Analysis and classification of radiological results and epidemiology of patients with COVID-19 pneumonia

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Abstract
The coronavirus disease-2019 (COVID-19) pneumonia which is caused by the severe acute respiratory syndrome coronavirus-2 (SARS CoV-2) virus is the current urgent issue world over. According to the Health Ministry of Turkey, the first COVID-19 patient was diagnosed on March 11, 2020. Since then, approximately 5.5 million patients have been confirmed to be positive SARS CoV-2 virus. In this retrospective study, we aimed at analyzing the epidemiological and radiological findings of COVID-19 cases at the Hospital of Grand National Assembly of Turkey from April 1, 2020 to December 31, 2020.

A total of 130 patients (84 male, 25–87 years) were diagnosed as positive with High Resolution Computed Tomography (HRCT) scans and 71 of them confirmed with positive Real Time Polymerase Chain Reaction using the patients’ nasopharyngeal and throat samples.

HRCT scans were classified into 4 stages. Stage I (39.2%) patients’ group; the HRCT results were found to be mosaic perfusion, whereas Stage II (39.2%) were found to be Ground Glass Opacity. Also, consolidation was detected in Stage III (20%). Finally, Stage IV, considered the most severe lung findings, and named as a crazy paving pattern was determined in 2 patients (1.53%). Furthermore, 20% of patients were found to be positive using IgG antibody against to SARS CoV-2 virus.

Our findings showed that HRCT could be most prominent technique compared to real time polymerase chain reaction for the diagnosis of COVID-19 pneumonia. The novel classification of HRCT findings will be helpful to early diagnosis of the disease, time saving and eventually cost-effective.

Abbreviations: COVID-19 = coronavirus disease-2019, GGO = ground glass opacity, HRCT = high resolution computed tomography, RT-PCR = real time polymerase chain reaction, SARS CoV-2 = severe acute respiratory syndrome coronavirus-2.

Keywords: consolidation, coronavirus disease-2019 pneumonia, crazy paving pattern, epidemiology, ground glass opacity, high resolution computed tomography, mosaic perfusion, radiology, severe acute respiratory syndrome coronavirus-2 virus

1. Introduction
The current pandemic of coronavirus disease 2019 (COVID-19) has a significant toll on people all across the world. COVID-19 pneumonia is caused by the severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) virus. The SARS CoV-2 infection mechanism is similar to other corona virus infections such as Severe Acute Respiratory Syndrome Coronavirus (SARS) and Middle East Respiratory Syndrome Coronavirus infection.[1–3] Almost every country has brought about a need for timely and high diagnostic performance tests for detecting COVID-19.[4] In December 2019, COVID-19 pneumonia started from Wuhan, China and spread to all over the world.[5] According to the World Health Organization (WHO) more than 200 million individuals infected with the SARS CoV-2 virus since December 2019. COVID-19 pneumonia was declared as a global pandemic in early March 2020.

In Turkey, the first SARS CoV-2 case was reported on 11 March 2020 and now approximately 6.5 million patients have been diagnosed with the COVID-19. Furthermore, approximately 60,000 patients died in Turkey due to the COVID-19 related illness. Although there are numerous vaccines approved and used in many countries like Turkey, early detection is essential for prevent the death and spread of SARS CoV-2 virus.

For the detection of SARS CoV-2 virus, real time polymerase chain reaction (RT-PCR) and high resolution computed...
tomography (HRCT) are commonly used.\[^{6,7}\] RT-PCR is a wet lab technique that is based on the amplification of the SARS-CoV-2 virus. Compared to the RT-PCR, HRCT is a high throughput technique used for the detection of the virus. HRCT uses thin slice thickness and it better evaluates the secondary lobule of the lungs.\[^{8}\] The advantage of HRCT is, classifying and analyzing the patients’ findings according to the lung status. The HRCT scans are classified as mosaic perfusion, Ground Glass Opacity (GGO), consolidation, and the crazy-paving pattern. This classification helps to understand the COVID-19 patients’ severity.\[^{9–11}\]

Studies performed by clinicians suggested that HRCT is a very prominent technique for the determination of COVID-19 patients in the early stages.\[^{5,7,11}\] Numerous studies have shown that the radiological findings changed in both mild and severe courses of COVID-19 pneumonia. Furthermore, recent research articles\[^{11–13}\] have found that approximately 94% of hospitalized patients have persistent lung parenchymal findings on their computed tomography scans. However, there is no comprehensive data about the lung symptoms classification of COVID-19 infection in the literature.

