# Chest CT as a complement to RT-PCR to confirm and follow-up COVID-19 patients

Aziza Ghanie Icksan[1], Muhammad Hafiz[2], Annisa Dian Harlivasari[2]

[1]*Department of Radiology, Persahabatan Hospital, Jakarta, Faculty of Medicine University Pembangunan Nasional Jakarta, Indonesia*
[2]*Department of Pulmonology and Respiratory Medicine, Budhi Asih Hospital, Jakarta, Indonesia*

**Citation :** Ghanie Icksan Aziza,Hafiz Muhammad. Chest CT as a complement to RT-PCR to confirm and follow-up COVID-19 patients
Medicinus. 2020 February; 8(1):31–37
**Keywords:** polymerase chain reaction; chest x-ray, chest HRCT, COVID -19
***Correspondance :** Aziza Ghanie Icksan, MD.
Department of Radiology, Persahabatan Hospital, Jakarta, Indonesia, Faculty of Medicine University Pembangunan Nasional
**E-mail** : azizagicksan@yahoo.com
**Online First :** January 2021

**Abstract**

**Background :** The first case of COVID-19 in Indonesia was recorded in March 2020. Limitation of reverse-transcription polymerase chain reaction (RT-PCR) has put chest CT as an essential complementary tool in the diagnosis and follow up treatment for COVID-19. Literatures strongly suggested that High-Resolution Computed Tomography (HRCT) is essential in diagnosing typical symptoms of COVID-19 at the early phase of disease due to its superior sensitivity (97%) compared to chest x-ray (CXR).
The two cases presented in this case study showed the crucial role of chest CT with HRCT to establish the working diagnosis and follow up COVID-19 patients as a complement to RT-PCR, currently deemed a gold standard.

## Introduction

In late December 2019, a newly emerging infectious disease of unknown origin caused an outbreak in Wuhan, China. The International Committee on Taxonomy of Viruses (ICTV) named the virus SARS-CoV-2 on 11 February 2020 and the disease was announced as COVID-19 by World Health Organization (WHO)[1]. Diagnosis of COVID-19 has been a real challenge, especially in some countries with limited resources and insufficient health system. Indonesia is one of many countries impacted by the virus. The first case was identified in Depok, West Java, on 2 March 2020. It spread to nearby cities, most notably to Jakarta, which has become the epicenter of COVID-19 in Indonesia.
RT-PCR, as a standard reference, has been reported to have some degree of false-negative results caused by some factors including sampling operations, specimens source (upper or lower respiratory tract), sampling timing (different period of the disease development) and Chest CT may be considered as a primary tool for the current COVID-19 detection in epidemic areas[3].

some experts have suggested that chest CT can be regarded as a diagnostic standard of COVID-19[3].The essential aspects of controlling COVID-19 are early diagnosis, early isolation, and early treatment[23]. Recently, some studies reported that chest HRCT has higher sensitivity compared to RT-PCR and CXR[2,3]. Chest HRCT, as a routine imaging tool for pneumonia diagnosis, is relatively easy to do and a fast modality for diagnosis. Chest HRCT provides typical radiologic features in almost allpatients with COVID-19, such as ground-glass opacities (GGO), multifocal patchy consolidation, and/or interstitial changes with a peripheral distribution. The sensitivity of chest CT was great in Wuhan (the most affected city by the epidemic) and the sensitivity values were very close to each

other (97%, 96%, and 99%, respectively). In the regions other than Wuhan, the sensitivity varied from 61 to 98%.[2] Study from Ai et al. showed the sensitivity, specificity, and accuracy of chest CT in indicating COVID-19 infection were 97%, 25%, and 68%[3]. The varieties of the sensitivity results were caused by inter-observer difference interpretation, severity, and disease progression at the time of examination[2].

We looked into the possibility of using chest HRCT as a complement of RT-PCR to diagnose COVID-19, especially during a limited supply chain and unavailability of fast results of RT-PCR and chest CT.

