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Abstract

Objective: To investigate the low-dose chest computed tomography (CT) presentation and dynamic changes in patients with novel coronavirus disease 2019 (COVID-19) to improve understanding of this highly infectious disease.

Methods: The clinical and CT data of 16 patients with COVID-19 were retrospectively analyzed. Dynamic CTs were performed continuously after admission.

Results: Of the patients, 14 were moderate cases, and 2 were severe. Twelve patients underwent CT at the early onset stage. Single nodules or ground-glass opacities (GGOs) were found in 2 patients and multiple bilateral pulmonary lesions in 8 (consolidation-like opacities with or without small nodules in five and large GGOs with interlobular septal thickening in three). Ten had lesion growth and enlargement on the second CT. Fourteen patients underwent CT during the progressive stage, which revealed GGOs and focal consolidation in 6 of them, lung consolidation opacities in 5, and simple, large GGOs with interlobular septal thickening in 3. In both severe cases, the lesions continued to enlarge and grow, and the extent of consolidation continued to expand.

Conclusion: Low-dose chest CT can clearly reflect the morphology, density, and extent of COVID-19 nodules, and is beneficial for observing dynamic nodule changes and disease screening and monitoring.

Keywords: Coronavirus; COVID-19; Diagnosis; Low dose; Computed tomography

1. Introduction

Since December 2019, multiple cases of novel coronavirus pneumonia caused by a new type of coronavirus have been successively discovered in Wuhan, Hubei Province, China. As the virus has spread, cases have also been found elsewhere in China and abroad. Deep sequencing of lower respiratory tract specimens from patients revealed that the source of infection was a novel coronavirus that has been named severe acute respiratory syndrome (SARS) coronavirus 2 (SARS-CoV-2) by the World Health Organization; the disease caused by this virus has been termed coronavirus disease 2019 (COVID-19).
Coronavirus is a large family of RNA viruses, of which 6 subtypes have been previously discovered. SARS-CoV-2 is a novel coronavirus strain that has not previously been found in humans and is currently considered to be the seventh subtype [1]. COVID-19 has a characteristic clinical and imaging presentation, and timely determination of the clinical and imaging data of affected patients can provide a reference for early clinical diagnosis and timely isolation and treatment, thereby improving the prognosis of patients. To further improve the radiographic examination and diagnosis of COVID-19, we retrospectively analyzed the clinical and imaging data of 16 patients.

2. Materials and methods

2.1. Clinical data

The institutional review board of Central People’s Hospital of Zhanjiang approved this retrospective study and waived the requirement for informed consent due to the nature of the study. We have abided by patient data confidentiality and compliance set out in the Declaration of Helsinki. The clinical and imaging data of 16 patients diagnosed with COVID-19 at our hospital between January 23, 2020 and February 14, 2020 were collected. All cases were confirmed on the basis of a positive test result for SARS-CoV-2 nucleic acid via reverse transcription polymerase chain reaction. Of the patients, 10 were men, and 6 were women, and their ages ranged from 24 to 68 years, with an average age of 36.2 years. All 16 patients had a history of travel to or residence in Wuhan within 2 weeks of onset, or exposure to or contact with patients from Wuhan with fever before onset. Eight of the patients comprised married couples, classifying them as familial clustered cases. The patients' general clinical data, including body temperature, peripheral WBC count, C-reactive protein level, procalcitonin level, D-dimer level, fibrinogen level, and lactate dehydrogenase level, are shown in Table 1. COVID-19 cases were clinically classified as mild, moderate, severe, or critical according to the Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (fifth draft edition) [2].

