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A Comparative Study of the Temporal Changes of CT Findings in Younger and Older Adults with COVID-19 Pneumonia

Research Article

Anand A, Rathod J, Hundekari M*, Disawal A, Jaybhay S and Deshmukh M

Department of Radiology, Government Medical College, Nagpur, India

***Corresponding author:** Hundekari M, Junior Resident, Department of Radiology, Government Medical College Nagpur, Hanuman Nagar-440024, Nagpur, India, Tel: 7798100399; E-mail: maherafsha@gmail.com

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Abstract

Objectives: To compare the temporal lung changes in Coronavirus Disease 2019 (COVID-19) pneumonia in younger (< 40 years) and older (≥ 40 years) adults and determine appropriate Computed Tomographic (CT) follow-up time.

Materials and methods: The chest CT images of 100 laboratory-confirmed SARS-CoV-2 infected patients were analyzed retrospectively, including 43 younger patients (27.95 ± 4.95 years) and 57 older patients (59.6 ± 10.71 years). The CT score and major CT findings were evaluated.

Results: An abnormal (positive) CT status in 33/43 (76.7%) of younger patients and 51/57 (89.5%) of older patients was recorded, when the initial CT was done at 4.88 ± 2.22 days and 5.75 ± 1.97 days respectively. On the initial scans, pure Ground-Glass Opacities (GGO) and crazy-paving patterns were common. On subsequent follow-up scans, the GGO plus reticulations, reticular pattern and pleural thickening were more commonly seen with significantly higher frequency in older patients. The mean total CT severity score in older patients was greater for initial as well as subsequent follow-up scans (all $P<0.001$). For the younger patients, the CT score reached a peak at 12 days and nadir at 30 days after symptom onset, while in older patients the peak CT score was reached at 14 days and lowest CT score was reached at 37 days.

Conclusion: The disease appeared to be milder in the younger population. The elderly patients are more likely to have extensive lung lobe involvement, interstitial and reticular changes, and pleural thickening. The appropriate follow-up time of CT scans is during the second week (approximately 12 days for younger patients and approximately 14 days for older patients) and after the fifth week (approximately 30 days for younger patients and approximately 37 days for older patients).

Keywords: COVID- 19; Coronavirus disease 2019; CT; Computed Tomography; Pneumonia; Follow-up

Introduction

As of December 8, 2020, a total of 6,72,10,778 confirmed COVID-19 cases, including 15,40,777 deaths have been reported worldwide to the World Health Organization (WHO) [1]. Amongst these, India has reported a total of 97,27,225 confirmed cases and about 1,42,388 deaths [2].

With the gradual recognition of COVID-19 pneumonia, professional consensus, guidelines, and criteria have steadily been established to facilitate diagnosis and treatment [3]. The diagnosis of COVID-19 is currently confirmed by identification of viral RNA in Reverse Transcriptase-Polymerase Reaction (RT-PCR). The specificity of most of the RT-PCR test results is theoretically 100% because the primer design is specific to the genome sequence of SARS-CoV-2. However, occasional false-positive results may occur owing to technical errors and reagent contamination. Furthermore, it should be realized that a positive RT-PCR test result reflects only the detection of viral RNA and does not necessarily indicate the presence of viable virus [4]. Another disadvantage of the RT-PCR test is that it takes some time before results are available, with estimated testing times ranging from 50 minutes to 4 hours for semiautomated to fully automated, walk-away assays and 6-14 hours for manually performed assays [5].

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On the other hand, many previously conducted studies have demonstrated CT having higher sensitivity (> 95%) as compared to RT-PCR results (60-70%) [6,7].

A recent meta-analysis also reported a chest CT pooled sensitivity of 94.6% and a pooled specificity of 46.0% in the detection of COVID-19 [8], hence CT has become an important tool for COVID-19 pneumonia screening, comprehensive evaluation and follow-up. But owing to the greater radiation dose of CT and the increased frequency of scans done presently, there is a growing concern regarding its long term effects on the human body such as cancer [9], thus it is of great importance to limit the number of scans done per person.

Furthermore, the disease course is found to be more severe with poorer prognosis in older adults [10]. Thus, we retrospectively analyzed the initial and follow-up CT scans of 100 RT-PCR confirmed COVID-19 cases to study and compare the imaging features and temporal evolution of the disease among young (< 40 years) and older adults (≥ 40 years)and to determine the appropriate CT follow-up time.

Materials and Methods

Patients and chest CT

This was a retrospective observational study approved by the ethical committee of our institute and the requirement of written informed consent was waived. Symptomatic COVID-19 infected patients between August 15 to October 15, 2020, were screened using the following criteria.

a. At least one positive RT-PCR for SARS- CoV-2 obtained with nasopharyngeal/oropharyngeal swabs.

b. Cases should have undergone ≥ 1 CT scan, the selection criteria for the follow-up scan were if the patient's symptoms changed or progressed.

Thus, about 100 patients were included in the study and they were stratified into two groups based on the age: Group A (< 40 years) and group B (≥ 40 years).