The purpose of this study was to evaluate the severity of HRCT scans and to establish a correlation between the HRCT scans and patients’ symptoms. This study, which evaluates and analyzes the results of tomography in COVID-19 pneumonia, could be helpful to determine the prognosis of COVID-19 pneumonia from a different perspective and could be beneficial to put the correct diagnosis. The outline of the study design is given in Figure 1.

### 2. Material and methods

#### 2.1. Patients

A total of 130 patients who have suspected from COVID-19 pneumonia or a history of close contact with an infected individual were retrospectively enrolled in this study. 130 patients (84 male, 25–87 years) underwent RT-PCR and/or HRCT between 1 April 2020- 31 December 2020 in the Hospital of The Grand National Assembly of Turkey. For diagnosis of SARS CoV-2 virus, using the patients’ nasopharyngeal and throat samples, RT-PCR was performed with the Bio-Speedy SARS CoV-2N RT-qPCR Kit (Bioeksen, Turkey). The kit amplifies both Nucleocapsid gene (N) and open reading frame 1ab (ORF1ab) gene of SARS CoV-2 virus and kit was also the first approved kit by the WHO in Turkey. All steps were done according to the manufacturer’s protocol by using the Bio-rad CFX-96 real-time PCR system. The RT-PCR results were extracted from the patients’ electronic records in the Ministry of Health system. Ethical approval was obtained from the Ministry of Health Ankara City Hospital Non-Interventional Clinical Research Ethics Board (Project No: E2–21–51) and informed written consent was obtained from all patients.

Determination of IgG antibodies to SARS CoV-2 virus, using the patients’ plasma samples the Siemens SARS-CoV-2 IgG assay (Siemens, Germany) was performed at the Ministry of Health Ankara City Hospital. According to the manufacturer’s protocol, the value of IgG antibody is given as U/mL, and 1 < IgG (U/mL) results accepted as positive. Antibody results were collected from the patients’ electronic records in the Ministry of Health system.

#### 2.2. Imaging technique

HRCT is an important and accurate tool for early detection of COVID-19 pneumonia, and it is commonly used for diagnostic evaluation of lung diseases.\[^{11}\] For chest HRCT images, in patients with the supine position the Alexion Advance CT system (Toshiba, Japan) was used. The scanning parameters were set at; tube voltage= 120 kVp, automatic tube current modulation (80mAs), matrix= 512 × 512, slice thickness= 1 mm. Data were reconstructed with a slice thickness of 10 mm. All images were viewed with both lung (width, 1600 HU; level, – 400 HU) and mediastinal (width, 380 HU; level, 40 HU) settings. The radiologist T.U. (25 years of experience) reviewed HRCT scans.

#### 2.3. Imaging interpretation

We evaluated HRCT scans as; Stage I (39.5%), Stage II (39.5%), Stage III (20.1%) and Stage IV (0.7%) respectively. Patients who have positive and/or negative RT-PCR results and did not show COVID-19 symptoms, included in Stage I and also mosaic perfusion was determined as single or multiple foci in Stage I. RT-PCR results with both positive and negative were included in Stage II. Patients with Stage II (mild symptoms) showed GGO as a
single focus or multiple foci in HRCT results. There were also micronodular infiltrative foci detected in some of Stage II patients. Patients with consolidation with multiple foci and mild pleural and/or pericardial effusion were added into Stage III (moderate symptoms). Massive consolidation in the lung parenchyma and massive pleural and/or pericardial effusion which are severe symptoms of the disease were named as Stage IV. Parameters of Stage I, II, III, and IV included in this study were summarized in Figure 2.

2.4. Statistical analysis
Statistical analyses were carried out using the SPSS version 25.0 (SPSS, Inc., Chicago, IL). The clinical and demographic parameters were classified as categorical variables and continuous variables. If parameters are categorical, descriptive statistics were used and x2 test or Fisher exact test were performed to statistical significance between the groups. Continuous variables were tested for normality using Shapiro-Wilk tests. For comparison of the continuous parameters between the groups, the ANOVA test was used. P value was set as <.05 for all comparisons. A power analysis of 130 COVID-19 patients was performed using G*Power 3.1 software. With an α=0.05; power=0.80, and effect size=0.4 parameters it was found that the total sample size needed was a minimum of 76 patients.

3. Results
3.1. RT-PCR and the SARS CoV-2 IgG assay results of patients
Among 130 patients 71 of them confirmed with positive RT-PCR and 59 patients RT-PCR results were found to be negative. As a result of the SARS CoV-2 IgG Assay, 26 patients (20%) found as a positive IgG antibody against SARS CoV-2 virus. The SARS CoV-2 IgG assay results, the clinical and demographic parameters, COVID-19 symptoms, duration of the symptoms, and ongoing symptoms of 130 patients were summarized in Table 1.

