Comparative Study of CT Characteristics in Imported Cases and Indigenous Cases with COVID-19

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Objective: The aims of the current study were to describe the serial CT characteristics of patients infected with COVID-19. In addition, in the light of the CT findings, we tried to determine whether virulence weakens during the transmission with quarantine management.

Methods: Demographics, comorbidity, clinical findings, CT scanning, and scores of the affected lung parenchyma were compared for 131 patients with abnormality on CT images classified as COVID-19 pneumonia and the patients were divided between an imported group (n = 83) and indigenous group (n = 48), according to infected location. Two reviewers scored chest CT examinations for segmental involvement, ground glass opacities, consolidation, and honeycombing opacities. The 55 patients with peak CT "severity score" were selected to make a comparative analysis.

Results: Patients' demographics and comorbidities and clinical findings did not differ significantly between the two groups. The CT scores distribution trendline of the third CT scanning was lower than the former CT scanning. The peak CT scores trendline of the 55 selected COVID-19 patients in the indigenous group was lower than the imported group. The ROC analysis revealed an area under curve of 0.714 for the CT scanning with an optimal cutoff scores of 2.55 for prediction of contact history, a sensitivity of 76.3%, and a specificity of 52.9%. The peak CT scores of the imported cases were higher than of the indigenous cases and the lung consolidation predominance on CT findings was remarkable in the imported patients (P < 0.05).

Conclusions: CT scanning not only monitored the progression of patients with COVID-19 but also reflected their exposure status to some extent. We suggest that a follow-up CT scanning interval of more than 5 days might be cost effective. The pathogenicity of novel coronavirus may be weakened through transmission under adequate quarantine measures, since indigenous cases have much better progression than imported cases.

Key words: COVID-19; CT; Coronavirus; Pathogenicity

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In December 2019, there was an outbreak of atypical pneumonia in Wuhan, the provincial capital of Hubei in China. The pathogens were identified as SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) and the disease caused by this SARS-CoV-2 was called COVID-19 by the World Health Organization (WHO). The epidemic was soon discovered in more than a dozen countries around the world. WHO declared the epidemic outbreak a Public Health Emergency of International Concern. SARS-CoV-2 is an RNA virus that mutates easily due to unstable-strand replication. The mutations to strengthen or reduce virulence occur

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randomly. But the human-to-human transmission and formidable transmissibility undoubtedly threaten the public health and the epidemic can now be characterized as a pandemic [1-4].

To control COVID-19, the Chinese government made intensive efforts toward epidemic prevention and control to curb the spread of the virus. Wuhan, where the earliest symptom onset of confirmed patients appeared, went into lockdown on January 23, 2020, with public transport suspended, roads out of the city blocked, and flights cancelled. Under the most restrictive measures, the patients with COVID-19 in other Chinese provinces turned gradually from imported cases to indigenous cases. The former cases contained patients infected by the first and second generation of the novel coronavirus; the latter cases included patients infected by subsequent generations. In China, the worst affected area was Wuhan, and the fatality rate in the Hubei Province was 3.1%, as the majority of the deaths occurred in this province, while the fatality rate outside Hubei was only 0.16%. It has been unclear whether the virulence weakens during the transmission under quarantine management, there is yet insufficient evidence yet to determine if it does.

Radiography plays important role in diagnosing pneumonia, but imaging manifestations of viral pneumonia are diverse and associated with the pathogenesis and progress of viral infection. The radiography appearances affected by the immune status of the host are similar to other viral pneumonia, such as Severe Acute Respiratory Syndrome (SARS) and the Middle East Respiratory Syndrome (MERS). CT has a definite advantage in diagnosis and monitoring of disease progression during medical treatment [5-7]. Our institution is one of the designated hospitals to treat patients infected with COVID-19. We observed signs of COVID-19 on a number of chest CT findings between imported patients coming from Hubei and indigenous patients infected in our province during the epidemic outbreak. The aims of the current study were to describe the serial CT characteristics of patients infected with COVID-19. In addition, we tried to determine whether the virulence weakens through transmission with control measures by identifying the imaging differences between imported cases and indigenous cases with peak severity scores in CT scanning.

