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Follow-up the severity of abnormalities diagnosed in chest CT imaging of COVID-19 patients: A cross-sectional study

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Abstract

Background and Aims: This study aimed to evaluate the severity of diagnosed lung abnormalities of coronavirus disease 2019 (COVID-19) patients based on the pre- and postrecovery follow-up chest computed tomography (CT) scan findings done at regular intervals.

Methods: This cross-sectional study was performed in three phases. The severity of lung abnormalities was recorded and compared based on the initial and follow-up chest CT findings carried out pre-and at regular intervals (3 and 6 months) of postrecovery of COVID-19 patients. Statistical data analysis was conducted using SPSS-Version 26. Pearson Chi-square test was used to analyze the results. p-value < 0.05 was considered statistically significant.

Results: Regarding the initial chest CT findings, although ground-glass opacity (GGO) was observed as the most common lung lesion, almost all the evaluated COVID-19 patients had multiple lung lesions and involvements, especially with more involvement of the lower lobes. concerning the frequency of lung lesions and involvements in all phases of the study, almost no statistically significant differences were observed between male and female COVID-19 patients and different age groups. However, older age groups had relatively more lung abnormalities due to Covid-19 based on initial CT images which take more time to be eliminated. Lung abnormalities of Covid-19 patients decreased significantly during the follow ups based on chest CT findings at different study phases.

Conclusion: According to evaluated pre- and post-recovery chest CT scans, the frequency of lung lesions and lung involvement distribution decreased significantly in COVID-19 patients, 3 and 6 months after recovery, and most of the recovered patients had no lung lesions or involvement anymore.

KEYWORDS

COVID-19, CT manifestations, follow-up study, lung involvement, lung lesion

1 | INTRODUCTION

The first cases of the novel coronavirus (COVID-19) were observed in December 2019 in Wuhan, China, and spread rapidly to all countries of the world.[1] The real-time reverse-transcription polymerase chain reaction (rRT-PCR) test is accepted as the standard method for screening COVID-19 suspected cases.[2] However, the current rRT-PCR test has limited sensitivity in some situations due to quality, stability, reproducibility, and insufficient viral materials in the samples.[3]

COVID-19 virus effectively multiplies in the upper and lower respiratory tracts and can lead to lesions in the lower respiratory tract.[4] Chest computed tomography (CT) images of COVID-19 patients showed the specific radiological characteristics of this disease.[5] Therefore, clinical experts turned to using chest CT examinations to diagnose COVID-19 in the early stages.[5] Compared with the RT-PCR test, CT imaging has shown a higher sensitivity for diagnosing the disease.[3] So that, the CT images may reveal lung abnormalities consistent with COVID-19 in patients with initial negative RT-PCR test results.[4] According to current experience, the symptoms of the disease appear earlier on chest CT images than other clinical symptoms. Chest CT imaging plays a very influential role in the clinical screening for COVID-19.[6] Chest CT is often used as a complementary examination in the diagnosis and management of the disease for COVID-19 patients.[6,7] Studies have also indicated the valuable role of chest CT images in monitoring the progress and evaluating the severity of COVID-19 pneumonia symptoms.[5]

Typical CT manifestations of COVID-19 pneumonia include lesions with ground-glass opacities (GGO), consolidation, bilateral patchy shadowing, pulmonary fibrosis, multiple lesions, crazy-paving pattern, and so forth.[6,7] These interpretations contain a key role not only in the diagnosis of COVID-19 but also in the monitoring of disease progression and the evaluation of therapeutic response.[8,9]

Follow-up chest CT scans are often carried out for COVID-19 patients to assess the recovery of the patient or the progress of the disease. These follow-up examinations can reveal temporal changes in characteristics of images for COVID-19 patients, in addition to helping radiologists in making quick and valid assessments.[10]

Concerning the limited number of follow-up studies on recovered COVID-19 patients to evaluate the severity of lung abnormalities, and the consequences of the disease on the lungs' function, and respiratory symptoms, this cross-sectional study aimed to follow up the recovered Covid-19 patients using CT examinations. The observed lung abnormalities based on the CT scans carried out initially in the hospital at the time of disease diagnosis and regular intervals following patient recovery were evaluated.

2 | METHODS

The present study was conducted at the Khatam Al-Anbia hospital (Shoushtar, Iran). The protocol was approved by the ethics committee of the Shoushtar Faculty of Medical Sciences (Ethics code: IR.SHOUSHTAR. REC.1399.014). Patients' informed consent was obtained for including in the study and before undergoing CT scan examinations. All images were anonymized before use. All patients' data was kept confidential in compliance with the principles of the declaration of Helsinki.