3.2. Radiological findings of stage I patients with COVID-19 pneumonia
Patients underwent both RT-PCR and/ or HRCT. In this stage, all patients have not showed severe symptoms of the disease. But the exposure history of patients within Stage I, all patients’ RT-PCR results were found to be positive. The mildest form of the Stage, Stage I-A, the lung damage did not determine on HRCT scans. There were no inflammation findings determined in this group (Fig. 3). The positive RT-PCR results were found to be positive in all patients with the Stage I-B. According to HRCT classification, the mosaic perfusion pattern as a single focus or multiple foci without any lung parenchymal architectural distortion were identified in Stage I-B patients. There were minimum inflammation symptoms were found in this group (Fig. 4).

3.3. Radiological findings of stage II patients with COVID-19 pneumonia
In this group patients were classed as moderate and almost all patients have showed the disease symptoms. Among 26 patients 13 patients (50.0%) detected as positive RT-PCR results in Stage I-B group (Fig. 6).

3.4. Radiological findings of stage III patients with COVID-19 pneumonia
In this group patients were classified as moderate and almost all patients have showed the disease symptoms. Among 26 patients 13 patients (50.0%) detected as positive RT-PCR results in Stage II-B group (Fig. 6).
| Characteristics                        | All (n = 130) | Stage I (n = 51) | Stage II (n = 51) | Stage III (n = 26) | Stage IV (n = 2) | P value |
|---------------------------------------|---------------|-----------------|------------------|-------------------|-----------------|---------|
| Age Median IQR, (range)              | 49 (25–87)    | 45 (31–55)      | 49 (25–81)       | 52 (34–87)        | 48 (29–71)      | .01<sup>†</sup> |
| Male (%)                              | 64 (48.6)     | 3 (6)           | 35 (70.2)        | 11 (45.8)         | 17 (65.4)       | .03<sup>†</sup> |
| Exposure history (%)                  |               |                 |                  |                   |                 |         |
| Work                                  | 31 (23.8)     | 1 (3.9)         | 14 (29.5)        | 9 (37.5)          | 2 (20.0)        | 0       |
| Family                                | 42 (32.3)     | 0 (0)           | 12 (25.0)        | 8 (33.3)          | 4 (40.0)        | 0       |
| Public                                | 21 (16.1)     | 1 (3.9)         | 5 (10.4)         | 4 (16.6)          | 1 (10.0)        | 0       |
| Unknown                               | 36 (27.6)     | 1 (3.9)         | 15 (31.2)        | 7 (29.1)          | 3 (30.0)        | .01<sup>‡</sup> |
| RT-PCR (%)                            | 71 (54.6)     | 3 (6)           | 24 (50.0)        | 12 (50.0)         | 7 (70.0)        | .836    |
| Antibody, IgG (%)                     | 26 (20.0)     | 0 (0)           | 9 (18.7)         | 2 (4.4)           | 2 (4.16)        | 2       |
| Smoking (%)                           | 16 (12.3)     | 1 (3.9)         | 7 (14.5)         | 3 (12.9)          | 1 (10.0)        | .01<sup>‡</sup> |
| Comorbidity (%)                       |               |                 |                  |                   |                 |         |
| Diabetes                              | 9 (6.9)       | 0 (0)           | 2 (4.1)          | 2 (8.3)           | 0 (0)           | <.001<sup>†</sup> |
| Hypertension                          | 25 (19.2)     | 0 (0)           | 10 (20.8)        | 4 (16.6)          | 1 (10.0)        | .01<sup>†</sup> |
| Cardiovascular diseases               | 13 (10.0)     | 0 (0)           | 4 (8.3)          | 2 (8.3)           | 0 (0)           | <.001<sup>†</sup> |
| Thyroid                               | 5 (3.8)       | 1 (3.9)         | 3 (6.2)          | 2 (8.3)           | 1 (10.0)        | 0       |
| Rheumatism                            | 2 (1.53)      | 0 (0)           | 1 (2.0)          | 1 (4.1)           | 0 (0)           | .734    |
| Chronic pulmonary diseases (%)        |               |                 |                  |                   |                 |         |
| Asthma                                | 6 (4.6)       | 0 (0)           | 4 (8.3)          | 0 (0)             | 0 (0)           | .228    |
| Bronchiectasis                        | 11 (8.4)      | 0 (0)           | 1 (2.0)          | 2 (8.3)           | 1 (10.0)        | .002<sup>‡</sup> |
| COPD                                  | 6 (4.6)       | 0 (0)           | 1 (2.0)          | 0 (0)             | 4 (40.0)        | .001<sup>‡</sup> |