All patients were imaged using a multidetector 128 slice SIEMENS CT scanner. Following were the scanning parameters: X-ray Tube parameters- 140 KVp; 234 mAs; rotation time - 0.5 s; pitch - 1.0; section thickness- 5mm; intersection space- 5 mm; additional reconstruction using the B80f ultra-sharp kernel and a slice thickness of 1 mm.

The clinical, demographic and imaging data of all the patients were recorded and various parameters were compared between these age groups.

CT image analysis

Two senior radiologists with 15- 20 years of experience in thoracic radiology evaluated the scanned images on the console using multiplanar reconstruction tools. Imaging was reviewed independently and a final decision was reached by consensus. The initial and follow-up CT images were assessed for following characteristics as per the Fleischner Society Glossary [11], such as pure Ground-Glass Opacity (GGO), crazy-paving pattern, consolidation, reticular pattern, GGO with consolidation, GGO plus reticulations, bronchiectasis and pleural thickening. The horizontal distribution of pulmonary lesions was noted as peripheral: involving mainly the peripheral one-third of the lung or central plus peripheral. The area of involvement was categorized as predominant anterior or posterior involvement (the area before or after the vertical line of the midpoint of the diaphragm in the sagittal position respectively). The number of lesions was noted as single or multiple (> 1) lesions.

A semi-quantitative CT severity scoring was used to evaluate the extent of lung involvement and was recorded for each of the five lobes during initial as well as each follow-up scan, based on anatomic involvement: 0, no involvement; 1, <5% involvement; 2, 5-25% involvement; 3, 26-50% involvement; 4, 51-75% involvement; and 5, >75% involvement. The total CT score was the sum of each lobar score, (0 to 25) [12]. The interval time between initial CT and onset of initial symptoms was defined as Initial CT interval, the interval between the first follow up CT and onset of initial symptoms was defined as first follow-up interval and so on.

We examined the relationship between the CT scores and follow-up time as well as the proportion of patients showing progression during each follow-up to determine the appropriate CT follow-up time. For all the patients, we also recorded imaging characteristics of the last CT scan to see if the lesions showed expansion, resolution into reticular opacities, combination of expansion and resolution or complete resolution.

Statistical analysis

Statistical analyses were performed using SPSS version 19.0. Continuous variables were expressed as Mean ± Standard Deviation (minimum-maximum), Numerical data were expressed as a percentage (%) of the total. The comparisons of the quantitative data were done using two-sample unpaired t-test and counting data were evaluated using the Pearson Chi-Square test. The difference was statistically significant with a P-value < 0.05.

Results

Demographic and clinical characteristics

The demographic and clinical characteristics are listed in Table1.

Imaging features of initial CT (Table 2)

The mean interval between the onset of initial symptoms and initial CT was 5.75 ± 1.97 days (range: 2-12 days) in group B, significantly higher than group A- Mean interval: 4.88 ± 2.22 days (range: 1-13) (P- 0.042). 33/43 (76.7%) patients in group A and 51/57 (89.5%) patients in group B showed parenchymal abnormalities in the first chest CT scan. The mean interval between initial negative CT status and subsequent positive CT status was 7.6 ± 2.63 days (5-12) for group A and 7.71 ± 3.94 (4-15) for group B (P-0.944). The predominant distribution pattern was peripheral in group A cases (26/43:60.5%) while the central plus peripheral pattern was more common in group B cases (33/57:57.9%). The posterior portion of lung was more commonly involved in both the groups, A- 27/43 (62.8%) and B- 36/57 (86.1%). The CT severity scores of each of the lung lobes were greater in group B than group A (all P<0.001), with

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Table 1: Demographic, clinical profile of the patients with COVID-19 infection.

	Group 1 (n=43)	Group 2 (n=57)	F value	P-value
Age	27.95 ± 4.95 (17-39)	59.6 ± 10.71 (40-87)	21.218	<0.001*
Gender				
Male	37 (86)	36 (63.2)		
Female	6 (13.9)	21 (36.8)		
Symptoms				
Fever	32 (74.4)	45 (78.9)		
Cough	25 (58.1)	36 (63.1)		
Fatigue	38 (88.3)	49 (85.9)		
Breathlessness	18 (41.9)	43 (75.4)		
Accompanying condition/ disease				
Hypertension	10 (23.2)	28 (49.1)		
Diabetes	4 (9.3)	20 (35)		
Total number of scans	113	156		
Mean number of scans	2.63 ± 0.53 (2-4)	2.74 ± 0.58 (2-4)	0.01	0.341
The mean interval between adjacent scans	8.51 ± 3.27 (3-20.5)	9.4 ± 4.11 (3.5-31)	0.218	0.245

Note: Quantitative data are represented as mean ± standard deviation (minimum-maximum), counting data are represented as count (%), * represents a statistically significant difference.

Table 2: Findings of initial CT between the two age groups.

