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Frequency of Chest Computed-Tomography Scan Findings in Patients with COVID-19 and the Characteristic Findings According to the Duration of Infection

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Abstract

Background: Over the last two years the world has been facing a pandemic caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), with initial cases mainly emerging from Wuhan, China. Real time Reverse Transcription-Polymerase Chain Reaction (RT-PCR) test is the standard of diagnosis for the virus. RT-PCR may be negative in the early phase of infection from the virus; however the viral shedding in the infected individual can still be a source of transmission to others during this time. Thus, Computed Tomography scan (CT scan), has emerged as a modality of early diagnosis of COVID-19 infection in RT-PCR negative patients.

Methods: A cross-sectional prospective study of 70 patients was conducted in the department of medicine at The Aga Khan university hospital, Karachi. Pakistan. Age, gender, duration of symptoms, RT-PCR of lower respiratory tract secretions, number of days between symptom onset and thedate of first positive test and the date on which CT scan was done with its findings were obtained.

Results: A total of 70 patients, 48 (68.6%) males and 22 (31.4%) females were included in the study. Mean age of patients was 57.3 ± 13.3; range: 25-84. The symptoms at presentation were fever (81.4%), shortness of breath (74.3%) and cough (57.1%) respectively. Ground glass opacity 31 (44.3%) was the most common finding on CT scan. The right lower lobe was most commonly involved in 59 (84.3%) patients. The total lobes mean severity score 7.5 ± 5.4; range: 0-20. Both ground glass opacity and consolidation were found early in the course of disease even before symptom onset.

Conclusion: The diagnostic findings in this study has illustrated that the characteristics of CT findings in COVID-19 are related to the time course of the infection. It can aid in diagnosing the disease when clinical suspicion is high and RT-PCR test for COVID-19 is negative. Additionally in case such patients are hypoxic they can be offered treatment such as remedesivir, which works best if given within a window period of 10 days from the onset of symptoms of COVID-19.

Keywords: COVID-19; RT-PCR; SARS-CoV-2; Remedesivir

Abbreviations: CT scan: Computed Tomography; COVID-19: Corona virus disease 19; RT-PCR: Reverse Transcriptase Polymerase Chain Reaction; GGO: Ground Glass Opacity

Introduction

In December 2019, a novel coronavirus, designated the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), was first reported in China [1]. The disease has spread quickly around the world since then. On 30th January 2020, the World Health Organization (WHO) declared the COVID-19 outbreak as the sixth public health emergency of international concern, following H_1N_1 (2009), polio (2014), Ebola in West Africa (2014), Zika (2016) and Ebola in the democratic republic of Congo (2019) [2]. COVID-19 was declared a pandemic by the WHO in March 2020 [3]. Millions of people are affected worldwide and the number is growing rapidly due to new outbreaks secondary to rapidly changing variants.

SARS-CoV-2 is part of the family of Coronaviridae. The main presenting features are fever, flu-like illness and cough. It is mostly known to affect the respiratory tract and in severe cases can cause dyspnea, and even progress to acute respiratory distress syndrome with bilateral infiltrates on chest imaging. Asymptomatic individuals also called carriers can transmit SARS-CoV-2 to other individuals. Some asymptomatic carriers can progress directly to ARDS. Real time Reverse Transcription Polymerase Chain Reaction (RT-PCR) testing for SARS-CoV-2 is the standard of diagnosis [4]. However, it has its limitations. The high false-negative result rate of SARS-CoV-2 RT-PCR causes the infected individual to miss the best timing for proper treatment and isolation which can cause spread of the disease to other individuals. While being highly specific the sensitivity of RT-PCR remains variable at 60-78% [5].

Due to lack of a better alternative chest imaging has emerged as a modality of great importance for the diagnosis and management of patients with COVID-19. Plain chest radiographs mostly provide non-specific findings or be

completely normal especially early in the course of the disease. Computed Tomography scan chest (CT scan), especially High Resolution Computed Tomography scan of the chest (HRCT chest) is however very useful for the early diagnosis of COVID-19 infection. CT scan is more sensitive than RT-PCR testing and many patients with an initially negative RT-PCR testing have been observed to have typical or atypical CT findings for COVID-19 [6-9]. CT scans can also show changes in asymptomatic patients with COVID-19. A study of 126 patients with COVID-19 showed that with serial CT examinations, disease progression and course can be comprehensively understood. Thus CT scan not only plays an important role in the diagnosis of the illness but also provides a non-invasive evaluation of disease progression [10].