2.2. Examination method

Low-dose chest CTs were performed using SIEMENS SOMATOM Definition 16-slice spiral CT. The patients were placed in the supine position, with their hands raised and scanned while holding their breath at the end of inspiration. The scan ranged from the apex to the base of the lungs. The scanning conditions were as follows: tube voltage, 100 kV; reference tube current, 50 mA (current was adjusted using CARE Dose4D automatic tube current modulation technology); slice thickness, 5 mm; and slice increment, 5 mm. After scanning, thin-layer MSCT reconstruction technology was used for reconstruction of the acquired images with a slice thickness of 1.0 mm and an interval of 1.0 mm. The windowing technique was used on the acquired images. For the
lung window, the window width was 1200 HU, and the window level was −600 HU. For the mediastinal window, the window width was 350 HU, and the window level was 50 HU. The computed tomography dose index volume (CTD1vol), dose-length product (DLP), and effective dose (ED) of the chest CT scans were calculated using the following formula: \[ ED = \frac{DLP}{k}, \] where \( k \) is equal to 0.014. The effective radiation dose per chest CT scan was \( 1.5 \pm 0.09 \) mSv.

2.3. Imaging analysis

The shape, distribution, density, and margins of and dynamic changes in the lesions on low-dose chest CT during the early stage of onset, progressive stage, and recovery stage were observed and analyzed. All images were independently analyzed by two radiologists, and consistent results were achieved via consensus.

3. Results

There were 14 moderate cases (14/16, 87.5%) (Figs. 1−4) and 2 severe cases (2/16, 12.5%) (Fig. 5 and Fig. 6). The imaging presentations of the 16 patients at different periods were divided into 3 stages, namely the early onset stage, lesion progression, and lesion recovery.

3.1. CT presentation at the early onset stage

Twelve of the 16 patients underwent CT on days 1−3 after onset. In the 4 remaining patients, the initial examination was performed ≥3 days after onset, classifying them as being in the progressive stage. At the early stage of onset, single nodules (Fig. 2) or ground-glass opacities (GGOs) (Fig. 3) were found in 2 patients (2/12, 16.7%), the 95% confidence interval is (0.044, 0.378), multiple bilateral pulmonary lesions in 8 (8/12, 66.7%), the 95% confidence interval is (0.400, 0.934), large GGOs accompanied by interlobular septal thickening (Figs. 4 and 5) in five (5/12, 41.7%), and primarily large GGOs with local consolidation accompanied by focal consolidation-like opacities with or without small nodules (Figures 6) in 3 (3/12, 25.0%). No abnormalities (Fig. 1), however, were found in 2 (2/12, 16.7%). Thickened vascular opacities and thick-walled bronchial passages were seen in all 8 patients with multiple bilateral pulmonary lesions.

3.2. CT presentation during disease progression

Of the 12 patients examined at the early stage of onset, 10 patients (10/12, 83.3%), the 95% confidence interval is (0.622, 1.044), showed growth and enlargement of lesions on the second CT on days 3−5, including progression from unilateral to bilateral involvement and from single-to multiple-lobe involvement, ultimately progressing to diffuse bilateral distribution (Figs. 1, 4, and 5, and Figure 6). In 4 patients, the initial examination was performed ≥3 days after the disease onset, classifying them as being in the progressive stage; among them, 2 exhibited primarily large patches of

Fig. 1. Case 1, male patient, aged 26 years. A, no abnormalities on chest CT on day 1 after admission. B, multiple flaky consolidation opacities in the bilateral lower posterior and lateral basal segments of the lungs, with unclear margins on day 5. C, bilateral lesions were generally dissipated with some residual linear opacities on day 10.
consolidation, and the other 2 exhibited large patches of ground glass shadows with blurry margins accompanied by interlobular septal thickening. Of the 14 patients in the progressive stage, 12 patients (12/14, 85.7%), the 95% confidence interval is (0.674, 1.040), exhibited diffuse bilateral distribution of lesions. The lesions were more commonly distributed in the lower lungs and located primarily in the outer band of the lungs or the subpleural space. There were 2 cases of unilateral involvement, both of which involved the right lower lung.

The main presentation was lung consolidation opacities in five patients (5/14, 35.7%), the 95% confidence interval is (0.106, 0.608) (Fig. 1). The lesions were primarily lung consolidation opacities, which may be accompanied by a small amount of patchy GGOs. There were thickening of the bronchovascular bundles and multifocal subpleural lung consolidation in 3 patients, and air bronchograms were visible. There was multifocal subsegmental atelectasis in 3 patients.