Case Report

Case 1. A 43-year-old female with a history of asthma and pulmonary tuberculosis (TB) presented to the emergency department with moderate fever for three days accompanied by dry cough, myalgia, vomiting, diarrhea, anosmia, and fatigue. Otherwise, the patient looked healthy. Vital signs showed increased body temperature (38.7ºC), slight tachycardia, and normal blood pressure, with the rest physical examination was unremarkable. Initial laboratory results showed normal white blood cell count without lymphopenia. Inflammation marker revealed the increase of C-reactive Protein (CRP) at 40 mg/L, other markers such as Erythrocyte Sedimentation Rate (ESR) and Lactate Dehydrogenase (LDH) within the normal limit (Table 1). Other blood samples taken for NS1 antigen dengue and serology (widal) for typhoid fever were negative.

The CXR (Figure 1) showed fibrosis in the right upper lung zone, consistent with scarred TB. Subsequent HRCT revealed bilateral, multifocal sub-pleural GGO and crazy paving consistent with minimal typical COVID 19 pneumonia (Fig 1 b-d). The nasopharyngeal swab was positive seven days later. Meanwhile, the patient has already been on oseltamivir 2 x 75 mg, chloroquine 2 x 300 mg, and azithromycin 500 mg daily for ten days. The second RT-PCR test 14 days apart showed conversion to negative, but three consecutive nasal and oropharyngeal swabs showed positive results again. The patient's husband was confirmed to have COVID-19 as well and both of them practiced self-isolation in their home, but unfortunately, they were still shared the same room. Contrary to the positive RT-PCR results, the symptoms resolved and the laboratory and inflammation marker turned back to normal. The second HRCT conducted 35 days from the first one revealed complete resolution of the lesion even though RT-PCR was still positive (Fig. 2 a-d).

CXR and HRCT case 1

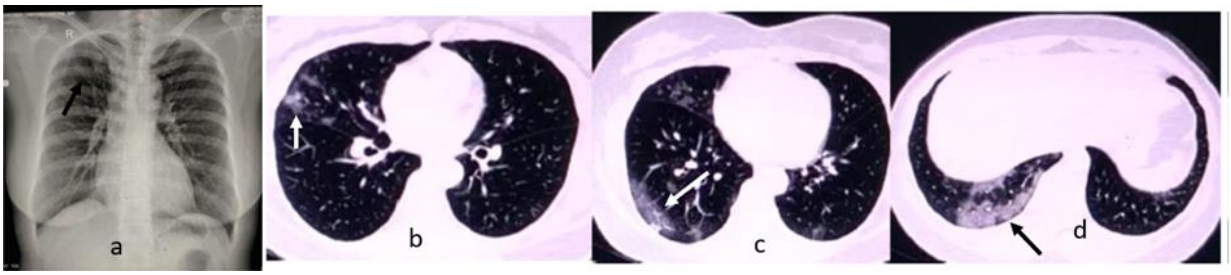


Figure 1. (case 1) CXR shows the right posterior upper lung fibrosis (a). HRCT shows multifocal sub pleural GGO in the middle and posterior right lung lobe (b.c). Subpleural nodule in the left lower lung lobe (head arrow c) and crazy paving found in the right subpleural posterior lung lobe (arrow d) suitable with minimal typical COVID 19

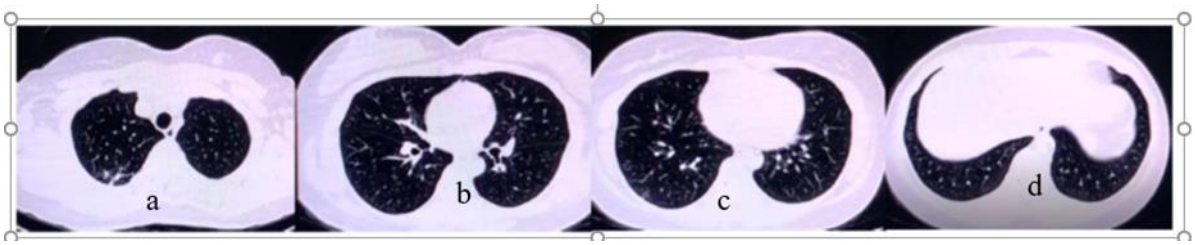


Figure 2. (Case 1) follow up HRCT was done 34 days after first HRCT and all of the lesions were disappear (b.c.d) except right upper posterior lung fibrosis same with old HRCT suggestive sequel TB ( a)