Features on Initial chest CT	Group 1 (n=43)	Group 2 (n=57)	X or F value	P-value
CT status				
Positive CT	33 (76.7)	51 (89.5)	2.955	0.086
Negative CT	10 (23.2)	6 (10.5)		
Interval between negative to positive CT status	7.6 ± 2.63 (5-12)	7.71 ± 3.94 (4-15)	1.09	0.944
CT characteristics				
Distribution				
Peripheral	26 (60.5)	18 (31.5)	4.805	0.091
Central + Peripheral	7 (16.3)	33 (57.9)		
Lung area				
Predominant Anterior	6 (13.9)	15 (26.3)	4.266	0.118
Predominant Posterior	27 (62.8)	36 (86.1)		
Number of lesions				
Single	10 (23.3)	6 (10.5)	7.301	0.026*
Multiple	23 (53.5)	45 (78.9)		
Lobar score				
Right Upper Lobe (RUL)	0.47 ± 0.73	1.46 ± 1.03	9.918	< 0.001*
Right Middle Lobe (RML)	0.47 ± 0.55	1.25 ± 1.04	18.019	< 0.001*
Right Lower Lobe (RLL)	1.37 ± 1.02	2.07 ± 1.03	1.951	< 0.001*
Left Upper Lobe (LUL)	0.65 ± 0.75	1.39 ± 1.09	9.806	< 0.001*
Left Lower Lobe (LLL)	1 ± 1.0	1.93 ± 1.17	0.587	< 0.001*
Patterns				
Pure GGO	30 (69.8)	31 (54.4)	2.438	0.118
Crazy-paving	31 (72)	36 (63.1)	0.885	0.347
Consolidation	0	13 (22.8)	11.272	0.001*
GGO with consolidation	7 (16.2)	31 (54.4)	15.107	< 0.001*
GGO plus reticulations	2 (4.6)	3 (5.3)	0.19	0.889
Reticular	0	1 (1.8)	0.762	0.383
Bronchiectasis	0	0	NA	NA
Pleural thickening	1 (2.3)	1 (1.8)	0.041	0.84

Note: Quantitative data are represented as mean ± standard deviation (minimum-maximum), counting data are represented as count (%), * represents a statistically significant difference, NA- not applicable.

the highest score, observed in the right lower lobe in both the groups (1.37 ± 1.02 in group A and 2.07 ± 1.03 in group B).

The predominant patterns during the initial scan were pure GGO and crazy-paving pattern: 30/43 (69.8%) and 31/72 (72%) in group A and 31/57 (54.4%) and 36/57 (63.1%) in group B, (P>0.005).Others patterns like consolidation and GGO with consolidation were greater in proportion in group B than the group A (13/57 [22.8%] *vs.* 0/43, P-0.001 and 31/57 [54.4%] *vs.* 7/43 [16.2%], P<0.001).

Temporal changes in CT scores (Table 3 and Figure 1)

The mean total CT severity score of group B was greater than that of group A during initial as well as subsequent follow-up scans (all P<0.001). About CT interval times, the initial CT interval and the first follow-up interval time was greater in group B than group A patients (P-0.042 and P-0.022), whereas not much difference was noted in second and third follow-up interval time between the two groups (P-0.528 and P-0.224).

For Group A patients, there was a marked increase in the mean CT score values after the initial CT scan (3.95 ± 3.33). The mean CT score peaked during the first follow-up interval; mean 12.49 ± 3.31 (8-20) days with a mean score value (7.26 ± 4.02). Afterwards, the mean CT score began to decrease, the score value was 5.50 ± 3.40 during the second follow-up interval: 21.27 ± 7.41 (6-43) days. Later on, the mean score dropped to the lowest value of 2 ± 0.0 during the third follow-up interval- 30 ± 2.82 (28-32) days.

In group A, 32/43 (74.4%) patients showed progress during the first follow-up interval, while 2/43 (4.6%) showed no interval change and 9/43 (20.9%) showed improvement during this interval. During the second follow-up interval, 3/26 (11.5%) patients showed progress, 21/26 (80.7%) cases showed improvement and 2/26 (7.6%)

Table 3: The difference of CT severity scores and CT follow-up time between groups.

	Group 1 (number of patients)	Group 2 (number of patients)	F value	P-value
CT severity score				
Initial CT	3.95 ± 3.33 (0-11) (n=43)	8.09 ± 4.92 (2-12) (n=57)	8.592	< 0.001*
First follow-up CT	7.26 ± 4.02 (1-17) (n=43)	11.95 ± 4.45 (7-40) (n=57)	0.128	< 0.001*
Second follow-up CT	5.50 ± 3.40 (2-13) (n=26)	11.45 ± 4.21 (15-34) (n=38)	1.192	< 0.001*
Third follow-up CT	2 ± 0 (0-2) (n=2)	9.25 ± 2.63 (25-42) (n=5)	0	0.5
Time interval				
Initial CT interval	4.88 ± 2.22 (1-13)	5.75 ± 1.97 (2-12)	0.211	0.042*
First follow-up interval	12.49 ± 3.31 (8-20)	14.77 ± 5.73 (7-40)	2.368	0.022*
Second follow-up interval	21.27 ± 7.41 (6-43)	22.24 ± 4.77 (15-34)	0.655	0.528
Third follow-up interval	30 ± 2.82 (28-32)	37.40 ± 6.98 (25-42)	0.867	0.224

Note: Quantitative data are represented as mean ± standard deviation (minimum-maximum), initial CT interval is the interval between onset of initial symptoms and initial CT, first follow-up interval is the interval between onset of initial symptoms and first follow-up scan and so on, * represents a statistically significant difference.

