CT Scan Finding Characteristics of Confirmed Covid-19 Patients Based on Clinical Symptom Onset Patterns

by Dewi Roziqo

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CT Scan Finding Characteristics of Confirmed Covid-19 Patients Based on Clinical Symptom Onset Patterns

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Abstract

Chest computed tomography (CT) scan is one of the main modalities to detect COVID-19 infection. Several CT scan findings are the hallmark to rapidly detect suspected COVID-19 infection, therefore timely treatment could be administered. This study aims to describe chest CT scan findings of confirmed COVID-19 patients based on clinical symptom onset patterns.

This study is a descriptive study with a retrospective design in confirmed COVID-19 patients. Data regarding characteristics of chest CT scan findings and the patient's history including clinical symptoms onset were collected.

There were 123 subjects in this study. The study data were categorized into modified clinical symptom onset patterns which were early, progressive, peak, absorption, and advanced phases. Most of male (57%) and female (43%) patients that were admitted to the hospital were in absorption phase of the disease with fever, cough, and dyspnea as the most prevalent symptoms. Chest CT scan findings of absorption phase included GGO (ground glass opacity) in 28 patients (76%), crazy paving pattern in 18 patients (49%), consolidation in 22 patients (59%), and fibrosis in 31 patients (84%). Chest CT scan findings of confirmed COVID-19 patients vary depending on the phase of the disease. Risk factors and secondary bacterial infection may contribute to long-term persistence of symptoms.

Keywords: *COVID-19, chest CT scan, clinical symptom onset patterns*

Introduction

The COVID-19 disease has symptoms similar to the common cold infection with an incubation period of about 2-14 days, therefore most cases go undetected and causes fast-growing transmission. Prompt diagnosis is essential to help prevent this disease transmission.(1) WHO and Center for Disease Control (CDC) guidelines stated that chest computed tomography (CT) scan is one of the main modalities in detecting COVID-19 infection. The typical chest CT scan findings of a patient infected with COVID-19 causing pneumonia are multiple areas of bilateral lobular and subsegmental consolidation and ground-glass opacity (GGO).(2) These findings are the key to rapidly detect a suspected COVID-19 infection, therefore timely treatment could be administered and could prevent further transmission.

Studies regarding correlation between symptom onset in COVID-19 patients and CT scan findings has been conducted by several researchers. A study by Pan

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et al.,2020, examined the time course of pulmonary changes on chest CT scans during recovery from COVID-19 pneumonia and divided them into four stages of chest CT scan findings based on the quartiles of the time course from day 0 to day 26. In stage 1 (early stage: 0-4 days) GGO was found; in stage 2 (progressive stage: 5-8 days) GGO was scattered with enhanced crazy-paving pattern findings; in stage 3 (peak stage: 9-13 days) consolidated consolidation, scattered GGO, crazy-paving pattern, and residual parenchymal bands were found; and in stage 4 (absorption stage: >14 days) the consolidation was gradually absorbed and no longer crazy-paving pattern was found.[3] This study aims to describe chest CT scan findings of confirmed COVID-19 patients based on clinical symptom onset patterns.

Methods and Materials

Study Design

This is a descriptive study with a retrospective design that used medical records and the examination results of non-contrast chest CT scan from patients with confirmed COVID-19 who were treated at Dr. Soetomo Surabaya General Hospital, Surabaya, Indonesia from June to October 2020.

Data Collection

Researchers identified medical record and history data of confirmed COVID-19 patients. The collected data were clinical symptoms, comorbid, and symptom onset patterns, which were calculated from the start of the patient's symptom until a non-contrast chest CT scan was performed. Evaluation of CT scan finding was conducted by 2 experimented radiologists senior (mean 10 years of experience) and one resident (mean 3 years of experience) using standardized CT reports. For cases with controversial results, two radiologists with more than 10 years experience jointly reviewed and evaluated the result.

Imaging Protocols

All patients were adults and non-pregnant who underwent non-contrast chest CT scan to detect COVID-19 pneumonia in supine position during full inspiration. A total of 69 patients were subjected to CT scans in the Emergency Room using multi-detector 128 slice CT scan (Toshiba Aquilion Vision) and 54 patients had CT scans at the Radiodiagnostic Installation using multi-detector 128 slice CT scan (Philips) and 16 slice CT scan (Hitachi). The protocol used was 120 kV voltage tube, automatic tube current (120–380) mA, 5 mm thickness, 0.5 mm slice interval, 0-5 second rotation speed, and 1-0.828 helical distance.