Materials and Methods

The study is a cross-sectional, prospective study conducted in the department of medicine of The Aga Khan university Hospital based in Karachi, Pakistan. Ethical approval was obtained from the institutional ethical review committee (No: 2020-4996-11235) before starting the study. The total duration of study was 3 months from 1st June 2020 to 31st August 2020 [11]. Seventy patients were enrolled in the study as per our inclusion criteria. Patients with pre-existing interstitial lung disease were excluded from our study. In addition to basic demographic data such as age and gender, patients symptoms and symptom duration, Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) of respiratory secretions obtained by broncho-alveolar lavage, endotracheal aspirate, nasopharyngeal swab, or oropharyngeal swab, number of days between symptom onset or date of the first positive RT-PCR test and the day on which first Computed Tomography scan (CT scan) was done and the CT scan chest findings including the following:

- Ground glass opacities,
- Consolidation,
- Laterality of ground glass opacity and consolidation,
- Characteristics of opacity including rounded, linear and crazy paving,
- Airway abnormalities like air wall thickening and bronchiectasis,
- Presence of other abnormalities like pneumothorax, pneumomediastinum, mediastinal lymphadenopathy, pleural effusion, tree in-bud appearance, presence of cavitation, fibrocystic changes, pleural effusion and cardiomegaly,
- Number of lobes involved,
- Degree of involvement of each lobe,
- Total severity score based on the sum of involvement of all lobes [12].

Each of the five lung lobes were assessed for degree of involvement and classified as: None (0%), minimal (1-25%), mild (26-50%), moderate (51-75%), or severe (76-100%). No involvement corresponded to a lobe score of 0, minimal to a lobe score of 1, mild to a lobe score of 2, moderate to a lobe score of 3, and severe to a lobe score of 4 [13]. An overall lung "total severity score" was reached by summing the five lobe scores (range of possible scores, 0-20) [14].

The time duration between the symptom onset and/or first positive COVID-19 test and date of changes on the CT scan was obtained. The findings on CT scan were then grouped according to the phases of illness which included:

- **Early phase:** Asymptomatic with positive RT-PCR or the maximum duration of symptoms from onset equal to 5 or less than 5 days.
- **Intermediate phase:** Duration of symptoms between 6-9 days.
- **Late phase:** Duration of symptoms 10 to 14 days.

Statistical analysis

The analysis was performed using SPSS 21.0. Descriptive statistics of patients' demographics, clinical results were reported as numbers and relative frequencies. Frequencies of CT scores were calculated and compared with other clinical variables [15]. The Pearson correlation coefficient test was used for correlations, and p value less than 0.05 was defined statistically significant.

Results

Descriptive characteristic of patients: A total of 70 patients (48 male and 22 female) were included in the study [16]. Mean age of patients was 57.3 ± 13.3; range: 25-84. The most common symptom at presentation was fever (81.4%), shortness of breath (74.3%) and cough (57.1%) (Table 1).

Table 1: Descriptive characteristics of study population (n=70).

Age, years	57.3 ± 13.3; range: 25-84
Gender	
Male	48 (68.6)
Female	22 (31.4)
Symptoms	
Fever	57 (81.4)

Cough	40 (57.1)
Shortness of breath	52 (74.3)
Headache	1 (1.4)
Sore throat	3 (4.3)
Myalgia	4 (5.7)
Diarrhea	9 (12.9)
Anorexia	2 (2.9)
Rhinorrhea	1 (1.4)
Vomiting	5 (7.1)
Generalized weakness	23 (32.9)

CT scan chest findings

The most common finding in our patients was presence of ground glass opacity in 31 (44.3%) presented in peripheral location in 41 patients (58.6%) and rounded in morphology in 49 (70%) patients followed by interlobular septal thickening in 13 (18.6) whereas 10 (14.3%) had no ground glass opacity or consolidation on CT scan [17].