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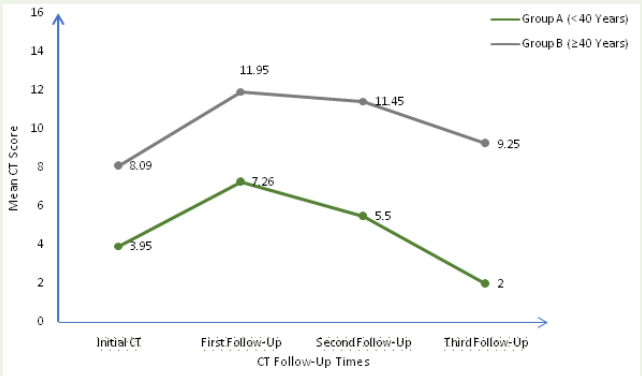

Figure 1: A line diagram showing the dynamic changes of the mean peak CT scores with CT follow-up times in which x= CT intervals and y= mean CT score. The mean CT scores showed increasing trend after initial CT with peak score during first follow-up and then showed a decreasing trend with the lowest scores occurring during the third follow-up in both groups A and group B.

cases showed no interval change whereas 2/2 (100% cases) showed significant improvement during the third follow-up interval.

The peak of mean CT score for group B patients (11.95 ± 4.45) was reached during the mean interval of 14.77 ± 5.73 (7-40) days after the onset of initial symptoms (first follow-up interval). It remained stable with a mean value- 11.45 ± 4.21 during the second follow-up interval: 22.24 ± 4.77 (15-34) days. After this time the mean score dropped to a value of 9.25 ± 2.63 around 37.40 ± 6.98 (25-42) days (third follow-up interval).

Of 57 patients in group B, 49 (85.9%) showed progress, 3 (5.2%) remained stable and 5 (8.7%) improved during the first follow-up interval. During the second follow-up interval, 10/38 (26.3%) patients showed progress, 20/38 (52.6%) cases showed improvement and 3/38 (7.8%) cases showed no interval change whereas 1/5 (20%) cases were stable and 4/5(80%) cases showed significant improvement during the third follow-up interval.

Temporal changes in the main CT characteristics (Table 4 and Figures 2-5)

During the first follow-up interval, the predominant finding was crazy-paving pattern in both group A (31/43, 72%) and B (36/57, 63.1%) (P-0.347). Pure GGO was more common in group A (15/43, 34.9%) than group B (4/57, 7%) (P<0.001). The following features: consolidation, GGO plus reticulations, reticular pattern and pleural thickening were significantly more common in group B than in group A (34/57[59.6%] *vs.* 10/43[23.2%], 47/57[82.4%] *vs.* 16/43[37.2%], 18/57[31.6%] *vs.* 4/43[9.3%] and 23/57[40.3%] *vs.* 4/43[9.3%]; all P<0.05). The GGO with consolidation pattern was more common in group B (30/57[52.6%]) than group A (16/43[37.2%]), but without a significant difference (P-0.126).

The GGO plus reticulations and reticular patterns were more common during the second follow-up interval. No significant difference was observed during this follow-up interval concerning the crazy-paving, consolidation and the GGO with consolidation patterns (P-0.178, P-0.142, P-0.088), whereas the GGO plus reticulations pattern, reticular pattern, bronchiectasis and pleural thickening were much more common in group B than in group A.(35/38[92.1%] *vs.* 17/26[65.4%], 35/38[92.1%] *vs.* 15/26[57.7%], 31/38[81.6%] *vs.* 3/26 [11.5%] and 16/38[42.1]% *vs.* 2/26 [7.6%]; all P<0.05).

During the third follow-up interval, pure GGO was predominant in group A, 1/2 (50%) than group B(0/5)(P-0.025) whereas reticular pattern, bronchiectasis and pleural thickening were common in group B as compared to group A, but without a statistically significant difference (all P>0.05).

During the analysis of the final follow-up scan, 11/43 (25.5%) patients of group A and in 1/57 (1.7%) patients of group B showed complete resolution of the lesions (P<0.001), expansion of the pre-existing abnormalities were noted in 7/43 (16.2%) patients of group A and 6/57 (10.5%) patients of group B(P-0.397). 20/43 (46.5%) patients of group A and 33/57 (57.9%) patients of group B showed absorption of the earlier lesions into reticulations (P-0.259), while 4/43 (9.3%)

Table 4: The findings of CT characteristics in the CT follow-up between two groups.