There were 3 cases (3/14, 21.4%), the 95% confidence interval is (−0.001, 0.429), of simple, large GGOs with interlobular septal thickening (Figs. 4 and 5). During dynamic observation, the lesions always exhibited large GGOs with blurred margins. Thickened vascular opacities and thick-walled bronchial passages accompanied by interlobular septal thickening were observed.

The primary presentation was GGO in 6 patients (6/14, 42.8%), the 95% confidence interval is (0.169, 0.687) (Figures 6). GGO was the primary component of the lesion. GGOs and lung consolidation opacities can occur in the same or different slices; lung consolidation opacities can also be seen inside GGO lesions. There were 4 cases with irregular morphology and two cases with fan-shaped opacities parallel to the pleura. There was increased vascular reticulation in the lesions in six cases, and air bronchograms were visible.

Fig. 2. Case 2, male patient, aged 29 years. A, an unclear halo consolidation nodule was seen in the posterior basal segment of the right lower lung on day 2 after admission. B, lesion dissipation presented as a thin ground-glass opacity on day 6.

Fig. 3. Case 3, female patient, aged 24 years, wife of case 2. A, flaky ground glass opacities in the basal segment of the left lower lung with thick-walled bronchial passage and thickening of the adjacent blood vessels on day 2 after admission. B, lesion dissipation presented as a thin ground-glass opacity with unclear margins on day 6.
3.3. Dynamic CT lesion changes and outcomes

Of the 14 moderate cases, 2 exhibited clear dissipation of lesions on the second CT on day 4. A third CT was performed in 12 cases within 3–9 days of onset, and the lesions showed some dissipation and reduction (Figs. 1–4). Of the 2 severe cases, a third CT was performed on the third and fifth days of onset, respectively. The lesions continued to enlarge and grow. In 1 case, the third CT on day 6 showed extensive consolidation of both lower lungs; however, pleural effusion and lymph node enlargement were still not observed (Figure 6). The fourth CT on days 10 and 15 showed general dissipation of pulmonary nodules presenting as thin GGOs and residual partial linear opacities (Fig. 5 and Figure 6).

In 3 of the 12 moderate cases and 1 of the 2 severe cases (making a total of 4 lesions), there was dissipation or reduction of certain lesions during progression or recovery; however, there were new lesion opacities in other locations or enlargement of other lesions (Fig. 4 and Figure 6). There were 14 cases of lesions with diffuse distribution during progression, after which the extent and density of the lesions decreased, and subpleural curvilinear lines and interlobular septal thickening appeared.

4. Discussion

4.1. Epidemiological characteristics

At the early stage, most admitted patients with COVID-19 had a history of exposure to the Huanan Seafood Market in Wuhan [3,4]. In this cohort, 10 were male and 6 were female; the male sex dominance is consistent with the findings in the study by Huang et al. [5]. All 16 patients had a history of travel to or residence in Wuhan within 2 weeks of onset, or of exposure to or contact with patients from Wuhan with fever and respiratory tract symptoms. Six of the patients were 3 married couples, classifying them as familial clustered cases characterized by person-to-person transmission. In this cohort, 12 were aged ≤40 years, accounting for 75% of the total patients. The disease was more common among young and middle-aged individuals mainly because the patients were mostly migrant workers returning to Wuhan for the Lunar New Year holiday and were imported cases.

4.2. Clinical presentation

With respect to the clinical symptoms of the 16 patients in this cohort, 11 patients presented with fever at the early stage and gradually developed other symptoms, such as cough and thickened blood vessel opacity on day 1 after admission. B, the crazy-paving pattern region in the lower left lung dissipated and lightened, and new flaky opacities and ground-glass opacities developed in the lower left lateral basal segment and the right central lung on day 4. C, lesions in the left lower lung and the right central lung had clearly dissipated with multiple linear opacities and some ground-glass opacities remaining on day 8.
sputum; 3 presented only with fever; and 2 presented only with cough but not fever. Some COVID-19 symptoms in this cohort were atypical and had hidden characteristics. At the early onset stage, laboratory tests often show that the total peripheral WBC count is normal or decreased and that the lymphocyte count is reduced. Some patients have increased liver enzyme, creatinine, or myoglobin levels; most patients have elevated C-reactive protein levels and erythrocyte sedimentation rate but a normal procalcitonin level; and patients with severe conditions often have elevated D-dimer levels [2]. The WBC counts were normal or decreased in all 16 patients in this cohort. Conversely, the lymphocyte count was decreased in eight patients (50%), suggesting significant damage to the immune cells in the body. This may be associated with SARS-CoV-2 infection of lymphocytes or the cytotoxic or pro-apoptotic effects of SARS-CoV-2.