2.1 | Study phases and patient selection

The present cross-sectional study was performed in three phases. In the first phase of the study, a retrospective analysis was conducted on the medical records of COVID-19-positive patients who were referred to the Khatam Al-Anbia hospital during the period from June 2020 to July 2021. Nasopharyngeal and/or oropharyngeal swabs were used to detect severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) nucleic acid by real-time reverse-transcriptase-polymerase-reaction (rRT-PCR) for all these patients. A two-step convenience random sampling method was applied to select the patients based on the COVID-19 patients' medical records number (ID) in the hospital. Inclusion criteria were: having a positive rRT-PCR test, availability of patient's initial chest CT images in the hospital PACS system, having lung involvement due to COVID-19, and age more than 15. Patients less than 15 years old were not included in the study due to our institutional ethics committee rules and considerations such as radiation protection restrictions which permitted us to evaluate only patients older than 15. Concerning the inclusion criteria, 347 patients were included in the first phase of the study, and their CT scan findings were evaluated to determine the type of lung lesions and lung involvement. In the second and third phases of the study, patients were asked to refer to the hospital to participate in the study and to take a follow-up chest CT scan if they wished after obtaining their informed consent. Eventually, 48 patients were referred to the hospital 3 months after recovery to participate in the second phase of the study and underwent a follow-up chest CT scan. Among them, 11 patients were referred for scanning in the third phase of the study 6 months after recovery. The number of participants in the second and third phases of the study reduced mainly for some reasons including death, complete recovery, and patients' fear of possible side effects of receiving ionizing radiation due to undergoing a CT scan or fear of being exposed to COVID-19 at hospital and recurrence of the disease.

2.2 | CT acquisition and data collection

All chest CT images were acquired with a multi-slice CT scanner (GE Healthcare). Patients were scanned in a supine position during breath-holding. Imaging parameters were as follows: kVp = 120, mAS = 115, matrix size = 512 × 512, slice thickness = 7.5 mm.

All the initial and follow-up CT images of patients were assessed by two radiologists blinded to clinical and para-clinical results, separately. These chest CT scans were evaluated for the main features of CT images in COVID-19 pneumonia which are described as: (1) presence of GGO; (2) presence of consolidation, (3) laterality of GGO and consolidation; (4) lobes affected by GGO or consolidative opacities; (5) presence of nodules; (6) presence of pleural changes such as pleural effusion or pleural thickening; (7) presence of thoracic lymphadenopathy; (8) airway abnormalities; (9) axial distribution of disease; (10) presence of underlying lung disease such as emphysema or fibrosis; and other abnormalities including linear opacities and opacities with a crazy-paving pattern. For cases of incompatible interpretations, the opinion of the radiologist with more work experience was accepted.

A checklist prepared by researchers was used to record patients' data including demographic characteristics of the patients and the results of evaluating the chest CT features by the radiologist.

2.3 | Statistical analysis

IBM SPSS software for Windows (version 26) was applied to analyze the collected data. Descriptive statistics were reported as mean ± standard deviation for quantitative values and as the frequency with percentage for qualitative variables. The frequency and distribution of lung lesions and lung involvements observed in the initial chest CT images were compared between males and females, likewise, six considered age groups (15–30, 31–45, 46–60, 61–75, 76–90, and >90) using Pearson Chi-square test. The same analysis was carried out for comparison of frequency and distribution of lung abnormalities between males and females based on follow-up scans obtained three months after recovery as well as comparing the frequency of lung abnormalities and involvements between the two first phases of the study. A *p*-value less than 0.05 was considered statistically significant for the Pearson Chi-square test. To compare the lung abnormalities' changes during the follow-ups, the frequency and percentages of different lung lesions and involvements for participants in three study phases are tabulated. The frequency and distribution of observed lung abnormalities are also tabulated for different age groups evaluated in the second and third phases of the study.

3 | RESULTS

Demographic characteristics of the evaluated patients in all three phases of the study are shown in Table 1. Total number of evaluated COVID-19 patients ($N = 347$) in the first phase of the study included 13 (4.1%) patients in the range of 15–30, 64 (20.2%) in the range of 31–45, 93 (29.3%) in the range of 46–60, 92 (29.0%) in the range of 61–75, 53 (16.7%) in the range of 76–90, and 2 (0.6%) patients in the range of >90). A total of 48 recovered COVID-19 patients participated in the second phase of the study carried out 3 months after recovery including 2 (4.5%) patients in the age range of 15–30, 10 (22.7%) in the range of 31–45, 13 (29.5%) in the range of 46–60, 10 (22.7%) in the range of 61–75, and 16.7 (20.5%) in the range of 76–90. The final 11 participants in the last phase of the study carried out 6 months after recovery comprised of 3 (37.5%) in the range of 46–60, 2 (25%) in the range of 61–75, 3(37.5%) in the range of 76–90.

Figures 1 and 2 show the frequency of detected lung lesions and the distribution of lung involvements, respectively, based on the initial chest CT findings of all 347 included patients in the first phase of the study.

Figures 3 and 4 represent the frequency of initially detected lung lesions and the distribution of lung involvements, respectively, for 347 evaluated COVID-19 patients in the first phase of the study based on patients' gender (175 males and 172 females). Figure 5 shows the initial and follow-up chest CT images for one of the evaluated COVID-19 patients as an instance.

The results of the Chi-Square test to compare the frequency and distribution of detected lung abnormalities due to COVID-19 between males and females based on the initial chest CT findings are reported in Table 2. Chest CT manifestations of COVID-19 and distribution of lung involvements in the second phase of the study compared with the initial CT findings for 48 participants including 22 (45.8%) males and 26 (54.2%) females are presented in Table 3. In addition, Table 4 shows the frequency and distribution of the detected lung lesions and lung involvements among three phases of the study for the 11 final participants including 8 (72.7%) males and 3 (27.3%) females.