Clinical and Imaging Interpretation

Identification of clinical symptom data categorized by clinical syndrome according to WHO, which includes: mild disease/non-specific symptoms, mild pneumonia, severe pneumonia, ARDS, sepsis and septic shock.[4] The analysis results were reported using The Covid-19 Reporting and Data System (CO-RADS) category.[5] Severity was assessed using a visual scoring system of each lobe involved. The scores for all lung lobes are summed to show lung involvement severity.[6] This study used a modified assessment of per-lobe severity. Score 0: if there is no lesion or 0%, score 1: when the estimated number of lesions visually is 1% to 25%, score 2: when the estimated number of lesions visually is 26% to 50%, score 3: when the estimated number of lesions is visual 51% to 75%, score 4: when the estimated number of lesions visually is more than 75%. The final results were categorized into mild (total score 7 or less), moderate (total score between 8 and 17), and severe (total score 18 or more).

Data Analysis

The collected data were categorical, which were processed using SPSS 21 software and then presented in tabular form with percentages (%).

Results

The study was conducted on 123 study subjects of COVID-19 pneumonia patients. The study data were

categorized into modified clinical symptom onset patterns. The categories included initial (0-4 days), progressive (5-8 days), peak (9-13 days), absorption (14-30 days), and advanced phase (>30 days).

Subject Characteristics Based on Clinical Symptom Onset Patterns

The age range of study subjects was 17-91 years, with a mean age of 52 years. Based on the characteristics of clinical symptom onset patterns, most patients were included in absorption phase with an age range of 32-70 years (mean= 55±9 years) with 37 patients. The number of subjects who were male was 70 people (57%), which was more than female subjects with 53 people (43%). In initial, peak, absorption, and advanced phases most patients were male with 18 (56%), 9 (64%), 21 (57%), and 10 (67%) patients, respectively. While in progressive phase most patients were female with 13 (52%) patients.

The 3 most common clinical symptoms were fever (66%), cough (70%), and dyspnea (58%). Fever was found mostly in initial and progressive phase, with 24 (75%) and 21 (84%) patients, respectively. Cough was mostly found in peak phase with 11 (79%) patients, while in absorption and advanced phase the number of patients who experienced cough and dyspnea were similar, with 28 (76%) and 10 (67%) patients in each phase, respectively. The study subjects in this study had variable comorbid, although some patients had no concomitant comorbid. In early, absorption, and peak phase, the most frequent comorbid was Diabetes Mellitus (DM) with 10 (31%), 11 (30%), and 3 (20%) patients, respectively. In progressive and peak phase, the most frequent comorbid was hypertension (HT), with 10 (40%) and 6 (43%) patients, respectively.

The study subjects were categorized into clinical syndromes based on WHO criteria. The results showed that most patients in early and progressive phase had mild pneumonia with 13 (41%) and 11 (44%) patients, respectively. In peak phase, there were the same number of patients for mild and severe pneumonia, which were 4 (29%) patients. Most patients in absorption and advanced phase had severe pneumonia, with 10 (27%) and 5 (33%) patients, respectively.

The subject characteristics are outlined in Table 1.

Table 1. Subject Characteristics

Characteristics	Early phase N (%)	Progressive phase N (%)	Peak phase N (%)	Absorption phase N (%)	Advanced phase N (%)	Total N (%)
Gender						
Male	18 (56)	12 (48)	9 (64)	21 (57)	10 (67)	70 (57)
Female	14 (44)	13 (52)	5 (36)	16 (43)	5 (33)	53 (43)
Age (Years)						
Mean ± Standard Deviation	43 ± 15	49 ± 16	59 ± 13	55 ± 9	59 ± 8	52 ± 14
Age Range	17 - 74	32 - 91	35 - 85	32 - 70	45 - 70	17 - 91
Symptoms						
Fever	24 (75)	21 (84)	8 (57)	19 (51)	9 (60)	81 (66)
Cough	17 (53)	20 (80)	11 (79)	28 (76)	10 (67)	86 (70)
Dyspnea	13 (41)	14 (56)	6 (43)	28 (76)	10 (67)	71 (58)
No Symptom	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.8)
Comorbid						
Chronic Kidney Disease (CKD)	2 (6)	3 (12)	0 (0)	2 (5)	2 (13)	9 (7)
DM	10 (31)	7 (28)	5 (36)	11 (30)	3 (20)	36 (29)
HT	7 (22)	10 (40)	6 (43)	7 (19)	2 (13)	32 (26)
Obesity	1 (3)	5 (20)	0 (0)	1 (3)	1 (7)	8 (6)
Malignancy	3 (9)	2 (8)	0 (0)	0 (0)	1 (7)	6 (5)
Others	13 (41)	4 (16)	2 (14)	8 (22)	5 (33)	32 (26)
No Comorbid	9 (28)	9 (36)	7 (50)	15 (40)	6 (40)	46 (37)
Clinical Syndrome (WHO)						
None	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.8)
Mild Disease / Non-Specific Symptoms	10 (31)	2 (8)	3 (21)	4 (11)	1 (7)	20 (16)
Mild Pneumonia	13 (41)	11 (44)	4 (29)	6 (16)	3 (20)	37 (30)
Severe Pneumonia	0 (0)	8 (32)	4 (29)	10 (27)	5 (33)	27 (22)
ARDS	3 (9)	0 (0)	2 (14)	7 (19)	4 (27)	16 (13)
Sepsis	3 (9)	1 (4)	0 (0)	6 (16)	0 (0)	10 (8)
Septic Shock	2 (6)	3 (12)	1 (7)	3 (8)	1 (7)	10 (8)