Materials and Methods

Our institutional review board approved the study and informed consent was waived for the use of patients’ medical and imaging data. To avert any potential breach of confidentiality, no link between the patients and the researchers was made available.

Subjects

Our retrospective cohort comprised 142 patients (age range, 17-75 years; mean ±SD age, 44.14 ± 13.38 years; 74 male and 68 female patients) who received a positive diagnosis from December 24, 2019 to February 20, 2020. Nasopharyngeal swabs obtained from the patient tested positive for 2019-nCoV on real-time reverse-transcription polymerase-chain-reaction (RT-PCR) assays (Sansure Biotech). The initial CT findings were obtained at 6.36 ± 4.98 days (mean ± SD; range 0–34 days) after the onset of symptoms. The subjects were divided into two different cohorts: imported cases (n = 88, 48 males and 40 females; mean age, 43.47 ± 1.35 SD; range, 21–70 years) and indigenous cases (n = 54, 26 males and 28 females; mean age 45.24 ± 1.97 range 17–75 years). All subjects received appropriate supportive care in hospital.

CT findings and evaluation

The Light Speed VCT, Bright Speed Elite CT and Brivo CT325 (120 kV and automatic tube current modulation technology; GE Healthcare) were used for all chest CT examinations. The patients held their breath in the supine position during end-inspiration and were imaged with 5-mm slice thickness CT. The scanning area ranged from the apex to the basis pulmones and phrenic angle. CT findings obtained on admission to the department of emergency medicine and subsequent CT findings obtained during the course of treatment were included in the study. Throughout the study period, routine CT scanning were obtained every 3 or 4 days.

Interpretation of CT findings

Serial CT findings obtained at initial presentation and during treatment were retrospectively reviewed and a consensus opinion was provided by two radiologists, none of who was aware of the clinical progress of the subjects. The radiologists involved in the review process had 10 and 20 years’ experience with CT reporting. The radiographs were viewed on a dedicated radiology PACS workstation (Neusoft, China). The radiographs were examined for the presence of ground-glass opacity, consolidation, and honeycombing opacity, and the findings were recorded using the Fleischner Society nomenclature [8]. In addition, other abnormalities were recorded.

An overall lung “severity score” was recorded at the initial presentation and on follow-up CT scans. Each lung was divided into upper and lower zones according to the oblique fissure of the lung and each zone was evaluated in terms of involvement. The degree of involvement within each lung zone was assigned a score ranging from
The remaining 131 patients with abnormality on CT categorized as upper respiratory tract infection (URI). did not have any radiographic abnormality and were who tested positive for the new strain of coronavirus were graphed by MedCalc. The parenchymal abnormality on CT images was graded on a 4-point scale: 1, normal attenuation; 2, ground-glass attenuation; 3, consolidation; and 4, honeycombing opacity. The ground-glass opacity was defined as an area of hazy increased lung opacity, within which margins of pulmonary vessels maybe indistinct. Consolidation appeared as a homogeneous increase in pulmonary parenchymal attenuation that obscured the margins of vessels and airway walls. Honeycombing opacity referred to destroyed and fibrotic lung tissue containing numerous cystic airspaces with thick fibrous walls. Points from all zones were added to arrive at a final total cumulative score (range of possible scores 0-16) (Fig. 1). At least consecutive follow-up chest CT scans were available for 142 of the patients during the study time window. These scans were evaluated to assess for progression over time. Then, the cases of peak "severity scores" were selected o analyze statistically. The peak CT score referred to the previous and the subsequent follow-up CT score both being lower than this score. The peak scores of two patients who died were the highest scores.

Although pleural effusions, discrete pulmonary nodules, and mediastinal lymphadenopathy were not typical radiographic features, they were also recorded. In terms of anatomic location, the distribution of parenchymal abnormalities was recorded according to five lobes.