Chi-Square test results for comparing the frequency of different detected lung lesions and the distribution of lung involvements between males and females, based on the follow-up chest CT findings carried out 3 months after recovery (second phase of the

TABLE 1 Demographic characteristics of the COVID-19 patients included in three different study phases

Study phase	Total number of patients (%)	Male *N* (%)	Female *N* (%)	Mean age ± SD (years)
Phase 1	347 (100%)	175 (50.4%)	172 (49.6%)	58.3 ± 16.6
Phase 2	48 (100%)	22 (45.8%)	26 (54.2%)	56.9 ± 17.5
Phase 3	11(100%)	8 (72.7%)	3 (27.3%)	66.8 ± 13.8

Note: Phases 1, 2, and 3 of the study refer to evaluating the initial chest CT scans of COVID-19 patients and the follow-up chest CT scans findings carried out 3, and 6 months after recovery, respectively.

Abbreviations: CT, computed tomography; COVID-19, coronavirus disease 2019; SD, standard deviation.

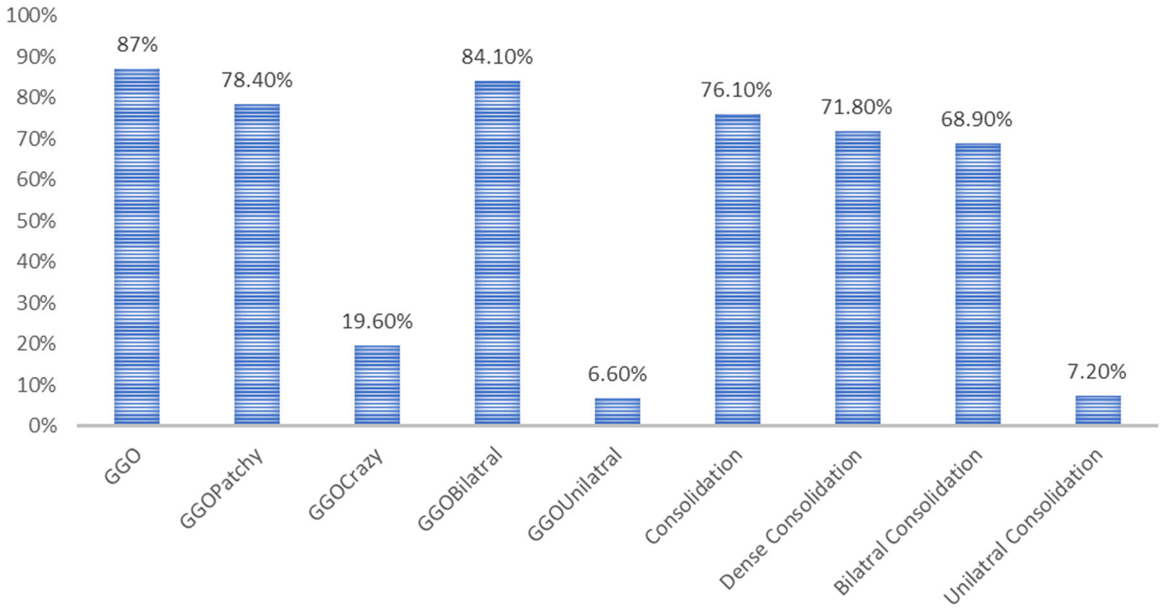

FIGURE 1 Frequency of different detected lung lesions regarding the initial chest CT of 347 evaluated COVID-19 patients. CT, computed tomography; COVID-19, coronavirus disease 2019.

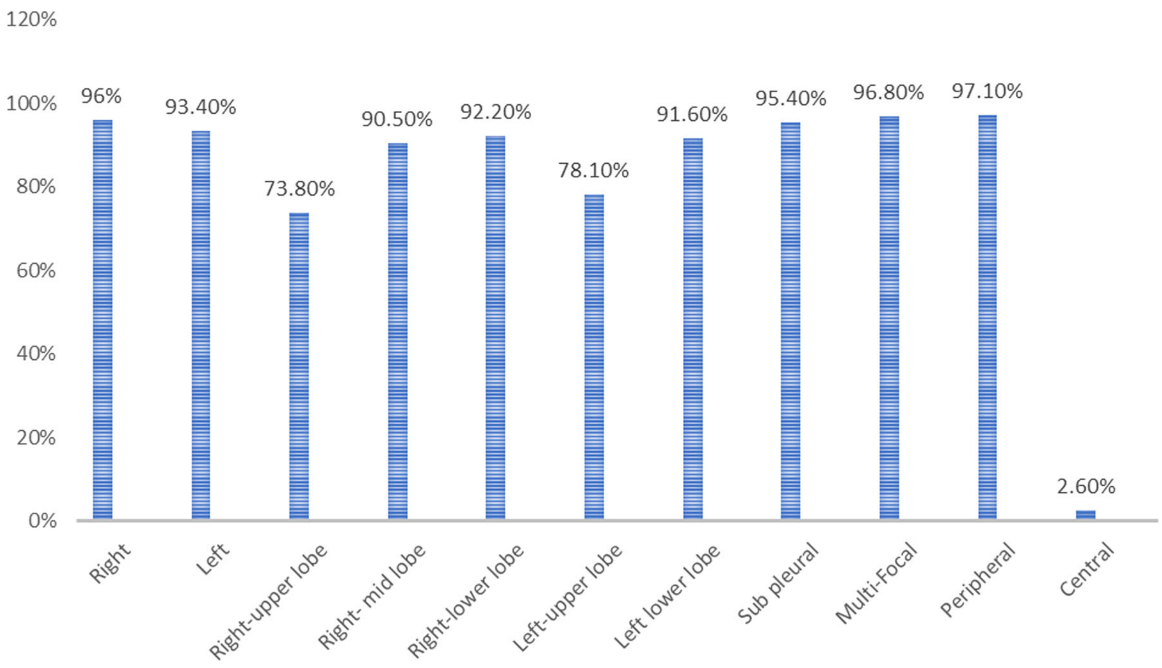

FIGURE 2 Frequency distribution of detected lung involvements regarding the initial chest CT of 347 evaluated COVID-19 patients. CT, computed tomography; COVID-19, coronavirus disease 2019.