Characteristics of Chest CT Scan Findings by Clinical Symptom Onset Pattern

The results of this study showed that the most common characteristics in early phase were GGO in 26 (81%) patients, crazy paving pattern on 8 (25%) patients, consolidation on 14 (44%) patients, and fibrosis on 23 (72%) patients. In progressive phase there were GGO in 17 (68%) patients, crazy paving pattern in 11 (44%) patients, consolidation in 15 (60%)

patients, and fibrosis in 22 (88%) patients. In peak phase, there were GGO in 11 (79%) patients, crazy paving pattern in 4 (29%) patients, consolidation in 7 (50%) patients, and fibrosis in 10 (71%) patients. In absorption phase there were GGO in 28 (76%) patients, crazy paving pattern in 18 (49%) patients, consolidation in 22 (59%) patients, and fibrosis in 31 (84%) patients. In advanced phase there were GGO in 8 (53%) patients, crazy paving patterns and consolidation in 1 (7%) patient each, and fibrosis in 12 (80%) patients. Bronchiectasis and bronchiolectasis were commonly found in absorption and advanced phases. The most common distribution for chest CT scan findings were bilateral predominantly peripheral in all clinical symptom onset patterns. Table 2 outlines these chest CT scan findings.

Table 2. Characteristics of Chest CT Scan Findings by Clinical Symptom Onset Pattern

Chest CT Scan Findings	Early phase N (%)	Progressive phase N (%)	Peak phase N (%)	Absorption phase N (%)	Advanced phase N (%)	Total N (%)
Characteristics						
GGO	26 (81)	17 (68)	11 (79)	28 (76)	8 (53)	90 (73)
Crazy Paving Pattern	8 (25)	11 (44)	4 (29)	18 (49)	1 (7)	42 (34)
Consolidation	14 (44)	15 (60)	7 (50)	22 (59)	1 (7)	59 (48)
Halo sign	4 (12)	2 (8)	2 (14)	1 (3)	1 (7)	10 (8)
Reverse halo sign	2 (6)	1 (4)	1 (7)	2 (5)	1 (7)	7 (6)
Air bubble sign	0 (0)	0 (0)	1 (7)	3 (8)	0 (0)	4 (3)
Reticular pattern	2 (6)	3 (12)	0 (0)	1 (3)	2 (13)	8 (6)
Nodule	1 (3)	1 (4)	2 (14)	3 (8)	3 (20)	10 (8)
Fibrosis	23 (72)	22 (88)	10 (71)	31 (84)	12 (80)	98 (80)
Bronchiectasis	2 (6)	4 (16)	2 (14)	20 (54)	8 (53)	36 (29)
Bronchiolectasis	2 (6)	3 (12)	3 (21)	22 (59)	7 (47)	37 (30)
Pleural efusion	3 (9)	2 (8)	1 (7)	4 (11)	2 (13)	12 (10)
Pleural thickening	2 (6)	5 (20)	2 (14)	7 (19)	2 (13)	18 (15)
Distribution						
Bilateral predominantly peripheral	20 (62)	20 (80)	13 (93)	35 (95)	12 (80)	100 (81)
Unilateral predominantly peripheral	8 (25)	3 (12)	0 (0)	0 (0)	0 (0)	11 (9)
Bilateral predominantly central	1 (3)	1 (4)	0 (0)	0 (0)	0 (0)	2 (2)
No predominance	1 (3)	1 (4)	0 (0)	0 (0)	1 (7)	3 (2)
No lesion	2 (6)	0 (0)	1 (7)	2 (5)	2 (13)	7 (6)