Case 2. A 51 years old male health care worker developed fever symptoms for four days, followed by myalgia, malaise, and dry cough. He was diagnosed with typhoid fever based on a Tubex test result, which increased to four (reference < 2). He was treated for typhoid fever with Ceftriaxone 2g/day intravenously for three days without any improvement. Because the serum antibody for SARS-CoV-2 was positive on days seven, he was recommended to get other examinations, which were nasopharyngeal swab, CXR, and HRCT. CXR (Fig.3a) showed GGO in the right lower lung zone. Four days later, a descriptive finding of the HRCT (Fig 3b-d) showed multifocal sub-pleural GGO, consolidation, and fibrosis both in the right superior and lower lung lobe, suitable to moderate typical pneumonia COVID-19 at the progressive stage. He was treated by standard regimen, including oseltamivir 75 mg twice daily, chloroquine 500 mg twice daily, and azithromycin 500 mg orally for ten days. He continued to do self-isolation at his home. The first two initial and days 14 of RT-PCR swabs were negative. On the $10^{th}$ day, he reported that he had no fever. However, he felt shortness of breath after a mild exercise, which never happened to him. Another chest CT obtained approximately 20 days later showed some resolutions of GGO and consolidation suitable for the convalescence stage (Fig. 4 d-f)

CXR and HRCT case 2.

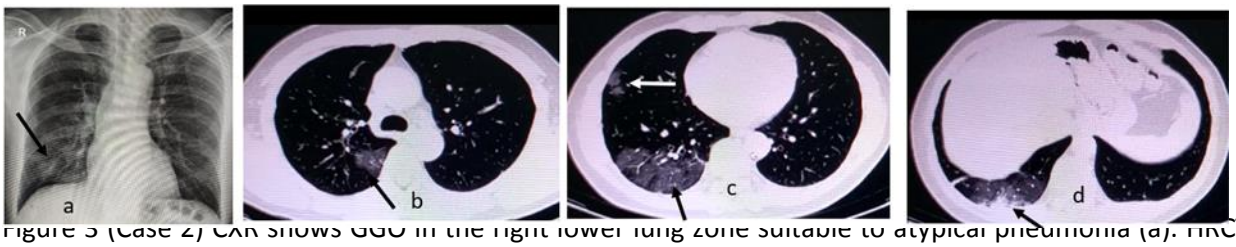


Figure 3 (Case 2) CXR shows GGO in the right lower lung zone suitable to atypical pneumonia (a). HRCT in the same day shows multifocal subpleural GGO (b c), subpleural consolidation and fibrosis in the right superior and lower lung lobe (d) suitable to moderate typical COVID-19 progressive stage

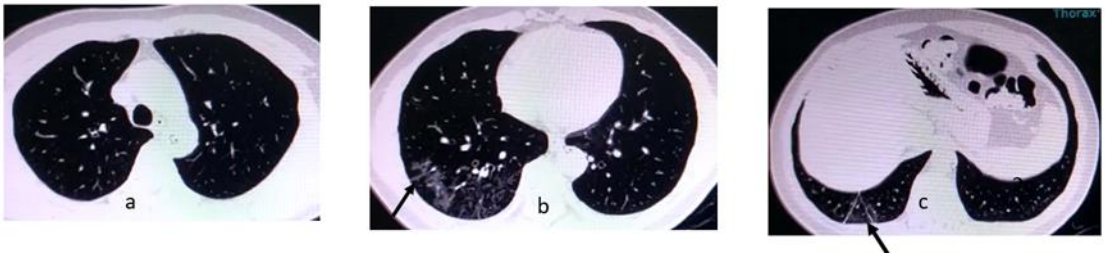


Figure 4. (Case 2) Follow up HRCT in 20 days from the first HRCT shows improvement. Decrease right lower GGO (b). Other lesions disappeared (a.c) suitable for convalescence stage.