4.3. Dynamic changes in chest CT findings and pathological mechanisms in patients with COVID-19

It has been reported in the literature that the histopathological changes obtained from the puncture sampling of the cadaver of covid-19 suggest that the pathological features of covid-19 are very similar to those caused by severe acute respiratory syndrome (SARS) and middle east respiratory syndrome (MERS) coronavirus [6]. Therefore, it is of certain reference value to refer to the pathological changes of SARS and MERS [7,8]. Taken together with the extent and type of lesions, CT presentations can be divided into an early stage, a progressive or severe stage, and a remission stage.

At the early stage, lesions are located primarily in the periphery of the lungs or in the subpleural space. They are more common in the lower lungs, which may be related to the small size of viral particles. Furthermore, there is involvement of the terminal bronchi and respiratory bronchioles around the lung parenchyma, followed by involvement of all secondary lobules; this distribution is consistent with the report by Chung et al. [8]. Lung lesions are often multiple, and single lesions are rare. In two cases in this cohort, the first CT showed only small patchy opacities or small nodular opacities. These imaging findings were nonspecific and could not be distinguished from the findings of common inflammation. In the early stage, GGO was more common, which was related to the formation of hyaline membrane in the alveolar walls. Thickened blood vessels and thick-walled bronchial passages can be seen inside GGO lesions, with or without local reticular interlobular septal thickening. There may also be consolidation opacities or nodular opacities, which are generally small and limited with unclear margins and halo signs. GGO often exists alone but

Fig. 5. Case 9, male patient, aged 55 years. A, multiple sheet-like ground-glass opacities in the bilateral lower and right central lungs with interlobular septal thickening on day 2 after admission; B, bilateral lesions were larger than those before; there was a crazy-paving pattern; and thick-walled bronchial passage and thickening of the adjacent blood vessels were visible in the lesion on day 5; C, bilateral lesions had clearly dissipated with multiple linear opacities and some ground-glass opacities remaining on day 10.
Fig. 6. Case 13, male patient, aged 35 years. Multiple patchy opacities and nodular opacities in the bilateral upper lungs on day 1 after admission. A, large lesions and consolidation in the upper right lung posterior segment, with unclear margins; B, lesions in the posterior segment of the upper right lung were reduced in size compared to those before, presenting as ground-glass opacities, and those in the upper left lung were enlarged compared to those before on day 3; C, lesions in the posterior segment of the upper right lung had clearly dissipated, and the remaining bilateral lesions were larger and more numerous than those before, presenting as nodular ground-glass opacities and local consolidation on day 6 (Fig. 6c); D, at a different slice on day 1, the ground-glass opacities in the dorsal segment of the left lower lung had unclear margins. E, halo lesions in the left lower lung exhibited large flaky ground-glass opacities with interlobular septal thickening, and a new ground-glass opacity appeared in the right lower lung on day 3; F, on day 6, the bilateral lower lung lesions became larger and consolidated, exhibiting air bronchograms, and new bilateral multiple ground-glass opacities were distributed along the bronchovascular bundles; G, bilateral lesions were significantly reduced, and consolidation of the lower lungs had generally returned to normal, with residual ground-glass opacities and a small amount of linear opacities on day 15.
can also exist simultaneously with consolidation. This presentation is consistent with reports in the literature [8,9]. In addition, the early-stage CT findings of 2 mild cases in this cohort were negative; however, positive findings appeared on re-examination, suggesting that CT findings may not be synchronized with clinical manifestations and that close follow-up is necessary.