Characteristics of Chest CT Scan Findings by CO-RADS Categories

In CO-RADS 1 group, most patients showed normal lung features and only 1 (14%) had fibrosis. In CO-RADS 2 category group, most patients had fibrosis and pleural thickening, with 7 (78%) and 4 (44%) patients, respectively. In CO-RADS 3 category group, most patients had consolidation and GGO with 4 (80%) and 3 (60%) patients, respectively. In CO-RADS 4 group, most patients had GGO and consolidation with 11 (85%) and 8 (61%) patients, respectively. In CO-RADS 5 group, most patients had GGO and fibrosis, with 35 (85%) and 33 (80%) patients, respectively. Finally, in CO-RADS 6 group, most patients had fibrosis and GGO, with 45 (94%) and 40 (83%) patients, respectively. All CO-RADS categories mostly had bilateral predominantly peripheral in their finding's distribution. Table 3 outlines these findings.

Table 3. Characteristics of Chest CT Scan Findings by CO-RADS Categories

Chest CT Scan Findings	CO-RADS						Total N (%)
	C1 N (%)	C2 N (%)	C3 N (%)	C4 N (%)	C5 N (%)	C6 N (%)	
Mean severity score ± standard deviation	0 ± 0	2 ± 1	5 ± 3	5 ± 4	10 ± 5	10 ± 5	8 ± 5
Characteristic							
GGO	0 (0)	1 (11)	3 (60)	11(85)	35 (85)	40 (83)	90 (73)
Crazy Paving Pattern	0 (0)	1 (11)	0 (0)	3 (23)	21 (51)	17 (35)	42 (34)
Consolidation	0 (0)	1 (11)	3 (60)	8 (61)	23 (56)	24 (50)	59 (48)
Halo sign	0 (0)	0 (0)	0 (0)	2 (15)	6 (15)	2 (4)	10 (8)
Reverse halo sign	0 (0)	1 (11)	0 (0)	1 (8)	4 (10)	1 (2)	7 (6)
Air bubble sign	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (8)	4 (3)
Reticular pattern	0 (0)	1 (11)	0 (0)	2 (15)	3 (7)	2 (4)	8 (6)
Nodule	0 (0)	1 (11)	0 (0)	1 (8)	2 (5)	6 (12)	10 (8)
Fibrosis	1 (14)	7 (78)	4 (80)	8 (61)	33 (80)	45 (94)	98 (80)
Bronchiectasis	0 (0)	2 (22)	0 (0)	1 (8)	6 (15)	27 (56)	36 (29)
Bronchiolectasis	0 (0)	0 (0)	1 (20)	0 (0)	3 (7)	33 (69)	37 (30)
Pleural efusion	0 (0)	3 (33)	1 (20)	4 (31)	1 (2)	3 (6)	12 (10)
Pleural thickening	1 (14)	4 (44)	1 (20)	1 (8)	2 (5)	9 (19)	18 (15)
Distribution							
Bilateral predominantly peripheral	2 (25)	1 (12)	1 (20)	9 (69)	40 (98)	47 (98)	100 (81)
Unilateral predominantly peripheral	0 (0)	5 (62)	3 (60)	3 (23)	0 (0)	0 (0)	11 (9)
Bilateral predominantly central	0 (0)	0 (0)	1 (20)	0 (0)	1 (2)	0 (0)	2 (2)
No predominance	1 (12)	0 (0)	0 (0)	1 (8)	0 (0)	1 (2)	3 (2)
No lesion	7 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	7 (6)

Discussion

The typical findings of a patient infected with COVID-19 that causes pneumonia on a chest CT scan are multiple areas of bilateral lobular and subsegmental consolidation and ground-glass opacity (GGO).[2] These findings are the key to rapidly detect a suspected COVID-19 infection, therefore a timely treatment could be provided and prevent further infection transmission. CT scan findings in this study included GGO, crazy paving pattern, consolidation, halo sign,

