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This manuscript has recently been accepted for publication in the European Respiratory Journal. It is published here in its accepted form prior to copyediting and typesetting by our production team. After these production processes are complete and the authors have approved the resulting proofs, the article will move to the latest issue of the ERJ online.

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Clinical and CT features of early-stage patients with COVID-19: a retrospective analysis of imported cases in Shanghai, China

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To the Editor,

Since December 2019, some patients with novel corona virus infectious disease (COVID-19) emerged in Wuhan, Hubei, China [1]. The pathogen analysis discovered a new type of coronavirus from infected airway epithelial cells [2] and named as sever acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) [3]. At the time of Chinese people were heading home for celebrating the Spring Festival, many latent cases left Wuhan, which led to the emergence of imported COVID-19 cases across the mainland of China and some other countries [4-5]. Shanghai is one of the major cities with imported cases [4-5].

COVID-19 are diagnosed mainly by real-time PCR (RT-PCR) to detect SARS-CoV-2 nucleic acid [4]. Due to the limited supply of RT-PCR kit and false-negative nucleic acid cases emerged, some experts have proposed to diagnose suspected cases using the time-saving chest computed tomography (CT) rather than RT-PCR [6]. CT features at the early-stage of COVID-19 have not particularly studied yet, which is vital to the early identification of suspected cases. The purpose of this study was to explore the early-stage clinical and CT features of nucleic acid-positive COVID-19.

From January 20 to 30, 2020, forty-four COVID-19 patients (male: female, 25:19; median age, 48.5 years; age range, 20-76 years) in our institution who met the entry criteria (patients’ interval time between onset symptom and CT scan was less than 4 days[7]), were enrolled in this
study. Their clinical data included the onset symptoms and main laboratory findings (divided into 3 groups; A, decreased; B, normal; C, elevated). Observation parameters on CT included lesions distribution, size (maximum diameter in axial images), attenuation category (type I, pure ground-glass opacities- pGGOs; type II, GGOs with consolidation; type III, GGOs with interlobular septal thickening; type IV, consolidation), lesion-related signs (vessel expansion, air bronchogram), mediastinal lymphadenectasis (>1 cm in short-axis diameter) and pleural effusion.

CT score was defined to quantify the pulmonary lesions in CT. The design formula was "size (cm) * attenuation category weight". The attenuation category weight was “1” for type I, “2” for type II/III, and “3” for type IV, which was discussed by two experienced chest radiologists, especially for the infectious disease diagnosis.

Of all the 44 patients, the onset symptoms were mainly fever (95.45%), followed by fatigue (15.91%), dry cough (13.64%), anorexia (13.64%), expectoration (11.36%), et al. 52.27% patients were with decreased lymphocyte count, while 50% for CD3+ T cell counts, 43.18% for CD4+ T cell and 45.45% for CD8+ T cell. All patients presented elevated level of erythrocyte sedimentation rate (ESR), while 75% for C-reactive protein (CRP), and 29.55% for procalcitonin (PCT). Nineteen patients (43.18%) had elevated lactic dehydrogenase (LDH) level, while 15.91% for alanine aminotransferase (ALT) and glutamytransferase (GGT), 13.64% for aspartate aminotransferase (AST). Many patients’ levels of total protein (TP), albumin (ALB), prealbumin (PAB), high-density lipoprotein (HDL) and low-density lipoprotein (LDL) were decreased (40.91%, 81.82%, 50%, 61.37% and 52.27%, respectively).

