the longer conversion time might be because RT-PCR results typically took 1–2 weeks and if the results were positive, the patients needed to wait for another 1–2 weeks until two negative tests were achieved. Comparison of other studies is shown in Table 6.

Wang et al. found that most COVID-19 patients had a patchy or combination of GGO and consolidation opacities similar to our studies [22]. This study also found that CT's time duration in COVID-19 was 1.54 days (±0.946) while our study showed that patients took longer days. While partly it could be explained by the much lower participant number (n = 13) in the study done by Wang et al., it could also be explained by the fact that asymptomatic patients are unlikely to be checked with CT scan for COVID-19 due to cost issues and limited availability of CT scan in primary clinics and hospitals. Therefore, patients could undergo a CT scan only after they were referred to our hospital, which prolonged the CT scan time duration [20].

Ai et al. found that CT scan was 97% sensitive (95% and 98%) for confirmed COVID-19 patients with an NPV of 68% (65% and 70%) and accuracy of 68% (65% and 70%) while we only found that the sensitivity for CT scan was 72.3% (65.5% and 78.5%) with an NPV of 18.8% (12.0% and 28.3%) and accuracy of 59.6% (52.7% and 66.2%). Meanwhile, we reported a higher specificity 57.9% (33.5% and 79.8%) with a higher PPV of 93.9% (90.9% and 96.0%) compared to Ai et al. which reported specificity of 25% (22% and 30%) with a lower PPV of 65% (62% and 68%). This might be because our samples were only 1/5 of the study done by Ai et al. and hence the sensitivity calculation lacks volume. Furthermore, the differences in study design might explain the differences in findings. While our study only included those who tested positive for RT-PCR or positive CT scan findings as inclusion criteria, Ai et al.

Table 2: Usefulness of chest CT scan in detecting lesions in COVID-19 patients

CT Scan	Confirmed	Patients under surveillance	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Accuracy (95% CI)
Typical	141	7	72.3 (65.5, 78.5)	57.9 (33.5, 79.8)	93.9 (90.9, 96.0)	18.8 (12.0, 28.3)	59.6 (52.7, 66.2)
Non-typical	54	10					

CT: Computed tomography, COVID-19: Coronavirus disease 2019, PPV: Positive predictive value, NPV: Negative predictive value.

Table 3: Usefulness of chest CT scan in detecting lesions in symptomatic COVID-19 patients

CT scan	Confirmed	Patients under surveillance	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Accuracy (95% CI)
Typical	104	7	88.1 (80.9, 93.4)	58.8 (32.9, 81.2)	97.4 (95.1, 98.9)	22.4 (14.0, 33.8)	62.3 (52.6, 70.5)
Non-typical	14	10					

CT: Computed tomography, COVID-19: Coronavirus disease 2019, PPV: Positive predictive value, NPV: Negative predictive value.

categorized their participants into four groups which included a combination of positive or negative RT-PCR and positive or negative CT scan [15].
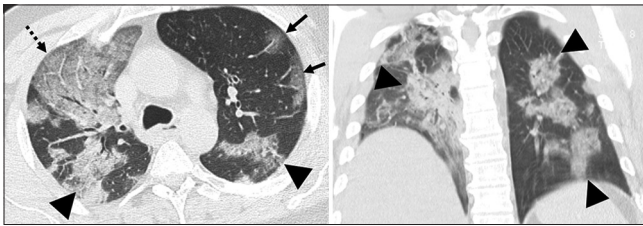

Figure 4: Severe coronavirus disease 2019 chest computed tomography scan axial view (left) and coronal view (right) indicating multifocal ground-glass opacities (black arrows), crazy paving (dotted black arrow), and consolidation (arrowheads)

Chest CT scans in symptomatic patients, however, seem to have a higher sensitivity and PPV. We found that chest CT scans' sensitivity in detecting COVID-19 was 88.1%, with a PPV of 97.4%. In their study of assessing the sensitivity of chest CT scan in patients with epidemiological or clinical features compatible with COVID-19, Fang *et al*. found that chest CT scans have a sensitivity 98% [12]. Smet *et al*. also compared the sensitivity and specificity of chest CT scans between asymptomatic and symptomatic patients. They found that the sensitivity of chest CT scans was 89.1%, while in asymptomatic patients, sensitivity was only 45.0%. They concluded that chest CT scans' sensitivity in asymptomatic patients was insufficient to justify it as a screening tool [23]. Therefore, as Shatri *et al*. pointed out, CT should not be used to screen asymptomatic patients for COVID-19, but may be considered in symptomatic patients [24].