study) are illustrated in Table SI. Also, Table SII shows the frequency and distribution of different lung abnormalities detected in CT scans carried out 6 months after recovery for males and females (Phase three of the study).

Likewise, lung lesions' frequency and the lung involvements' distribution for the evaluated patients in all three phases of the study between six considered age groups (15–30, 31–45, 46–60, 61–75, 76–90, and >90) are reported in Tables SIII–SV.

4 | DISCUSSION

High-resolution computed tomography (HRCT), during the COVID-19 pandemic, played an incredibly important role in detecting the disease in the early phases and evaluating the lesion nature.[11] Chest CT features have a crucial role not only in the detection of COVID-19 but also in the monitoring of disease severity and progression in addition to evaluating the therapeutic

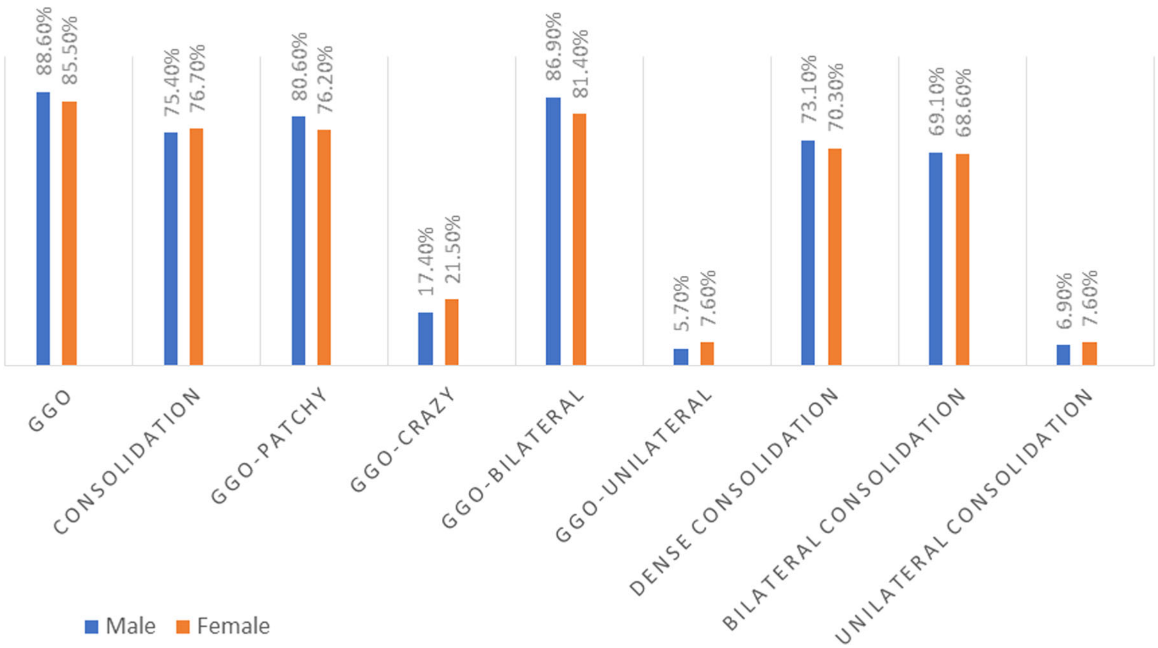

FIGURE 3 Comparing the percentages of different detected lung lesions for males and females based on the evaluated initial chest CT images (347 COVID-19 patients including 175 males and 172 females). CT, computed tomography; COVID-19, coronavirus disease 2019.