Statistical analysis

Statistical analysis was executed using SPSS Statistics20 (IBM company). Differences in the clinical-radiological characteristics of the patients who were infected in Hunan and those who were infected in Hubei were assessed using the Mann-Whitney U test for continuous variables and Fisher’s exact test for categorical variables. All analyses were considered significant at p values of less than 0.05 (single-tailed). Receiver operating characteristic (ROC) curve was plotted to select the appropriate cutoff value of peak CT scanning scores to assess maximum sensitivity and specificity for differentiate groups according to contact history. Dot-and-line diagram and Box-and-whisker plots were graphed by MedCalc.

Results

Demographics and clinical characteristics

Among 142 laboratory-confirmed cases, 11 patients who tested positive for the new strain of coronavirus did not have any radiographic abnormality and were categorized as upper respiratory tract infection (URI). The remaining 131 patients with abnormality on CT images were classified as COVID-19 pneumonia (72 men, 65 women; median 44.68 ± 13.40 years). Patients were classified into two categories according to contact history. Indigenous group patients were exposure to infected people in Hunan. Patients who recent travelled to or lived in Wuhan were imported infectious cases. In terms of premorbid condition, of 11 patients with URI, 2 (2/11) had cardiopathies. Underlying co-morbidities were documented in 46 of the patients (46/131) with COVID-19 pneumonia, including diabetes mellitus (n = 9), surgery history (n = 9), hypertension (n = 19), hepatobiliary disease (n = 8), coronary heart disease (n = 4), cerebral infarction (n = 4), lung disease (n = 3, including 1 pneumonia case of unknown etiology in 2003, 1 case of tuberculosis, and 1 case of chronic bronchitis), thyroid disease (n = 3), gastrointestinal diseases (n = 2), and hernia (n = 1). 15 patients suffered from more than one underlying co-morbidity. On initial presentation, most patients complained of fever (102/113), followed by respiratory symptoms such as cough, sputum, and dyspnea (75/113), fatigue (18/113), pharyngalgia (5/113), gastrointestinal symptoms such as nausea, vomiting, and diarrhea (10/113), myalgia (5/113) and headache (5/113). There were no significant differences between the imported cases and indigenous cases in terms of patients’ demographics and clinical characteristics among patients with COVID-19 pneumonia (P > 0.05) except that the 11 patients with URI were younger than patients with COVID-19 (P = 0.044). Detailed patient characteristics are shown in Table 1 and Table 2.

CT findings

The average time to CT scans from the symptom commencement was 6.24 ± 3.63 days. All of the patients had at least 3 consecutive follow-up CT scans in the hospital. Dot-and-line diagram and Box-and-whisker plots of sequential CT scores appear in Figure 2. CT scores of imported and indigenous patients were no different in the three scans (Fig. 2A and 2B). The peak CT scores trendline of the 55 selected COVID-19 patients was lower in the indigenous group than the imported group (Fig. 2C). The 11 patients with URI did not show any radiographic abnormalities.

The imaging of 131 patients with pneumonia changed with the progression of the disease. Of the 131 patients, the 55 with a peak CT "severity score" were selected o analyze in Table 3, and the CT scores of the remaining 76 patients that showed a tendency either upward or downward were excluded. In the receiver operating characteristic curve (ROC) analysis, an optimal cutoff value of a peak CT score 2.55 had a sensitivity of 76.3% and a specificity of 52.9% for the prediction of close
contact history in Wuhan (Fig. 3). The area under the ROC curve was 0.714 (95% confidence interval: 0.564, 0.863). Table 3 compares the patients' demographics and premorbidity as well parenchyma abnormalities and lung lobes involvement on chest CT findings between imported and indigenous groups with peak CT scores in hospital.