| Symptoms (%)                          |               |                 |                  |                   |                 |         |
| Cough                                 | 39 (30.0)     | 0 (0)           | 17 (35.41)       | 8 (33.3)          | 6 (60.0)        | .074    |
| Fever                                 | 32 (24.6)     | 0 (0)           | 10 (20.8)        | 8 (33.3)          | 6 (60.0)        | 2       |
| Headache                              | 20 (15.3)     | 0 (0)           | 7 (14.5)         | 5 (20.8)          | 2 (20.0)        | .01<sup>‡</sup> |
| Loss of taste or smell               | 19 (14.6)     | 0 (0)           | 6 (12.5)         | 5 (20.8)          | 3 (30.0)        | .761    |
| Shortness of breath                   | 27 (20.7)     | 0 (0)           | 7 (14.5)         | 4 (16.6)          | 3 (30.0)        | .013<sup>‡</sup> |
| Sore throat                           | 11 (8.4)      | 0 (0)           | 5 (10.4)         | 2 (8.3)           | 2 (20.0)        | .951    |
| Diarrhea                              | 10 (7.6)      | 0 (0)           | 5 (10.4)         | 3 (12.5)          | 1 (10.0)        | .794    |
| Rash                                  | 38 (29.2)     | 2 (6.6)         | 14 (29.1)        | 9 (37.5)          | 6 (60.0)        | .80     |
| Anxiety                               | 33 (25.3)     | 0 (0)           | 15 (31.2)        | 8 (33.3)          | 3 (30.0)        | .733    |
| No disease symptoms (%)               | 36 (27.6)     | 1 (3.9)         | 13 (27.0)        | 4 (16.6)          | 3 (30.0)        | .152    |
| Duration of symptoms (%)              |               |                 |                  |                   |                 |         |
| 0–5 d                                 | 13 (10.0)     | 1 (3.9)         | 8 (16.6)         | 2 (8.3)           | 1 (37.5)        | .022    |
| 5–7 d                                 | 15 (11.5)     | 1 (3.9)         | 5 (10.4)         | 3 (12.5)          | 1 (10.0)        | .799    |
| 8–10 d                                | 21 (16.1)     | 1 (3.9)         | 9 (18.7)         | 4 (16.6)          | 1 (10.0)        | .785    |
| 2 wk                                  | 18 (13.8)     | 0 (0)           | 9 (18.7)         | 2 (8.3)           | 4 (40.0)        | .880    |
| 15–25 d                               | 7 (5.3)       | 0 (0)           | 2 (4.1)          | 2 (8.3)           | 1 (37.5)        | .639    |
| 1 mo                                  | 5 (3.8)       | 0 (0)           | 1 (2.0)          | 2 (8.3)           | 0 (0)           | <.001<sup>†</sup> |
| Not determined                        | 51 (39.2)     | 0 (0)           | 14 (29.1)        | 9 (37.5)          | 3 (30.0)        | 0       |
| Ongoing symptoms (%)                  |               |                 |                  |                   |                 |         |
| Cough                                 | 7 (5.3)       | 0 (0)           | 2 (4.1)          | 0 (0)             | 1 (37.5)        | <.001<sup>†</sup> |
| Arrhythmia                            | 4 (3.0)       | 0 (0)           | 1 (2.0)          | 0 (0)             | 2 (8.3)         | .930    |
| Headache                              | 8 (6.1)       | 0 (0)           | 1 (4.1)          | 2 (8.3)           | 3 (30.0)        | 0       |
| Forgetfulness                         | 6 (4.6)       | 0 (0)           | 3 (6.2)          | 1 (4.1)           | 1 (10.0)        | <.001<sup>†</sup> |
| Shortness of breath                   | 13 (10.0)     | 0 (0)           | 5 (10.4)         | 3 (12.5)          | 2 (20.0)        | .313    |
| Insomnia                              | 5 (3.8)       | 0 (0)           | 3 (6.2)          | 0 (0)             | 2 (20.0)        | .292    |
| Temporary loss of vision              | 1 (0.7)       | 0 (0)           | 1 (2.0)          | 0 (0)             | 0 (0)           | .688    |
| Rash                                  | 10 (7.6)      | 1 (3.9)         | 3 (6.2)          | 3 (12.5)          | 2 (8.3)         | .150    |
| Anxiety                               | 17 (13.0)     | 0 (0)           | 7 (14.5)         | 5 (20.8)          | 2 (8.3)         | .511    |

For continuous variables data were analyzed as median (range) and ANOVA test were used for statistical significance. For categorical variables data were analyzed as count (percentage) and x² test or Fisher exact test were used for statistical significance. COPD = chronic obstructive pulmonary disease, RT-PCR = real-time polymerase chain reaction. Differences between Stage I-II and III indicate P value.