## Discussion

Viral nucleic acid test by RT-PCR assay, the current diagnostic criteria, plays a vital role in diagnosing COVID-19, despite its moderate sensitivity and long processing time. A nasopharyngeal swab is the most popular site for obtaining a viral sample, with sensitivity reported from previous reports ranging from 30-60%[4,5]. Several factors that can influence the RT-PCR test are the sampling procedure, the disease phase, and the detection kit's performance[6]. Supplementing a non-invasive imaging modality such as chest CT will enhance the diagnostic interpretation in suspected cases[3].

In case no 1, the first HRCT carried out on the third day of symptoms showed bilateral, multifocal sub-pleural GGO and crazy paving consistent with minimal typical COVID 19 pneumonia. The therapy was started based on the clinical, inflammatory marker, and HRCT report because the RT PCR result was only positive in the next seven days[7,8]. The subsequent HRCT was done 34 days after the first HRCT and all of the lesions have disappeared. According to several studies, COVID 19 patients have a GGO image on chest CT at the early stages of the disease, which is from day one to four of infection, then at the period of consolidation during the disease progression from day five to 13, and at the peak stage of the disease. Additionally, several patterns such as GGO, consolidation, crazy paving patterns, linear curves, and parenchymal bands can be found at the peak stage of the disease. During recovering phase of COVID-19, the lungs' initial finding on chest CT scan is a small subpleural GGO that grows larger with a crazy paving pattern and initial consolidation. Lung consolidations increase until two weeks of the first symptoms and the lesions were gradually absorbed,

leaving extensive GGO and sub-pleural parenchymal bands over the time[9,10].

A recent report regarding SARS-CoV-2 stated that about 21,4% of patients experienced prolong nucleic acid detection by RT-PCR test for SARS CoV-2 after a negative result.[3] It was reported that RT-PCR conversion's median time was 19,5 days (range 17-24 days). Our female patient's (case1) RT-PCR positivity timeline from the first to the fourth swab nasopharyngeal was 35 days. Previous studies in SARS-CoV-1 and MERS-CoV indicated that viral RNA could be detected in clinical specimens of patients for more than 30 days after the onset of symptoms[2]. Another study reported a certain number of COVID-19 patients might experience a prolonged nucleic acid conversion regardless of symptoms or radiology. Trace of viral detected by RT-PCR was not necessarily correlated with the ability of transmission[3], because upper respiratory tract was thought to be the main target of SARS-CoV-2 which is often located higher in the upper respiratory tract specimen. This should potentially be caused by prolonged viral shedding in the upper and lower respiratory tract[2,5]. Two negative SARS-CoV-2 RNA PCR tests, at least 24 hours apart, was recommended by the WHO as one of several criterias to release COVID 19 patient from isolation. Prolonged periods of detectable SARS-CoV-2 RNA has suggested a sustained viral replication in some kinds of host cells in patients with COVID-19.

RT-PCR conversion was compatible with the improvement of radiological abnormalities in majority cases. However, extensive studies are urgently needed to explore the duration of infectivity[2]. There is a discrepancy in CT and RT-PCR findings, as there are patients who have positive RT-PCR results without lesion on initial chest CT[1]. At the same time, some case evaluations showed the existence of about 3.5% of disease progression after RT-PCR results turning negative. Even though, after recovery, radiologic abnormalities showed mark improvement, but fibrotic changes remain the same.[1,5] Typical chest CT findings had a high sensitivity for initial false-negative RT-PCR, asymptomatic, and mild symptoms patients. Our second case, the male patient was treated by COVID 19 standard regimen based on the clinical symptoms, typical HRCT findings and positive serum antibody for SARS-CoV-2 result, despite negative RT-PCR result.

From another review, 5% of patients had initial false-negative RT-PCR results and then turned positive after the test are repeated. Many cases with initial false-negative RT-PCR have been reported to have typical COVID 19 chest CT[9]. Although the RT-PCR offers a valuable method in the diagnostic process, we have to be careful in interpreting the duration of viral shedding and infectivity status because it does not distinguish between infectious and non-infectious virus.