inverted halo sign, bubble air sign, reticular pattern, nodule, fibrosis, bronchiectasis, bronchiolectasis, pleural effusion and pleural thickening. These findings were in accordance to several previous studies.[3,7,8] Based on clinical symptom onset patterns, the findings in progressive, peak, and absorption phases in this study were mostly GGO, crazy paving pattern, consolidation, and fibrosis, with mostly bilateral predominantly peripheral distribution. These were similar to several previous studies which reported the presence of GGO with and without consolidation in subpleural visceral with peripheral ($p<0.001$) or bilateral multifocal distribution.[3,8,9] The virus ability to reach terminal bronchi and alveoli might be the main cause of this peripheral distribution.[10] Fibrosis was found in the early phase of this study. However, fibrosis due to COVID-19 usually occurs in chronic or healing phase.[8] It could be assumed that this finding is not a COVID-19 infection process and existed before COVID-19 infection. Statistically, Indonesia is a tuberculosis endemic area with a prevalence of bacteriological confirmed tuberculosis in 2013-2014 of 759 per 100,000 population aged 15 years and over.[11]

In this study, the lung severity was in line with the CO-RADS category. Lung severity scoring progresses with clinical onset. Lung severity scoring in initial phase was mild, then increased in progressive, peak, and up to absorption phase, and then decreased in advanced phase. Study by Guan et al.,2019 compared chest CT scan findings between progressive and recovery phase. From this study, several alterations were found in progressive phase: rounded image of GGO developed into uneven GGO, increased consolidation, and sometimes pleural effusions. In recovery phase, the crazy paving pattern and air bronchogram findings decreased significantly.[12] In this study, there were prolonged clinical symptoms and CT scan findings that still showed GGO, consolidation and crazy-paving patterns in absorption (14-30 days) and advanced (> 30 days). We assumed that there are several risk factors for these events. In this study, it was found that the average age of study subject was 52 years (SD±14), with mostly male patients in all phases of clinical symptom onset pattern. We also noted the presence of comorbid factors such as DM, HT, CKD, obesity and other comorbidities. In absorption and advanced phases, it was found that most of patients still had cough and dyspnea. This is in accordance to a study by Miyazato et al.,2020 who reported prolonged or delayed symptoms of coronavirus disease. The findings of this study were dyspnea, fatigue, cough, dysosmia, and dysgeusia, which lasted more than 120 days after symptom onset.[13]

A meta-analysis study by Biswas et al.,2021 estimated risk factors such as sex, age, or comorbidity with mortality in COVID-19 patients, and proved that male patients aged ≥50 years or that had comorbidities was significantly associated with an increased mortality risk. Age ≥50 years and male sex have higher expression of angiotensin-converting enzyme 2 (ACE2) regulated by male sex hormones, making men more prone of SARS-CoV-2 infection and had worse symptoms. Another hypothesis stated that women could fight the development of SARS-CoV-2 infection due to X-linked heterozygous alleles, which is called sex dimorphisms.[14] Comorbidity is associated with decreased immune function, as in DM patients. Natural immune function is substantially reduced, which could restrict the body from producing antibodies against any infection. ACE-2 is highly expressed in lungs, intestines, kidneys, and blood vessels epithelial cells and is predominantly upregulated in DM or HT patients treated with ACE inhibitors (ACEIs) and angiotensin II type-I receptor blockers (ARBs).[15]

Secondary bacterial infection might also be the cause of prolonged symptoms. A study by Zhang et al.,2020 reported that COVID-19 patients who received invasive mechanical ventilation or were in critical condition had a higher likelihood of developing secondary infection ($p<0.0001$). The most common infections are respiratory, haematogenous and urinary tract infections. Secondary infection will

lead to a higher mortality rate.[15]

This study has some limitations. Medical intervention as well as comorbid histories of confirmed patients with concomitant infection might interfere the CT scan findings. A history of comorbid such as malignancy, CKD, and others could also raise a bias with overlapped CT findings. We have a lack of standardized timeline of evaluation in overall patients, since the CT scan has not been as the routine protocol in patient's evaluation. CT scanning is perfomed mainly to follow up the disease's progression. Some cases of this study obtained were in the state of prolonged disease onset, approximately from 30-120 days.

Conclusion

CT scans are able to reveal distinct confirmed COVID-19 findings that are variable according to clinical symptom onset. The typical finding in early phase is GGO with a bilateral predominantly peripheral distribution. The next phases have variable findings, with GGO, crazy paving pattern, and consolidation as the most common findings with bilateral predominantly peripheral distribution. This study also showed that most patients were in absorption phase with dominant findings of fibrosis. However, GGO, consolidation, and crazy paving patterns were still found. Cough and dyspnea were still found in this phase. These results show long-term COVID-19 findings from both the symptoms and CT scan findings.

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