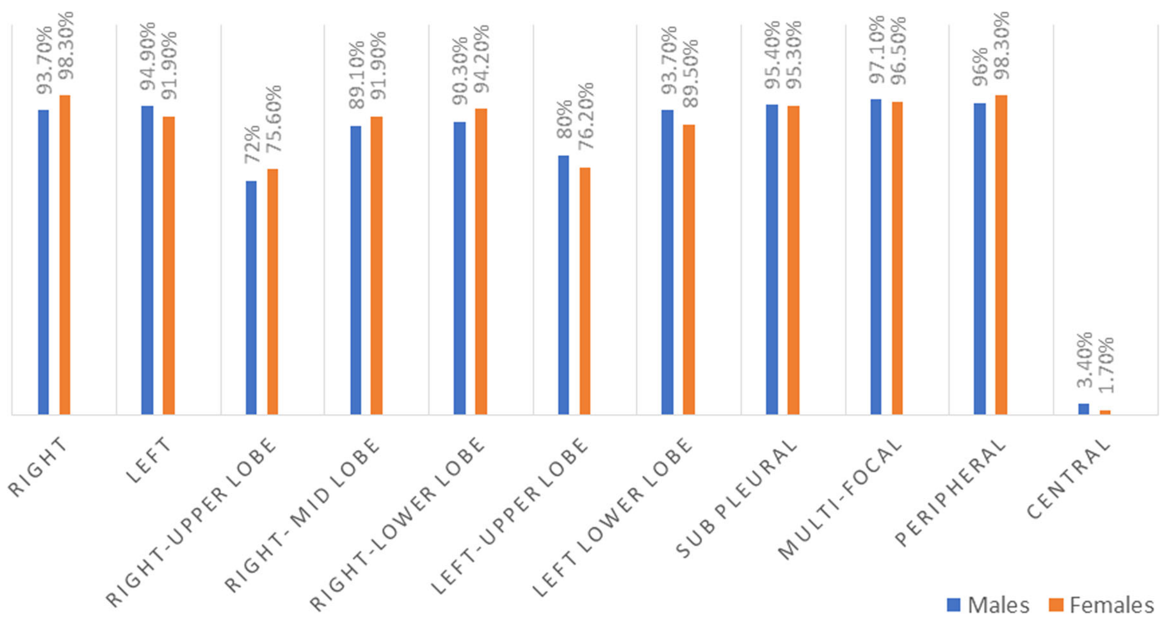

FIGURE 4 Comparing the detected lung involvements for males and females using the 347 initial chest CT images of COVID-19 patients (175 males and 172 females evaluated in the first phase of the study). CT, computed tomography; COVID-19, coronavirus disease 2019.

response.[8,9] Therefore, the current study was conducted to assess the extent of lung involvement and lung lesions among COVID-19 patients based on the initial and follow-up chest CT manifestations to evaluate the duration of lung lesions existence after patients' recovery. For this purpose, chest CT images were obtained at the time of disease detection and also 3 and 6 months after recovery and were assessed according to the extent of lung involvement and the type of detected lesions.

According to the initial chest CT images of COVID-19 patients, GGO and consolidation manifestations were the most common detected lesions, respectively. Although all COVID-19-positive patients had bilateral lung involvement, the lower lobes were more involved. Our results agree with literature. Studies by Liu et al. and Chung et al.[12,13] also reported the GGO as the most frequent manifestation on the chest CT images of COVID-19 patients. GGO manifestation is characterized as the areas of shadow hazy increased

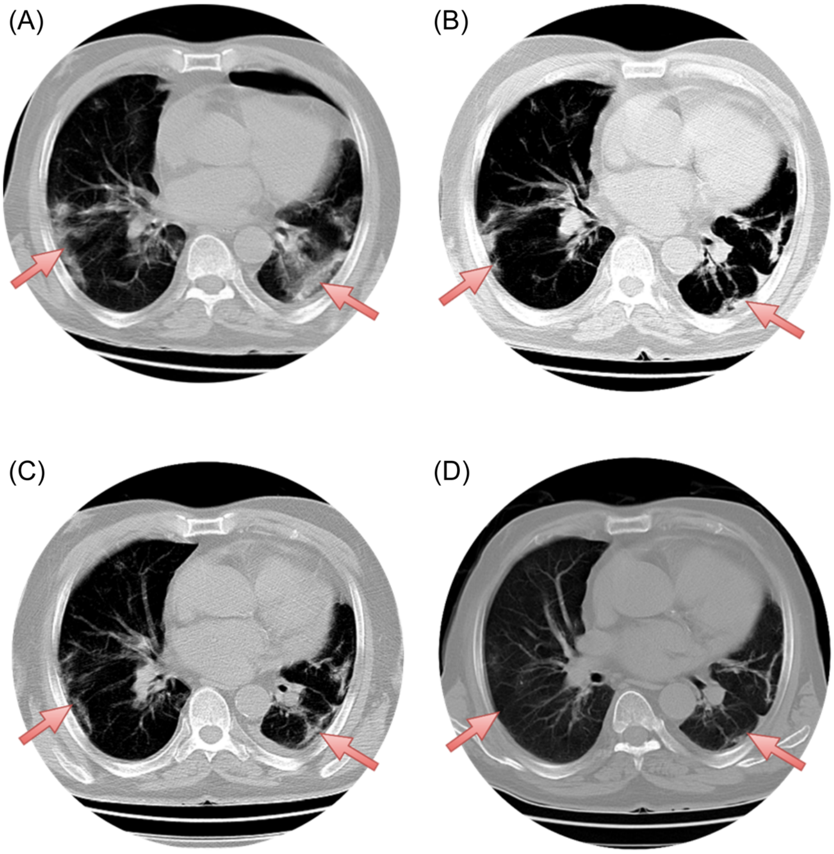

FIGURE 5 Chest CT images from one of the evaluated COVID-19 patients. (A) Initial chest CT, (B) chest CT 3 months after recovery, (C) chest CT 6 months after recovery, and (D) chest CT 9 months after recovery. CT, computed tomography; COVID-19, coronavirus disease 2019.