**Recommendation**

These two cases proved the pivotal role of thoracic HRCT scan in diagnosing and following up the case of confirmed COVID-19. As RT-PCR has some limitations, we suggest implementing multiple modalities besides RT-PCR, including clinical features, serial chest HRCT, an inflammation marker, antibody testing, and perhaps lung function test. Chest HRCT can be used in the management of diagnosing COVID-19 as well as follow up treatment.

Table 1. Clinical and laboratory findings

| | Patient 1 | Patient 2 | Reference |
|---|---|---|---|
| Sex | Female | Male | |
| Age | 43 | 51 | |
| Comorbidities | Asthma | | |
| Symptoms | | | |
| Fever | yes | yes | |
| Cough | yes | yes | |
| Nausea | yes | no | |
| Malaise | yes | yes | |
| Anosmia | yes | no | |
| Laboratory results | | | |
| Haemoglobin (g/dL) | 13.3 | 13.6 | 13.2 – 17.3 |
| Thrombocyte ($10^3$/uL) | 185 | 149 | 150 - 440 |
| Leukocyte ($10^6$/uL) | 4.9 | 3.2 | 3.8 – 10.6 |
| Lymphocyte (%) | 32 | 33 | 25 - 40 |
| Eosinophil (%) | 0 | 1 | 2 - 4 |
| Monocyte (%) | 21 | 14 | 2 - 8 |
| CRP (mg/L) | 40 | 80 | < 5 |
| ESR (mm/hr) | 26 | 62 | 0 – 30 |
| LDH (U/L) | 349 | 507 | < 480 |
| Therapy | | | |
| Oseltamivir | yes | yes | |
| Chloroquine | yes | yes | |
| Azitromycine | yes | yes | |
| RT-PCR | +.-,+,+,+ | -,-,- | |
| Antibody test | Non-reactive (14 days) | Reactive twice (7 and 14 days) | |

**References :**


1. Coronavirus Resource Center [Internet]. Cited [2020 Apr 19]. Available from: https://www.Coronavirus.jhu.edu/map.html.
2. Xu B, Xing Y, Peng J, Zheng Z, Tang W, Sun Y et al. Chest CT for detecting COVID-19: a systematic review and meta-analysis of diagnostic accuracy. Eur Radiol.2020.5;1-8.
3. Ai T, Yang Z, Hou H, Zhan C, Chen C, Lv W et al. Correlation of Chest CT and RT-PCR testing in Coronavirus Disease 2019 (COVID-19) in China: a report of 1014 cases.Radiology. 2020;1-23.
4. Feng Y, Ling Y, Bai T, Xie Y, Huang J, Li J et al. COVID-19 with different severity: A multi-center study of clinical features. Am J Respir Crit Care Med. 2020:4: 1-53.
5. Atkinson B. Petersen E. SARS-CoV-2 shedding and infectivity. Lancet. 2020;395(10233):1339-40.
6. Xiao AT, Tong YX, Zhang S. False-negative of RT-PCR and prolonged nucleic acid conversion in COVID-19: Rather than recurrence. Jour Med Virol.2020;4:1-6.
7. Wang L, Gao Y, Lou L-L, Zhang G. The clinical dynamics of 18 cases of COVID-19 outside of Wuhan,China. Eur Respir J.2020;in press.
8. Koo HJ, Lim S, Choe J, Choi SH, Sung H, Do KH. Radiographic and CT features of viral pneumonia. Radiographics. 2018;38:719-39.
9. Kanne JP. Chest CT findings in novel Corona virus 2019 ( 2019-nCOV) infections from Wuhan, China : key point for the radiologist. Radiology 2020;4.295(1):16-17.
10. Pan F,Ye T, Sun P, Gui S, Liang B, Lingli L et al. Time course of lung changes on Chest CT during recovery from Coronavirus Disease 2019 (COVID-19). Radiology.2020;295:715–21.


Conflict of interests: The authors declare that they have no competing interest

Contributions: All the authors contributed equally for the conception or design of the work; the acquisition, analysis, or interpretation of data for the work; drafting the work or revising it critically for important intellectual content; final approval of the version to be published. All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Consent for publication: The patients gave their written consent to use their personal data for the publication of this case report and any accompanying images. The patient understands that their name and initials will not be published.