In the progressive stage, the distribution of lesions widens, and their extent increases, which could gradually involve multiple lobes in both lungs. Some lesions can expand and merge, and the extent of the consolidation or the original consolidation increases. GGO can coexist with consolidation opacities and linear opacities and may be accompanied by interlobular septal thickening, exhibiting a “crazy-paving pattern.” The pathological mechanism may be related to viral involvement in the alveolar wall at the early stage, which leads to intralobular interstitial thickening and bronchial and vascular wall thickening.

Severe cases usually progress to diffuse lesions in multiple lobes and segments of both lungs, primarily consolidation, and air bronchograms combined with GGOs and linear opacities can be seen. The lesions change rapidly, and they progress from interstitial-parenchymal-diffuse bilateral distribution. In the 2 severe cases in this cohort, the disease progressed to diffuse multiple GGOs in the lungs with consolidation only 3–4 days after onset. In addition, the lesions in the right lung were more severe and more widely distributed than those in the left lung; conversely, the lesions in the lower lobes and the posterior region were more severe than those in the upper lobes and the anterior region, suggesting that lesions may be gravitationally distributed.

After active treatment or improvement of inherent immunity, the patient enters the remission stage, and the lesions in both lungs gradually exhibit dissipation and improvement. CT showed that the lesions and their extent were reduced; the exudative lesions had dissipated significantly; the original lung consolidations had recovered; and some residues in both lungs have been dispersed as linear opacities. During the progression or dissipation process in some cases in this cohort, the lesions in one part dissipated or were reduced; however, new lesions appeared in other parts, or the lesions in other parts became larger, suggesting that the imaging finding changes are not only restricted by patterns of disease progression but are also associated with the method of treatment and its efficacy, presence or absence of underlying diseases, age, and immune function.

4.4. COVID-19 imaging method

Chest CT can detect millimeter-scale lung lesions, has high sensitivity, and is currently the preferred imaging method for the routine screening, diagnosis, and severity assessment of COVID-19 [9]. Because viral pneumonia often progresses rapidly, multiple CT re-examinations may be needed in a short period to assess the condition. Therefore, low-dose CT is recommended to reduce the effective radiation dose. This imaging method was used in the 16 patients in this study. CARE Dose4D automatic tube current modulation was used during the scan to reduce the radiation dose and clearly display the lesions, which was beneficial for observing the dynamic changes in the lesions and can serve as an effective method for disease screening and monitoring.

COVID-19 overlaps with other viral pneumonias, organizing pneumonia, and eosinophilic pneumonia in terms of imaging presentation and is somewhat difficult to distinguish. Additional consideration of the travel history, contact history, clinical symptoms, and laboratory test results of the patient is helpful in distinguishing from pneumonias caused by SARS, avian influenza, and other pathogenic conditions. In addition, it should be noted that its clinical manifestations are not synchronized with its CT manifestations, or the CT manifestations are consistent with the changes seen in viral pneumonia despite a confirmed epidemiological history; thus, a diagnosis cannot be completely ruled out even with a negative nucleic acid test result. In short, the advantages of low-dose CT screening and nucleic acid testing are complementary, with both being helpful for epidemic prevention and control. With respect to the relationship between clinical manifestations, imaging signs, and nucleic acid test results, further large-sample studies are needed.

Author contributions

Yue Zhao, Bin Yang conceived the study. Yue Zhao, Bin Yang, Xiaolong Liu and Jian Zhong collected data. Wenshuai Duan and Wei Du performed image analysis. Bin Yang and Yue Zhao wrote the manuscript. Yue Zhao performed the statistical analysis. Bin Yang, Xinhua Wu, and Wei Du edited and reviewed the manuscript. All the authors discussed the results and commented on the manuscript.

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Ethical statement

The Institutional Review Board of Central People's Hospital of Zhanjiang approved this retrospective study and waived requirements for informed consent from the patients.

Conflict of interest

The authors have no conflict of interest to declare.

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