CT follow-up	Pure GGO	Crazy-paving	Consolidation	GGO with consolidation	GGO plus reticulations	Reticular	Bronchiectasis	Pleural thickening
First follow-up CT								
Group 1 (n=43)	15 (34.9)	31 (72)	10 (23.2)	16 (37.2)	16 (37.2)	4 (9.3)	0	4 (9.3)
Group 2 (n=57)	4 (7)	36 (63.1)	34 (59.6)	30 (52.6)	47 (82.4)	18 (31.6)	7 (12.2)	23 (40.3)
Chi Square Statistic	12.367	0.885	13.75	2.347	21.527	7.088	5.678	11.988
P-value	< 0.001*	0.347	< 0.001*	0.126	< 0.001*	0.008*	0.017*	0.001*
Second follow-up CT								
Group 1 (n=26)	7 (26.9)	5 (19.2)	0	0	17 (65.4)	15 (57.7)	3 (11.5)	2 (7.6)
Group 2 (n=38)	1 (2.6)	21 (18.9)	3 (7.8)	4 (10.5)	35 (92.1)	35 (92.1)	31 (81.6)	16 (42.1)
Chi Square Statistic	8.329	1.814	2.154	2.919	7.235	8.911	30.411	9.044
P-value	0.004*	0.178	0.142	0.088	0.007*	0.003*	< 0.001*	0.003*
Third follow-up CT								
Group 1 (n=2)	1 (50)	0	0	0	1 (50)	0	0	0
Group 2 (n=5)	0	0	0	0	1 (20)	3 (60)	3 (60)	1 (20)
Chi-Square Statistic	5	NA	NA	NA	1.875	1.875	1.875	0.313
P-value	0.025*	NA	NA	NA	0.171	0.171	0.171	0.576

Note: Counting data are represented as count (%), * represents a statistically significant difference, NA- not applicable.

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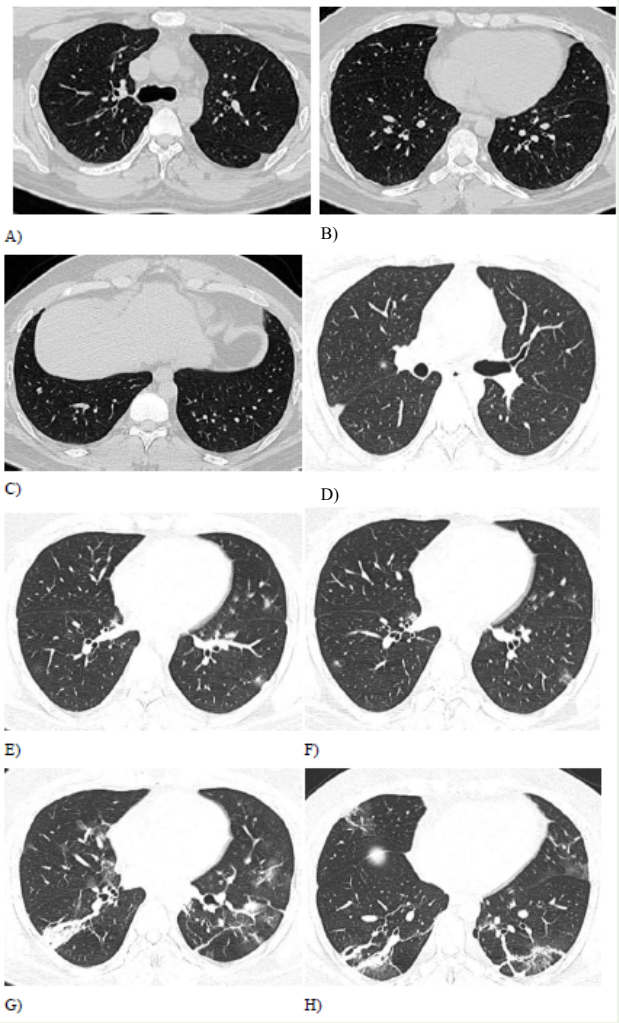

Figure 2: A 30-year-old male patient with COVID-19 pneumonia.
A, B, C: Initial axial thin section CT images (Day 3 after symptom onset) showed no involvement. D, E, F: First follow-up CT on day 8 after symptom onset showed newly developed subpleural GGO in bilateral lower lobes.
G and H: Second follow-up CT on day 17 after symptom onset showed the presence of multiple reticular streaks along with GGO in bilateral lung parenchyma.