Based on our data, symptomatic COVID-19 patients were more eight times more likely to have typical (104/118; 88%) than non-typical features (14/118; 12%) in their chest CTs. This contrasts to asymptomatic patients, where typical (37/77; 48%) and non-typical features (40/77; 52%) were almost equally likely to be found in their chest CTs. This finding draws similarities to a study conducted on the "Diamond Princess" cruise ship in Japan, which found that 79% had lung opacities in symptomatic patients. In comparison, in asymptomatic patients, they were present in only 54%. All asymptomatic patients with lung opacities had GGOs with or without interlobular septal thickening or consolidation. The lung opacities in 90% of the asymptomatic patients with lung opacities had peripheral or mixed distribution, while the rest had lung opacities of central distribution. In 78% of the asymptomatic patients with lung, opacities had multifocal lesions, while 22% had unifocal lesions. In another study of asymptomatic patients conducted by Hu *et al*., 50% of patients had COVID-19 typical features of GGOs, while 20% had atypical findings, with the rest having normal chest CTs [25]. A study conducted in Wuhan, China, by Meng *et al*. found that the predominant CT findings in asymptomatic patients were GGOs (94.8%) that were multifocal (62.1%) and peripherally distributed (75.9%), but unilaterally located (58.6%) [26].

Our data show that patients with a severe chest CT scan severity on admission are 4.4 times more likely to be admitted to the ICU than those with only mild-moderate chest CT scan severity. This is in concordance to a study conducted by Chen *et al*., in which it was found that COVID-19 patients admitted to the ICU had more lobes involved and more widespread distribution of lesions than those who have been discharged [27]. A similar finding was found in a study by Ruch *et al*., in which patients with over 50% of lung involvement in their chest CTs were associated with ICU admission and early death [28]. Therefore, initial chest CT may play a prognostic value in COVID-19 patients and help predict their outcome.

Our study has several limitations. First, using RT-PCR assays with a relatively low positive rate as the reference standard, the chest CT scan sensitivity for COVID-19 may be overestimated, and the specificity is underestimated. The second limitation is that due to this study's nature, we could not assess the time taken for patients to undergo CT scan after an initial positive RT-PCR test. Any correlations with clinical and laboratory data could not be obtained due to the hospital's overload. Third, since this is a cross-sectional study using past data, we could not include any control samples. Finally, since our hospital was not the referral

Table 4: Usefulness of chest CT scan in detecting lesions in confirmed COVID-19 patients

CT scan	Symptomatic	Asymptomatic	OR (95%CI)	p-value
Typical	104	37	8.0 (3.9–16.4)	<0.001
Non-typical	14	40		

CT: Computed tomography, COVID-19: Coronavirus disease 2019.

Table 5: Admission to ICU based on severity of CT scan

CT scan	ICU	Non-ICU	OR severe (95%CI)	p-value
Mild-moderate	2	103	4.4 (3.0–6.5)	<0.001
Severe	17	26		

CT: Computed tomography, ICU: Intensive care unit.

Table 6: Comparison of other studies

Author	Title	Year	Country	Sensitivity	Specificity	PPV	NPV	Accuracy	Sample size
Ai *et al*. [15]	Correlation of chest CT and RT-PCR testing for coronavirus disease 2019 (COVID-19) in China: A report of 1014 cases	2020	China	97	25	65	83	68	1014
Falaschi *et al*. [30]	Chest CT accuracy in diagnosing COVID-19 during the peak of the Italian epidemic: A retrospective correlation with RT-PCR testing and analysis of discordant cases	2020	Italy	90.7	78.8	86.4	85.1	85.9	773
Arslan *et al*. [31]	Correlation of chest CT and RT-PCR testing in coronavirus disease 2019 (COVID-19) in Turkey	2020	Turkey	43	74	96	6	44	610
Caruso *et al*. [32]	Chest CT features of COVID-19 in Rome, Italy	2020	Italy	97	56	59	96	72	158
Mirahmadizadeh *et al*. [33]	Sensitivity and specificity of chest CT scan based on RT-PCR in COVID-19 diagnosis	2021	Iran	78.6	42.3	59.5	64.7	60.2	54

CT: Computed tomography, COVID-19: Coronavirus disease 2019; RT-PCR: Reverse transcription-polymerase chain reaction, ICU: Intensive care unit.

hospital for COVID-19, there were few study samples available. However, despite the circumstances, this study provided another perspective from Indonesia in using CT scan as a feasible screening method for COVID-19.

Conclusion

The chest CT scan has good sensitivity for COVID-19 patients, which improves symptomatic patients. A high PPV suggests that chest CT scan can detect COVID-19 lesion, but the absence of the lesions would not exclude the disease's presence. Future studies should also assess follow-up chest CT scan in COVID-19 patients as it was reported that reactivation of COVID-19 could also contribute to radiological changes in chest CT scan [29].

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