### Table 1  Baseline characteristics of patients with URI and COVID-19 separately

| Demographic data                      | URI (n = 11) | COVID-19 (n = 131) | P value |
|---------------------------------------|--------------|--------------------|---------|
| Age (year)                            | 36.82±10.48  | 44.76±13.44        | 0.044   |
| Sex (M/F)                             | 4/7          | 70/61              | 0.439   |
| Premorbid condition (No/Yes)          | 9/2          | 85/46              | 0.419   |
| Time from Symptom onset to CT scans (day) | 5.91±8.28   | 6.24±3.63          | 0.073   |
| Symptoms (n/N)                        |              |                    |         |
| Fever                                 | 3/11         | 102/131            | 0.172   |
| Respiratory symptom                   | 3/11         | 75/131             | 0.398   |
| Fatigue                               | 1/11         | 18/131             | 0.938   |
| Myalgia                               | 0/11         | 5/131              | 0.828   |
| Gastrointestinal symptom              | 1/11         | 10/131             | 0.673   |
| Pharyngalgia                          | 2/11         | 12/131             | 0.736   |
| Headache                              | 1/11         | 5/131              | 0.984   |

Data are Mean ± SD or n/N, where N is the total number of patients with available data. URI, upper respiratory tract infection.

### Table 2  Baseline characteristics of patients with COVID-19 between imported and indigenous cases

| Demographic data                      | Imported cases (n = 83) | Indigenous Cases (n = 48) | P value |
|---------------------------------------|-------------------------|---------------------------|---------|
| Age (year)                            | 44.00±12.79             | 46.06±14.54               | 0.412   |
| Sex (M/F)                             | 45/38                   | 25/23                     | 0.478   |
| Premorbid condition (No/Yes)          | 54/29                   | 31/17                     | 0.552   |
| Time from symptom onset to CT scans (day) | 6.47±3.71   | 5.83±3.50                | 0.279   |
| Symptoms (n/N)                        |                         |                           |         |
| Fever                                 | 67/83                   | 35/48                     | 0.206   |
| Respiratory symptom                   | 47/83                   | 28/48                     | 0.498   |
| Fatigue                               | 12/83                   | 6/48                      | 0.487   |
| Myalgia                               | 4/83                    | 1/48                      | 0.394   |
| Gastrointestinal symptom              | 5/83                    | 5/48                      | 0.279   |
| Pharyngalgia                          | 6/83                    | 6/48                      | 0.241   |
| Headache                              | 4/83                    | 1/48                      | 0.431   |

Data are Mean ± SD or n/N, where N is the total number of patients with available data. M, male; F, female.

The predominant CT findings at presentation consisted of pulmonary consolidation in 41 patients (41/55), subpleural distribution in 32 patients (32/55), and crazy paving pattern in 27 patients (27/55). A small pleural effusion was found in 3 patients (2/55). Discrete pulmonary nodules were observed in 1 patient (1/55).
Lymphadenopathies were not seen on CT. There was no statistically significant difference in terms of patient demographics and premorbidities on chest CT findings between imported and indigenous groups with peak CT scores in the hospital. The lesions in the imported group had more left lower lobe involvement than those in the indigenous group ($P = 0.044$). But the peak CT scores of imported cases were higher and the lung consolidation predominance on CT findings was more remarkable in the imported group compared with indigenous group ($P < 0.05$).

**Table 3** Comparison of radiological characteristics of 55 COVID-19 pneumonia cases between imported and indigenous group