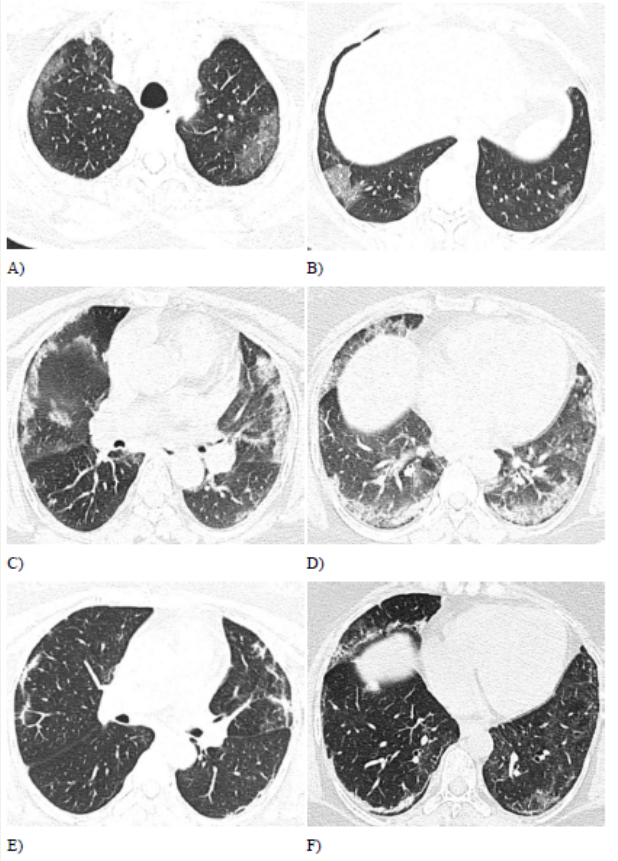

Figure 3: A 55-year-old- female patient with COVID-19 pneumonia.
A, B: Initial axial thin section CT images (Day 7 after symptom onset) showed multiple subpleural areas of pure ground glass opacities (GGO) and crazy-paving pattern scattered in both the lung lobes. C, D: First follow-up CT on day 13 after symptom onset showed newly developed GGO with consolidations in bilateral lung lobes. E and F: Second follow-up CT on day 23 after symptom showed resolution of previous lesions into subpleural reticular streaks.

patients of group A and 18/57 (31.57%) patients of group B showed simultaneous expansion and resolution of the previous lesions (P-0.008).

Discussion

We investigated the initial CT imaging features of COVID-19 pneumonia and their imaging evolution during follow-up in the two age groups in a sample of 100 patients with a total of 269 scans.

We reported an abnormal (positive) CT status in 33/43 (76.7%) of group A patients and 51/57 (89.5%) of group B patients, when the initial CT was done at a mean interval of 4.88 ± 2.22 days in group A and 5.75 ± 1.97 days in group B. Thus, to know about the presence of pneumonia, the appropriate time for the initial scan is usually 5 days after the symptom onset [13].

In a study conducted by Fang Y et al. describing the CT image visual quantitative evaluation and clinical classification of COVID-19, 71.8 % symptomatic confirmed cases had CT evidence of pneumonia [14]. Zhan J et al. reviewed CT scans of 110 patients describing CT pattern of evolution of COVID-19 pneumonia and reported an overall rate of 8.1 % negative scans [15]. Similarly, Liu X et al. found a pooled positive CT rate of 89.7% cases among 2378 COVID-19 cases in a meta-analysis which included a total of 13 studies [16]. Thus, a comparable positive rate in this study could reflect the possible similar course of disease in Indian population as well as the fact that this study included only symptomatic positive patients. Also the findings of this study are in concordance with that of Yuhui et al. who reported that the extent of lung abnormalities usually peaked during days 6-11 of illness [13].

Our results showed a predominant peripheral pattern of distribution (26/43; 60.5%) in the younger age group (A: < 40 years) while central plus peripheral involvement (33/57; 57.9) in the older age group (B: ≥ 40 years). Initially, the virus is believed to attack mainly the terminal and respiratory bronchioles, manifested as the

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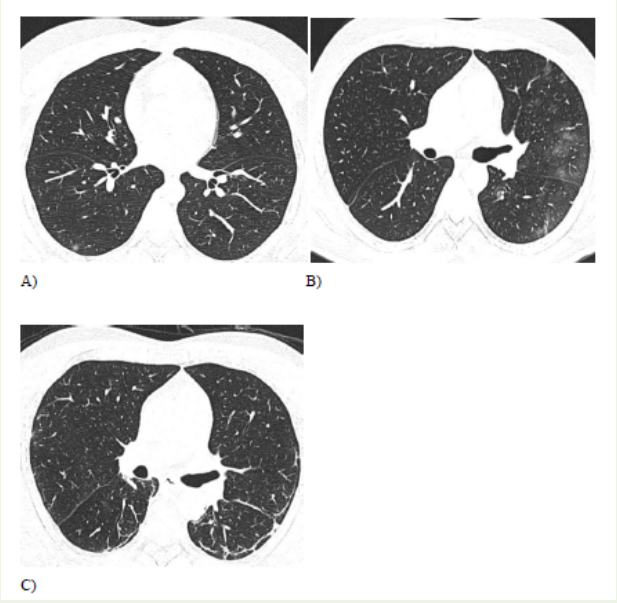

Figure 4: A 22-year-old male patient with COVID-19 pneumonia.
A: Initial axial thin section CT images (Day 5 after symptom onset) showed presence of a single focal subpleural pure GGO in the superior segment of right lower lobe. Rest of the lung parenchyma was normal. B: First follow-up CT on day 12 after symptom onset when patient insisted himself for the scan (without a clinical deterioration), showed development of additional subpleural ground glass opacities in the left lung parenchyma. C: Second follow-up CT obtained on day 27 after symptom onset showed resolution of the previous opacities in the form of subpleural reticular lines in bilateral lung parenchyma.

predominant peripheral pattern of lung involvement. However, the diffuse distribution of lesions, along with higher mean lobar CT severity scores on the initial chest scan observed in the older age group could represent more extensive parenchymal involvement in the older adults during the initial course of the disease. The highest CT severity score was observed in the right lower lobe due to shorter right lower lobe bronchial anatomy.