lung attenuation with conservation of vascular and bronchial margins. Likewise, Guan et al.[14] found that 56.4% of COVID-19 patients had GGO in chest CT imaging. Ai et al.[15] also reported that even in suspected COVID-19 patients with an initial negative RT-PCR test, GGO was one of the main CT manifestations. Han et al.[16] mentioned that GGO with or without consolidation is the early chest CT finding, which is mostly observed in the peripheral zones of lungs and attended by a halo or air broncho gram signs. Salehi et al.[17] conducted a systematic review study to evaluate the imaging findings of COVID-19 patients and found out that in the intermediate stage of the disease, GGOs are tending to increase in number and size and often progressively convert into multifocal consolidative opacities and septal thickening. Xu et al.[18] demonstrated that in COVID-19 patients, lung lesions' density is mostly in agreement with GGO, since the primary manifestation is usually attended by partial consolidation and fibrosis. Wu et al.[19] investigated 80 COVID-19-positive patients and found out that 73% of patients with clinical signs such as cough and fever, demonstrated multiple imaging features including GGO, consolidation, and interlobular septal thickening. In the study by Zhao et al.,[20] vessel enlargement and similar features were also reported for Covid-19 patients.

Some researchers revealed that besides GGO, bilateral patchy shadows are also common in chest CT images of COVID-19 patients.[8,14,17] Wang et al.[21] and Chen et al.[22] investigated the percentage of bilateral lung involvement in patients with COVID-19 and reported bilateral involvement for COVID-19 patients up to almost 100%. Similarly, the study by Huang et al.[23] stated that most of the patients suffered from bilateral involvement based on the chest CT findings. They reported the subsegmental consolidation and bilateral multiple lobular involvements as the typical CT findings for patients who were admitted to the ICU.

As discussed, consolidation is known as a typical CT feature in COVID-19 patients. Song et al.,[24] concluded that the lesions with consolidation can act as a marker of disease severity or progression. Also, Liu et al.[13] reported consolidation as a common lesion in pregnant women. Sun et al.[25] observed the increased risk of pulmonary fibrosis due to Covid-19 infection and recommended to the clinicians to be alert to the occurrence of pulmonary fibrosis in COVID-19 patients.

Based on our findings, which are in line with other studies, multiple lesions and crazy-paving patterns are also common in COVID-19-positive patients. Zhou et al.[26] revealed that COVID-19 is more probable to manifest as multiple lesions rather than a single lesion. Moreover, they revealed that coronavirus is more likely to invade the right inferior lobar bronchus and cause infection. Li et al.[27] showed that crazy-paving patterns can be seen in chest CT images of 36% of patients, specifically those with a severe form of the disease, which could be a sign of poor condition.

Based on our results, almost no statistically significant differences were seen in the frequency of different lung lesions and involvements between males and females, in the first phase of the study. On the other hand, all 347 evaluated patients (males and

TABLE 2 Chi-square test results for comparing the frequency of different detected lung lesions and lung involvements between males and females based on the first chest CT findings carried out at hospital pre-recovery of patients, the total number of evaluated patients $N = 347$ including 175 males (50.4%) and 172 females (49.6%)

Lesion type	Total frequency (%)	Frequency (%) for males	Frequency (%) for females	Chi-square	*p*-value
GGO	301 (86.7%)	155 (51.5%)	146 (48.5%)	0.8	0.38
Consolidation	263 (75.8%)	132 (50.2%)	131 (49.8%)	0.1	0.80
GGO-Patchy	271 (78.1%)	141 (52.0%)	130 (48.0%)	1.1	0.31
GGO-Crazy	68 (19.6%)	31 (45.6%)	37 (54.4%)	0.8	0.36
GGO-Bilateral	291 (83.9%)	152 (52.2%)	139 (47.8%)	2.0	0.16
GGO-Unilateral	23 (6.6%)	10 (43.5%)	13 (56.5%)	0.5	0.48
Dense Consolidation	248 (71.5%)	128 (51.6%)	120 (48.4%)	0.4	0.54
Bilateral Consolidation	238 (68.6%)	121 (50.8%)	117 (49.2%)	0.02	0.88
Unilateral Consolidation	25 (7.2%)	12 (48.0%)	13 (52.0%)	0.1	0.79
Lung involvement	**Total frequency (%)**	**Frequency (%) for males**	**Frequency (%) for females**	**Chi-square**	***p*-value**
Right	332 (95.7%)	164 (49.4%)	168 (50.6%)	4.6*	0.03
Left	323 (93.1%)	166 (51.4%)	157 (48.6%)	1.3	0.26
Right-upper Lobe	255 (73.5%)	126 (49.4%)	129 (50.6%)	0.5	0.47
Right- mid Lobe	313 (90.2%)	156 (49.8%)	157 (50.2%)	0.7	0.40
Right-lower Lobe	319 (91.9%)	158 (49.5%)	161 (50.5%)	1.8	0.18
Left-upper Lobe	270 (77.8%)	140 (51.9%)	130 (48.1%)	0.8	0.37
Left lower Lobe	317 (91.4%)	164 (51.7%)	153 (48.3%)	2.0	0.16
Subpleural	330 (95.1%)	167 (50.6%)	163 (49.4%)	0.002	0.96
Multi-Focal	335 (96.5%)	170 (50.7%)	165 (49.3%)	0.1	0.73
Peripheral	336 (96.8%)	168 (50.0%)	168 (50.0%)	1.6	0.21
Central	9 (2.6%)	6 (66.7%)	3 (33.3%)	1.0	0.32

Note: Total percentages for each lung abnormality were calculated as the frequency of that kind of observed lung lesion or lung involvement divided by the total number of evaluated chest CT images (347participants), multiplied by 100. Percentages of each type of lung abnormality for males and females were calculated as the ratio of that detected lesion or involvement frequency for each group relative to the total number of that lesion or involvement detected in evaluated images, multiplied by 100.