| Characteristics                        | Imported cases ($n = 38$) | Indigenous cases ($n = 17$) | $P$ value |
|----------------------------------------|---------------------------|----------------------------|-----------|
| Age (year)                             | 45.97±13.55               | 44.94±15.60                | 0.870     |
| Sex (M/F)                              | 21/17                     | 11/6                       | 0.362     |
| Premorbid condition (No/Yes)           | 21/17                     | 12/5                       | 0.221     |
| Peak CT score                          | 4.51±2.50                 | 2.82±2.02                  | 0.018     |
| CT opacification pattern and distribution (n/N) |               |                             |           |
| Ground-glass opacification only        | 1/38                      | 1/17                       | 0.527     |
| Ground-glass opacification predominance| 8/38                      | 3/17                       | 0.540     |
| Consolidation predominance             | 28/38                     | 13/17                      | 0.033     |
| Consolidation only                     | 1/38                      | 0                          | 0.679     |
| Subpleural distribution                | 23/38                     | 13/17                      | 0.201     |
| Crazy paving pattern                   | 17/38                     | 10/17                      | 0.201     |
| Honeycombing                           | 2/38                      | 0/17                       | 0.473     |
| Linear opacities                       | 18/38                     | 4/17                       | 0.084     |
| Discrete pulmonary nodules             | 1/38                      | 0/17                       | 0.679     |
| Lymphadenopathy                        | 0/38                      | 0/17                       | N/A       |
| Pleural effusion                       | 3/38                      | 0/17                       | 0.322     |
| Frequency of lobe involvement in GGO   |                           |                            |           |
| Right upper lobe                       | 28/38                     | 11/17                      | 0.498     |
| Right middle lobe                      | 26/38                     | 8/17                       | 0.056     |
| Right lower lobe                       | 34/38                     | 14/17                      | 0.464     |
| Left upper lobe                        | 24/38                     | 10/17                      | 0.759     |
| Left lower lobe                        | 31/38                     | 10/17                      | 0.073     |
| Frequency of lobe involvement in consolidation (n/N) |            |                            |           |
| Right upper lobe                       | 18/38                     | 6/17                       | 0.404     |
| Right middle lobe                      | 32/38                     | 10/17                      | 0.041     |
| Right lower lobe                       | 18/38                     | 5/17                       | 0.212     |
| Left upper lobe                        | 11/38                     | 2/17                       | 0.166     |
| Left lower lobe                        | 35/38                     | 14/17                      | 0.284     |

Data are Mean ± SD or n/N, where N is the total number of patients with available data. N/A, not applicable.
Discussion

SARS-CoV-2 has become a global health concern. The virulence and transmissibility remains unclear and to be investigated [10]. In China, the strict measures for epidemic control seemed to take effect. The conditions of patients outside Hubei province were not as severe as Wuhan. One possible reason might be the pathogenicity of subsequent SARS-CoV generation was reduced through transmission with intervention. Successful isolation of most pathogenic agents led to weaker virulence of subsequent generations, since the disseminated viruses were less pathogenic with transmissibility [11].

In this study, we analyzed 142 laboratory-confirmed SARS-CoV-2 positive cases. Imported cases referred patients from the epidemic region. Indigenous cases in our paper were all import-linked secondary or tertiary infection cases. 11 cases suffered acute URI and had no radiographic abnormality, and all were younger than the 131 cases with COVID-19 ($P = 0.044$). The records of 83 imported cases and 48 indigenous cases with COVID-19 pneumonia were evaluated. There were no differences in the demographic and clinical data between the imported group and indigenous group.

There were 2 deceased cases in imported group. One was 64-year-old man with a 10-year history of chronic obstructive pulmonary disease.

Figure 1 4-point scale CT scanning scoring system. (A) Normal attenuation scores 1 point. (B) Ground-glass opacities scores 2 points. (C) Consolidation scores 3 points. (D) Honeycombing opacity scores 4 points.

Figure 2 (A and B) Dot and line diagram of CT scores on 3 sequential CT scans between imported cases and indigenous cases. (C) Box and whisker plots of peak CT scores in 55 COVID-19 cases.

Figure 3 ROC analysis of CT scanning score for prediction of imported history. $N = 55$; AUC = 0.714, 95% CI: 0.576-0.827.

Figure 4 64-year-old male with history of recent travel to Wuhan and laboratory-confirmed SARS-CoV-2 presented with fever. CT images of score 10.9 showed honeycombing opacity that most appeared at subpleural areas of bilateral pulmonary. There also appeared diffuse ground-glass opacities change mixed with a hint of consolidative opacities and slight effusion in the right pleural cavity. Emphysema change displayed since the patients had a 10-year history of chronic obstructive pulmonary disease.
chronic obstructive pulmonary disease and the other was 59-year-old male with a history of pneumonia with unknown etiology in 2003. Figure 4 displays CT findings of the deceased case coexistent with chronic obstructive pulmonary disease. The CT images were obtained 6 days before his death. Consistent with previous studies, patients in critical condition tended to be elderly. They had some level of sensitized immune system following exposure to SARS-CoV-2 and died of systemic inflammatory response syndrome. The 2 deceased cases showed parenchyma abnormality of honeycombing. Irregular linear opacities were observed in progression.