Zhou et al. studied the evolution of CT features in 100 confirmed COVID-19 pneumonia patients. Based on imaging, they described the course of disease into the early rapid progressive stage: 1 to 7 days after symptom onset, advanced stage: 8-14 days after symptom onset and advanced stage: ≥ 14 days after symptom onset [17]. They reported that the pure GGO, GGO with consolidation were more common during the early rapid stage, a sharp increase in the consolidation and GGO plus reticular pattern was observed during advanced stage while repairing signs- reticular pattern and bronchiectasis were predominant during the absorption phase.

In our study, the spectrum of CT characteristics observed was pure GGO, crazy-paving, consolidation, GGO with consolidation, GGO plus reticulations, reticular pattern, bronchiectasis and pleural thickening, findings similar to previous studies [18-20]. During the initial chest scan, the most common patterns seen were pure GGO and crazy-paving patterns with no significant difference between the groups [17], finding consistent with a previous study [21]. In early stages, the virus attacks the peripheral vessels and terminal

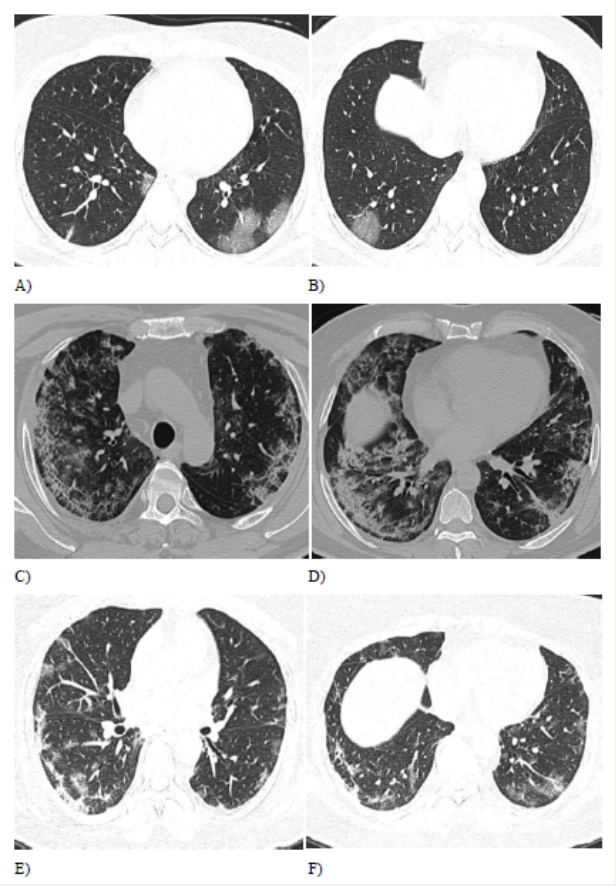

Figure 5: A 69-year-old-male patient with COVID-19 pneumonia.
A, B: Initial axial thin section CT images (Day 7 after symptom onset) showed multiple subpleural areas of pure ground glass opacities (GGO) along with crazy-paving pattern scattered in both the lower lung lobes. C, D: First follow-up CT on day 13 after symptom onset (on clinical deterioration) showed newly developed GGO with consolidations in bilateral upper as well as lower lung lobes. E and F: Second follow-up CT scan obtained on day 28 after symptom showed resolution of previous lesions into subpleural reticular streaks.

bronchioles causing an increase in the intraductal pressure which results in exudation, manifested as subpleural pure GGO. Over time, the collagen fibres are laid down by the proliferating fibroblasts which result in interstitial thickening and together along with the ground glass opacities crazy-paving pattern is formed. Further, as the disease progresses, the thickened lobular septum limits the absorption of the alveolar exudation, resulting in the alveolar consolidation formation. The significantly higher proportion of group B patients showing GGO with consolidation and consolidation patterns during the initial chest scan could represent more rapid advancement of the disease course in the older age group.

The first follow-up study (approximately 13 days after symptom onset) in group A, showed a predominance of crazy-paving pattern over other patterns while the dominant patterns observed in group B patients during their first follow-up interval (approximately 15 days after symptom onset) were crazy-paving, GGO with consolidation, consolidation and GGO plus reticular patterns. This finding also supports the fact that disease progression is much faster in the elderly.

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The appropriate time for the patients to undergo CT re-examination should be when the CT severity scores are at the peak and also when the extent and the density of lung opacities are more severe. The mean CT score peak was observed at a mean of 12.49 ± 3.31 days in group A and 14.77 ± 5.73 days in group B cases. This finding is comparable to the results of other studies [13].