Abbreviations: CT, computed tomography; GGO, ground-glass opacity.

*Shows significance ($0.01 < p\text{-value} \le 0.05$)

females) had one or more lung lesions or lung involvements based on initial CT scan findings. The only exception was statistically significant differences between males and females in right lung involvement (Pearson Chi-square = 4.57 and *p*-value = 0.032) which seems women had more right lung involvement based on initial chest CT images although the differences were not clinically significant.

Concerning the chest CT images undertaken in the second phase of the study (3 months after patient recovery), no statistically significant differences were observed between the frequency and distribution of remaining lung involvement and lung lesions for males and females. This is while, almost no lung lesion or involvement was seen in followed female patients based on the CT scans carried out in the third phase of the study (6 months after recovery).

Based on findings, the frequency of the detected lung lesions and involvements for recovered COVID-19 patients decreased statistically significant 3 months after recovery (Table 3). Also, most lung abnormalities due to COVID-19 were removed completely 6 months after recovery (Table 4).

According to our results, the most common manifestations in the initial, second, and third chest CT images of these evaluated participants in three phases of the study comprised of patchy GGO, GGO bilateral, GGO, and consolidation with different involvements. Due to the pathogenesis of COVID-19 infection, cytokines such as tumor necrosis factor-alpha (TNF-alpha) are the main mediators of pulmonary edema in COVID-19 patients with pulmonary symptoms. TNF-alpha reduces fluid absorption in lung epithelial cells by disrupting the transfer of sodium and chloride ions, while the

TABLE 3 The frequency of lung lesions and lung involvements detected in the follow-up chest CT scans (undertaken 3 months after recovery) for 48 participants compared to their initial CT scan findings and the Chi-square test results

	Frequency (%)			
Lesion type	**Phase 1**	**Phase 2**	**Chi-square**	***p*-value**
GGO	36 (75.0%)	20 (41.7%)	**10.9****	**0.001**
Consolidation	34 (70.8%)	16 (33.3%)	**13.5****	***p* < 0.001**
GGO-patchy	37 (77.1%)	21 (43.6%)	**11.2****	**0.001**
GGO-Crazy	6 (12.5%)	1 (2.1%)	**3.9***	**0.05**
GGO-bilateral	37 (77.1%)	19 (39.6%)	**13.9****	***p* < 0.001**
GGO-unilateral	2 (4.2%)	0 (0.0%)	2.0	0.15
Dense consolidation	28 (58.3%)	14 (29.2%)	**8.3****	**0.004**
Bilateral consolidation	28 (58.3%)	13 (27.1)	**9.1****	**0.003**
Unilateral consolidation	4 (8.3%)	3 (6.3%)	0.2	0.69
	Frequency (%)			
Lung involvement	**Phase 1**	**Phase 2**	**Chi-square**	***p*-value**
Right	43 (89.6%)	24 (50.0%)	**17.8****	***p* < 0.001**
Left	41 (85.4%)	23 (47.9%)	**15.2****	***p* < 0.001**
Right-upper lobe	27 (56.3%)	11 (22.9%)	**11.2****	**0.001**
Right-mid lobe	38 (79.2%)	22 (45.8%)	**11.4****	**0.001**
Right-lower lobe	38 (79.2%)	21 (43.8%)	**12.7****	***p* < 0.001**
Left-upper lobe	33 (68.8%)	16 (33.3%)	**12.1****	**0.001**
Left-lower lobe	39 (81.3%)	20 (41.7%)	**15.9****	***p* < 0.001**
Subpleural	42 (87.5%)	23 (47.9%)	**17.2****	***p* < 0.001**
Multifocal	42 (87.5%)	22 (45.8%)	**18.8****	***p* < 0.001**
Peripheral	42 (87.5%)	23 (47.9%)	**17.2****	***p* < 0.001**
Central	3 (6.3%)	0 (0.0%)	3.1	0.08

Note: Phase 1: Initial images obtained at disease detection time, Phase 2: follow-up chest CT obtained three months after recovery. Percentages for each lung abnormality were calculated as the frequency of that kind of observed lung lesion or lung involvement divided by the total number of evaluated chest CT images (48 participants), multiplied by 100.
Abbreviations: CT, computed tomography; GGO, ground-glass opacity.
*Shows significance (0.01 < *p*-value ≤ 0.05).
**Shows significance (*p*-value ≤ 0.01).