A total of 456 pulmonary lesions were detected by CT in 44 patients, of them 1 patient had no lesions (2.3%), five had solitary focal lesion (11.4%), seventeen had more than 10 lesions (38.6%). The lesions number of type I was 127 (27.85%), type II 286 (62.72%), type III 22 (4.82%), type IV 21 (4.61%). The lesions were mainly distributed in the peripheral (92.11%) and posterior part (71.71%, type I: 51.17%) of the lung. The size of type I was 1.37±1.08 cm (range, 0.34-8.53 cm), significantly smaller than that of type II (2.12 ± 2.00 cm, 0.3-13.53 cm, P < 0.001), but no statistically difference with type IV (1.52 ± 0.88 cm, 0.38-3.12cm, P = 0.2553). The size of type II was significantly smaller than that of type III (4.7 ± 2.58 cm, 1.36-11.90 cm, P < 0.001), but no statistically difference with type IV (P = 0.4632). The size of type III was also significantly
larger than that of type IV ($P < 0.001$). The CT score was $38.44 \pm 34.56$ (range, 0-136.13). Finally, there were 11 indicators in the multiple linear regression model (abnormal rate $\geq 40\%$; without multicollinearity; indicators: lymphocyte, CD4+ T cell, CD8+ T cell, CRP, TP, ALB, ALB/GLB, PAB, LDH, HDL, LDL) to evaluate their linear relation to the CT score. The adjusted $R^2$ was 0.509. Only CD4+ T cell ($B = -25.738$, $P = 0.018$), CRP ($B = 20.565$, $P = 0.044$) and LDH ($B = 23.201$, $P = 0.010$) got statistically significance of the linear regression with CT score. 28.95% lesions were with vessel expansion, while 40.13% with air bronchogram. 6.82% patients had mediastinal lymphadenopathy, while 6.82% patients had pleural effusion (bilateral: 2/44; unilateral: 1/44). All patients obtained follow-up CT at least once. During our study period, we recorded all patients’ first follow-up CT (interval of 2-7 days; median, 4 days). 81.82% patients showed lesions progression, while 13.64% patients showed lesion absorption. We also achieved a patient’s first and twice follow-up CT (Figure).

In our study, most patients’ onset symptoms were fever, which was similar to SARS-CoV\cite{8} and MERS-CoV\cite{9}, but the other symptoms of COVID-19 is mild. 52.27% patients’ lymphocytes count decreased which is valuable to the early diagnosis. Some experts suggested that COVID-19 might mainly act on lymphocytes, especially T lymphocytes, as does SARS-CoV\cite{10}. Many patients’ CD3+ T, CD4+ T, and CD8+ T cell counts also decreased which indicated COVID-19 could attack immunocyte and lead to the imbalanced immune regulation. The CD4+ T cell counts, as well as CRP and LDH got linear regression to the severity of pulmonary lesions on CT, which was not depicted before. Significantly, those indicators enrolled in the model were the first value and divided as the category variable, which might indicate the patients’ onset pulmonary severity levels. Similar to MERS-CoV or SARS-CoV infection\cite{9}, some patients presented elevated level of liver aminotransferase, which may indicate the potential liver injury\cite{11}.

13.64% patients’ pulmonary lesions are mild in the early stage, which are easy to be misdiagnosed. All the lesions of COVID-19 have a predominant distribution in the peripheral part of the lung (92.11%). Pulmonary lesions, except type I, have a predominant distribution in the posterior part of the lung, which is vital to the early diagnosis and had not depicted previously. In the early stage of COVID-19, most pulmonary lesions represent as type II, followed by type I, while type III and type IV are rare. The size of lesion represents as type IV is small, nearly to type
I and II, in contrast to the advanced COVID-19 which may show wide consolidation \cite{7}. The consolidation is also common in H7N9 pneumonia \cite{12}, bacterial pneumonia, invasive fungal disease \cite{13} and some other virus pneumonia \cite{14}. 81.82% patients’ follow-up CT showed disease progression, which is in accordance with the time course of lung changes that the greatest severity approximately 10 days after onset symptoms \cite{15}.

In conclusion, fever is the main onset symptom of COVID-19. Decreased lymphocyte count is an important indicator for diagnosis. The features of early-stage COVID-19 include GGOs-based lesions with rare small size consolidation mainly distributed in the peripheral and posterior part of the lung. Some patients’ pulmonary lesions are small and focal, which should capture physicians’ attention. The level of decreased CD4\(^+\)T cell, elevated CRP and LDH may prompt the severity of CT imaging.

Acknowledgement: We express our sincere wishes and greatest respects to the front-line workers, who are fighting against the COVID-19.

References:


Figure: A 64 years old female, the first CT shows lesions manifested as type II and III with pleural thickening and adhesion, mainly located in the peripheral and posterior part of the lung (A-C). Seven days follow-up CT shows lesions size broaden, and density increased, which means progression (D). While then 3 days follow-up CT shows lesions partly absorption and fibrosis, which means relief (E).