58 (82.9%) had bilateral disease involvement. The right upper lobe was involved in 34 (48.6%), the right middle lobe was involved in 41 (58.6%), the right lower lobe was involved in 59 (84.3%), the left upper lobe was involved in 31 (44.3%) and left lower lobe was involved in 58 (82.9%). We found that the lower lung lobes were most commonly involved by COVID-19. The total lobes mean severity score 7.5 ± 5.4; range: 0-20 [18]. Pneumothorax, pneumo-mediastinum, cardiomegaly, mediastinal lymphadenopathy, cavitation, tree in-bud appearance were also seen in patients. The time between symptom onset and the first CT scan was divided into four phases.

The frequency of ground glass opacities was lower in early phase groups when compared to the intermediate and late phase groups (Table 3). Bilateral lung involvement was found in 34 (58.62%) imaged in late phase of the disease [19]. Additionally opacities both rounded and linear were found most commonly in the late phase of illness (Tables 2 and 3).

Table 2: CT scan chest findings.

GGO and consolidation	
Presence of GGO without consolidation	31 (44.3)
Presence of consolidation without GGO	1 (1.4)
Presence of both GGO and consolidation	28 (40)
Normal	10 (14.3)
Distribution of opacity	
Central	2 (2.9)
Peripheral	41 (58.6)
Central and peripheral	14 (20)
Sub pleural	3 (4.3)
Normal	10 (14.3)
Opacity characteristics	

Rounded	49 (70)
Linear	3 (4.3)
Crazy paving	7 (10)
None	11 (15.7)
Airways	
Interlobular septal thickening	16 (22.9)
Bronchiectasis	7 (10)
Normal	47 (67.1)
Lobes affected	
Normal	10 (14.3)
1-2	15 (21.4)
3-5	45 (64.3)
Bilateral disease	58 (82.9)
Lobar distribution	
Right upper lobe	34 (48.6)
Right middle lobe	41 (58.6)
Right lower lobe	59 (84.3)
Left upper lobe	31 (44.3)
Left lower lobe	58 (82.9)
Total score	7.5 ± 5.4; range: 0-20
Right upper lobe	
0-2	65 (92.9)
3-4	5 (7.1)
Right middle lobe	
0-2	55 (78.6)
3-4	15 (21.4)
Right lower lobe	
0-2	36 (51.4)
3-4	34 (48.6)
Left upper lobe	
0-2	62 (88.6)

3-4	8 (11.4)
Left lower lobe	
0-2	39 (55.7)
3-4	31 (44.3)

Table 3: CT scan chest findings according to time course.

	Early	Intermediate	Late	p value
GGO	8 (40)	8 (50)	15 (44.1)	0.002
Consolidation	1 (5.0)	0	0	
Both GGO and	3 (15)	7 (43.8)	18 (52.9)	
consolidation				
Normal	8 (40)	1 (6.3)	1 (2.9)	
Distribution	0	1 (6.3)	1 (2.9)	0.003
Central	11 (55)	10 (62.5)	20 (58.8)	
Peripheral	1 (5.0)	2 (12.5)	11 (32.4)	
Central and peripheral Sub plural	0	2 (12.5)	1 (2.9)	
Normal	8 (40)	1 (6.3)	1 (2.9)	
Opacity characteristics Rounded	9 (45)	12 (75)	28 (82.4)	0.004
Linear	1 (5.0)	1 (6.3)	1 (2.9)	
Crazy paving	1 (5.0)	2 (12.5)	4 (11.8)	
Normal	9 (45)	1 (6.3)	1 (2.9)	
Lobes affected	8 (40)	1 (6.3)	1 (2.9)	0.001
Normal	6 (30)	3 (18.8)	6 (17.6)	
1-2	6 (30)	12 (75)	27 (79.4)	
5-Mar				

Discussion

Due to the variability in the sensitivity of RT-PCR for COVID-19 chest CT scan became a very common modality for testing for SARS-CoV2 respiratory illness. The guidelines for diagnosis and treatment of COVID-19 proposed by the national health commission of China had made CT scan chest a part of the diagnostic criteria for de initive diagnosis of COVID-19 [6]. In its latest seventh version chest imaging indings are included in case de inition of suspected case but not de initive case [15,16].