TABLE 4 The frequency of lung lesions and lung involvements detected in the follow-up chest CT scans undertaken 6 months after recovery for 11 participants compared to their initial and second CT scan findings

	Frequency (%)		
Lesion type	**Phase 1**	**Phase 2**	**Phase 3**
GGO	9 (81.8%)	3 (27.3%)	3 (27.3%)
Consolidation	9 (81.8%)	4 (36.4%)	2 (18.2%)
GGO-patchy	9 (81.8%)	3 (27.3%)	3 (27.3%)
GGO-crazy	1 (9.1%)	0 (0.0%)	0 (0.0%)
GGO-bilateral	8 (72.7%)	3 (27.3%)	1 (9.1%)
GGO-unilateral	1 (9.1%)	0 (0.0%)	0 (0.0%)
Dense consolidation	9 (81.8%)	4 (36.4%)	2 (18.2%)
Bilateral consolidation	8 (72.7%)	3 (27.7%)	1 (9.1%)
Unilateral consolidation	3 (27.3%)	1 (9.1%)	1 (9.1%)
	Frequency (%)		
Lung involvement	**Phase 1**	**Phase 2**	**Phase 3**
Right	8 (72.7%)	5 (45.5%)	1 (9.1%)
Left	9 (81.8%)	4 (36.4%)	3 (27.3%)
Right-upper lobe	5 (45.5%)	2 (18.2%)	0 (0.0%)
Right- mid lobe	8 (72.7%)	4 (36.4%)	0 (0.0%)
Right-lower lobe	7 (63.6%)	5 (45.5%)	1 (9.1%)
Left-upper lobe	7 (63.6%)	3 (27.3%)	0 (0.0%)
Left lower lobe	9 (81.8%)	4 (36.4%)	3 (27.3%)
Subpleural	9 (81.8%)	4 (36.4%)	3 (27.3%)
Multifocal	9 (81.8%)	4 (36.4%)	3 (27.3%)
Peripheral	8 (72.7%)	4 (36.4%)	3 (27.3%)
Central	0 (0.0%)	0 (0.0%)	0 (0.0%)

Note: Phase 1: Initial images obtained at disease detection time, Phase 2: follow-up chest CT obtained three months after recovery, Phase 3: follow-up chest CT obtained 6 months after recovery. Percentages for each lung lesion or lung involvement were calculated as the frequency of that kind of observed lung abnormality divided by the total number of evaluated chest CT images (11 participants), multiplied by 100.
Abbreviations: CT, computed tomography; GGO, ground-glass opacity.

exchange of respiratory gases requires a moist environment. Based on published studies related to chest CT findings of Covid-19 patients as well as the clinical and pathological assessment of COVID-19 disease, there is an inflammatory process that causes the accumulation of fluid in the interstitial and alveolar part of the lungs followed by pulmonary edema due to a decrease in the clearance of alveolar fluid.[28] Trepos et al.[29] reported the efficiency of anti-TNF alpha antibodies administration for the treatment of COVID-19 pulmonary symptoms. The evaluated COVID-19 patients in our study with pulmonary involvement received medications based on approved treatment protocols in our hospital, which probably took 6 months for the complete resolution of pulmonary symptoms in the follow-up CT of these patients.

Moreover, a comparison of lung involvement distribution and different detected lung lesions among six considered age groups of patients in the first phase of the study (Table SIII) showed almost no significant differences among them. Although GGO lesions with crazy-paving patterns were higher in the age group of 61–75 years, patchy GGO was more frequent for 61–75 years, and GGO bilateral was higher for both age groups of 45–60 and 61–75 years. This shows that almost all lung lesions were seen equally in all age groups at the initial phase of the study (pre-recovery CT images).

Also, evaluating the distribution of lung lesions and involvements in different age groups of followed patients in the second and third phases of the study (post-recovery phases) revealed that detected abnormalities remained mainly in older age groups while for younger patients almost all symptoms were eliminated 3 months after recovery. However, it should be mentioned that one of our study limitations is the small number of participants in the second and third phases of the study due to factors such as death, complete recovery, fear of probable side effects of receiving ionizing radiation during undergoing CT scan, and fear of being exposed to disease and recurrence of COVID-19, a during conducting this study we had two heavy peaks of COVID-19. The small number of evaluated recovered patients makes generalization of the results hard and more studies with larger sample sizes are needed to make more accurate and general conclusions based on the results.

5 | CONCLUSIONS

This cross-sectional follow up study was conducted to evaluate the extent of lung involvements and lung lesions among COVID-19 patients, based on the initial and follow-up chest CT findings (pre- and at regular intervals post-recovery). Based on the pre-recovery chest CT findings, almost all the evaluated Covid-19 patients had one or more lung lesions or almost suffered from lung involvement with no significant differences for males or females or different age groups. The lung involvements and the disease symptoms decreased significantly during the follow ups and most of the followed patients had no lung lesions orinvolvement based on CT findings carried out 3 or 6 months post-recovery. However, the time duration needed for CT manifestations of Covid-19, to be eliminated completely was longer for older age groups of evaluated patients.

AUTHOR CONTRIBUTIONS

Fatemeh Honarmandpour: Conceptualization; data curation; methodology. **Azam Jahangirimehr**: Conceptualization; data curation; methodology. **Marziyeh Tahmasbi**: Data curation; formal analysis; methodology; writing – original draft; writing – review & editing. **Azam Khalighi**: Conceptualization; data curation; methodology; supervision. **Azam Honarmandpour**: Conceptualization; data curation; funding acquisition; investigation; methodology; project administration; supervision; writing – original draft; writing – review & editing.

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CONFLICTS OF INTEREST

The authors have no conflict of interest. The financial support received from the Shoushtar Faculty of Medical Sciences covered the costs of undertaking follow-up CT scans for participants in the second and third phases of the study. We declare that the Shoushtar Faculty of Medical Sciences as the financial supporter of the study was not involved in the study design; collection, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication.

TRANSPARENCY STATEMENT

The lead author Azam Honarmandpour affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

DATA AVAILABILITY STATEMENT

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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