Figure 5. A 36-year-old man who had close contact history with COVID-19 pneumonia patients in indigenous group presented with fever and vomiting. (A) Initial CT scan at 2 days after admission showed ground glass opacity in subpleural regions of right middle lung. (B) CT image obtained at 5 days after admission displayed that the lesion in right middle lung expanded and opacity increased. (C) CT images obtained at 8 days after admission showed apparent bilateral patchy ground-glass opacities. (D) CT images obtained at 11 days after admission displayed obvious consolidative pulmonary opacities with air bronchogram sign. (E) The lesions shrunk after 15 days in the hospital and there appeared irregular line opacity. (F) The extent of lesions was further lessened with the trend of absorption and dissipation on CT images obtained at 18 days after admission.

Viruses in the same viral family share a similar pathogenesis; therefore, CT images have many similar features to SARS and MERS [12-14]. A young patient in the indigenous group with hypertension had 6 sequential CT scans. The progression of the pulmonary lesions has dynamic changes from mild to severe and to mild again over time (Fig. 5). The most common type of opacity observed in the beginning was peripheral ground-glass, followed by consolidation and a combination of both ground-glass opacity and consolidation. Consolidation predominance (41/55) were observed in the time of peak CT scanning deterioration was more significant in imported cases.

Subpleural distribution (32/55) were typical in COVID-19 pneumonia, and there were no significant differences in lobes involvement ($P > 0.05$). We found the severity scores trend in indigenous group were lower than imported cases on three consecutive CT scans. Moreover, CT scores distribution trendline of the third CT scanning were lower than the former CT scanning. There was no difference between the first and the second time of sequential CT scores due to the every 3- or 4-day CT scanning interval. We picked up 55 cases with peak CT scores during the study date range. Imported cases were more accessible to pulmonary consolidation than indigenous cases. A peak CT score of 2.55 might justify the virus patients infected were more pathogenic.

Several studies have discussed the imaging findings and epidemiological status of SARS-CoV-2 [15-18]. However, most of them focused on case reports and radiographic findings of COVID-19 pneumonia. Our study highlights the peak CT scores differences between imported and indigenous cases, which could reflect the fact that subsequent generations of SARS-CoV-2 were less pathogenic than the first and second generation. As to the abnormality of CT scanning, we proved the COVID-19 pneumonia was limited to transmitted disease under quarantine management. It did transmit from people to people, but the severity in the indigenous patients was milder than in the imported patients.

There were several limitations in this study. First, it was a retrospective study and might have limited power in identifying prognostic factors. Second, the imported cases included a few people who might have been
infected by the second generation or more of the virus in the affected area. But the indigenous cases only included patients infected by the second generation or more of the novel coronavirus. Lastly, all patients were treated with a variety of medications and the CT scores we collected were the first three times of CT scanning. So the individual differences of CT images were inevitable. The sensitivity, specificity and AUC of peak CT scores might not be sufficiently high enough. We found that CT scanning may be the most efficient diagnostic or prognostic tool for patients with COVID-19, but there was no significant difference in the trendline between the first two times of follow-up CT scanning. We should not overlook the highly contagious disease would increase risk of occupational exposure and patients would increase radiation exposure. So we suggest that the interval of CT scanning to COVID-19 should be more than 5 days. Prospective studies on CT manifestation with large-sample are still needed.

Conclusions

An epidemic of SARS-CoV-2 has threatened public health worldwide. CT scanning could not only play a vital role in the management of patients with the disease but also reflect exposure status to some extent. Indigenous cases have much better outcome than imported cases. The pathogenicity of novel coronavirus may be weakened through transmission under adequate quarantine measures. Based on our findings, we suggest that a follow-up CT scanning interval of more than 5 days might be cost effective.

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Conflict of Interest

The authors have no conflict of interest to declare.

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