The absorption phase of COVID-19 pneumonia is characterised by the decrease in the inflammatory cells with a progressive increase in the amount of the fibroblasts and the collagen fibres resulting in interstitial fibrosis- reticular pattern (repairing sign). Previously conducted studies have shown that the onset of the absorption phase starts approximately 14 days after symptom onset [17,22]. We found that the GGO plus reticulations and reticular pattern were predominant during the second follow-up interval (mean interval of 21.27 ± 7.41 days in group A and 22.24 ± 4.77 days in group B). And about 92.1 % patients in the older age group (B) showed reticular pattern as compared to 57.7% patients in younger age group (A), thus older patients are more likely to have the reticular pattern (a sign of pulmonary fibrosis). Deterioration of lung structure and function, weaker immune system of the body along with pre-existing medical diseases could result in the reduction of the lung compliance and thus a more severe extent and pattern of pneumonia in the elderly population.

The mean CT scores dropped to the lowest value about 30 days after symptom onset in group A and 37 days after symptoms onset in group B patients, with the conversion of the previous lesions into reticulations. Thus a CT re-examination to look for disease remission could be done during this period. All recommendations were made to regulate the frequency of CT scans to reduce the radiation dose and to show timely changes in the disease course.

The findings are similar to those conducted by Cheng yang et al. who studied temporal lung changes in eighty-six COVID-19 pneumonia patients and concluded that the appropriate follow-up time of CT scans is during the second week (approximately 12 days) and the fourth to fifth weeks (approximately 23-36 days) from the onset of illness [23].

In our study, we also recorded the imaging features of the final CT scan during the follow-up. About 25.5% of patients belonging to the younger age group showed complete resolution of the abnormalities as compared to only 1.7% of patients among the older age group. This finding suggested that younger patients are associated with easier absorption of lesions.

Limitations

Firstly, the sample size was smaller and heterogeneous. The number and follow-up interval of CT scans per patient were different which could result in selection bias. Also, patterns like reticulations and bronchiectasis need further follow-up to determine whether the fibrosis seen in COVID-19 is reversible or irreversible. Finally, no lung biopsies were performed to assess the correlation between radiological and histopathologic findings.

Furthermore, CT imaging also has many pitfalls. The imaging findings except for the higher prevalence of peripheral distribution, involvement of upper and middle lobes, COVID-19, and non-COVID viral pneumonia have overlapping chest findings [24]. Also, bilateral GGOs have a much broader differential, present in atypical infections, non-infectious processes, and even in healthy individuals [25,26]. Moreover, the CT scanner may act as a fomite of COVID-19 transmission.

Also, the results of a meta-analysis showed that 10.6% of symptomatic patients with RT-PCR test-proven COVID-19 have normal chest CT findings [8], which suggests that true sensitivity may be considerably lower than that reported by many of the initial studies on this topic. Thus, a negative chest CT examination result certainly does not exclude COVID-19. The proportion of false-positive chest CT examination may also be due to overlapping imaging features with other viral pneumonia. Also, the interpretation of chest CT examinations may become particularly challenging during influenza season.

Katal et al. studied CT imaging findings in patients with pre-existing lung malignancies and stated [27], although peripheral GGOs and consolidations are usually highly suggestive of superimposed COVID-19 pneumonia, these findings can be hardly distinguishable from an underlying lung malignancy or other opportunistic infections in patients with known lung cancer and warrant clinical, epidemic and laboratory correlation with PCR testing. Similarly it is very difficult to differentiate post COVID fibrosis especially in elderly patients with a pre-existing Interstitial Lung Disease (ILD) especially Idiopathic Pulmonary Fibrosis (IPF) which is the commonest form of ILD typically affecting the older age groups. Alveolar hemorrhage and adult Acute Respiratory Distress Syndrome [ARDS] may also present with features similar to COVID-19 pneumonia. Thus, it is important to realize that CT is not the standard for the diagnosis of COVID-19, but its findings help suggest the diagnosis in the appropriate setting. It is crucial to correlate chest CT findings with epidemiologic history, clinical presentation, and RT-PCR test results.

Conclusion

Differences in chest CT features, such as the distribution, number of lesions, lobar CT severity scores and patterns of lung abnormalities were observed in younger (< 40 years) and older-aged (≥ 40 years) patients with COVID-19 pneumonia. The disease appeared to be milder in the younger population. The elderly patients are more likely to have extensive lung lobe involvement, interstitial and reticular changes, and pleural thickening. These characteristics may have a role in the progress as well as prognosis of the disease. To confirm the presence of pneumonia, the appropriate time for the initial scan is usually 5 days after the symptom onset. The appropriate follow-up time of CT scans is during the second week (approximately 12 days after symptom onset for younger patients and approximately 14 days after symptom onset for older patients) and after the fifth week (approximately 30 days after symptom onset for younger patients and approximately 37 days after symptom onset for older patients). In the former time, patients are in the progression of the disease and a CT re-examination aims to help determine the extent of the disease, while in the later time, patients are in recovery and a re-examination aims to determine the absorption of the lesions. All recommendations aim to reduce the CT radiation dose to the patients.

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