A review article looking at specificity of CT findings in RT-PCR negative patients with COVID-19 concluded that in patients with negative RT-PCR, CT scan should be done to diagnose COVID-19 if there is enough evidence from history and symptoms and epidemiological data [17]. Also a prospective observational study on 250 intensive care unit patients revealed that HRCT can be used as an alternative to RT-PCR for COVID-19 [18]. WHO has recommended use of CT in diagnosis of COVID-19 under certain circumstances [19]? Our study showed that 10 (*i.e.* 14.3%) patients had no findings on CT scan out of a total of 70 patients.

This establishes the role of CT scan as an aid to diagnosis in COVID-19 in RT-PCR negative patients if clinical suspicion is high. With regards to CT findings previous studies show that the most common finding of COVID-19 on CT is GGOs, crazy paving pattern, consolidation and linear opacities [20-22]. A review article showed that common CT findings in COVID-19 comprised of GGO, consolidation, interlobular septal thickening, adjacent pleura thickening, air bronchogram, pleural effusion, bronchiectasis, lymphadenopathy, crazy paving, pulmonary fibrosis, subpleural line, centrilobular nodules, distortion, bronchial wall thickening, reticulation, and vascular enlargement. These could be peripheral or central in location and could be unilobar to multilobar, unilateral or bilateral [23,24]. Similarly a review of studies by Bernheim, Wu and Pan et al. have touted GGO to be the most common findings of COVID-19 CT but the next most common finding in 2 of these studies was consolidation [25]. The diagnostic findings in our study portray that the characteristic of CT findings and time course of infection is related. Rounded opacities and GGO were the most common findings in the early, intermediate and late phase of the disease. In all three phases the predominant distribution of all CT abnormalities was peripheral. However as the disease progressed the CT abnormalities became more frequent (8 CT scan normal in early phase versus 1 CT scan normal in the late phase) [26]. Also consolidation and crazy paving became more prominent as late phase features rather than early phase features. Also more lung lobes become affected in late phase of the disease. Yan and colleagues demonstrated that CT findings show GGO in mild cases and GGO and consolidation in severe cases [27]. Our study looks at the time course and changes in CT (regardless of illness severity) and shows that while GGO is seen in the early phase it is often accompanied by consolidation in the late phase. Fengjun has showed in a review of 449 CT scans that the CT score and the area involved reached a peak (median 10) on illness days 7-12, and then, continued to be at a high level and 90% of discharged patients had residual lesions on the final CT scans [28]. However according to a meta-analysis conducted by Zhou, while initial CT findings in radiological studies consisted of the sub-pleural distribution, thickening of small vessels, GGO and patchy infiltrates, late findings showed deterioration of progressive lesions to be the second most common dynamic change in CT findings, the first being that the initial lesions deteriorated to a peak level followed by improvement (55% *vs.* 80%). The other patterns seen in this meta-analysis were the following in decreasing order: lesions being gradually absorbed and improved (46%), lesion remaining stable (26%), fluctuation of lesions (22%) [29]. Our study found that bilateral lung involvement was more frequent along with right and left lower lobe involvement. According to Bernheim et al. CT scan can show an increasing percentage of bilateral lung involvement from 28% in early phase (0-2 days) to 88% in late phase (6-12 days). Unlike our study in studies done by Berinheim and Wu et al. there was more right lower lobe involvement than left. There are several limitations to our study. Firstly, it has relatively small sample size and was done in a single center. Secondly fluid administration, ejection fraction of the patient, use of anti-microbial therapy, superimposed bacterial pneumonia and clinical condition of the patient correlating with CT scan findings are not taken into account. We have also not correlated illness severity to the findings of the CT scan. Due to resource limitations we were not able to do serial CT scans.

Conclusion

Computed tomography scans can aid in diagnosing disease when suspicion is high and RT-PCR is negative and characteristically show ground glass opacities in the early phase and consolidation in peripheral location in the late phase of COVID-19 pneumonia.

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