* P < .05.

† P < .01.

‡ P < .001.
III. The HRCT findings were showed that the consolidation occurred with multiple foci in Stage III-A (Fig. 7). In the Stage III-B, there was infection detected as consolidation with multiple foci and mild pleural and/or pericardial effusion (Fig. 7).

3.5. Radiological findings of stage IV patients with COVID-19 pneumonia

A total of 2 patients included in this group and disease symptoms was found to be severe. In Stage IV all patients were found to be positive RT-PCR results. Furthermore, in Stage IV, the HRCT findings showed that distribution of increased lung opacity as massive consolidation with smoothly thickened interlobular septa within the areas of air space disease, resulting in crazy-paving pattern appearance was in the last stage of lung involvement (Fig. 8). Also, it was detected massive pleural and/or pericardial effusion and also a differentiation was identified in the heart shape patients with Stage IV (Fig. 9).

4. Discussion

Since December 2020, COVID-19 disease is one of the most health problems in countries. COVID-19 pneumonia starts with inflammation like all viral infections. This inflammation becomes increasing by the time and aggravate. Clinical exacerbation generally began with fever, shortness of breath, and cough. To detect COVID-19 disease suspected patients RT-PCR and radiological approaches are commonly used. Compared to tomography RT-PCR is a more cost-effective, and also reachable method for the patients because of the absence of the tomography device in every health center. However, a comparison of efficacy between RT-PCR and tomography, tomography is more powerful technique for the actual results. One of tomography type is the HRCT. In this study, to evaluate radiological findings we used HRCT scans. Because, HRCT has decreased slice thickness and increased spatial resolution. So, it represents identification and characterization of diffuse parenchymal abnormalities better than routine CT. Our aim was to classify which was not determined before in the literature, of the radiological findings and to correlate with clinical parameters. For this purpose, HRCT positive 130 patients who have found positive or negative RT-PCR results, retrospectively enrolled in this study. Radiologist T.U. evaluated HRCT findings according to patients’ lung damages (mosaic perfusion, GGO, consolidation and crazy paving pattern). As a result of this evaluation our study populations classified as 4 stages.

Stage I (39.2%) patients were found to be clinically asymptomatic. However, lung inflammation was detected as mosaic perfusion areas in Stage I-B patients. In the RT-PCR positive (54.6%) patients screened by HRCT, we detected inflammation as mosaic perfusion areas and nodules infiltrations. Especially, in the Stage I-B (36.92%) and Stage II-A (18.46%)
groups. The progression of the disease can be prevented by anti-COVID treatment of these early stages. However, using HRCT like other tomography techniques it is an easy way to determine inflammation in the pre-clinical stage but carries the risk of radiation exposure.

Patients with Stage II (39.2%), the inflammation had started to progress, and signs of infection were in the form of GGO densities. Furthermore, nodules which have been shown as a single focus Stage II-A (18.46%) had started to be commonly diffused in Stage II-B (20.76%). In our study, we described Stage II-A as early detection of inflammation. Therefore, it was significant because the treatment response was close to Stage I patients. However, the Stage II patients who have especially >40 years old were resistant to the treatment, chronic lung, and heart diseases cases.

Stage III (20.0%), progressive infection in the form of pneumonia was detected in HRCT as consolidation. Just like in the literature the infection in Stage III-A (7.69%) was observed as a consolidation area. Furthermore, in Stage III-B (12.30%) the pleural (pericardial) effusion was seen accompanying consolidation areas also. Stage III-B (12.30%) and Stage IV results (1.53%) showed that a very difficult and long treatment is needed and showed the complications of the inflammation.

Stage IV (1.53%) patients were the most severe group of our study population, and it was observed with advanced foci of lung infection of the crazy paving pattern. These patients were being followed up in intensive care units and all of them were intubated.

In patients with HRCT findings favoring COVID-19 pneumonia, especially in Stage II-B, III-A, III-B and IV patients with negative RT-PCR results (24.61%), there was a history of close contact, and clinical findings overlapped with COVID-19 symptoms. Treatment of patients with increased of GGO, consolidation and crazy paving pattern was long, especially in cases with chronic disease of > 40 years old. In the diagnosis of patients with COVID-19 lung infection, the literature showed common GGO densities on computed tomography. But with this study, early-stage tomographic findings of COVID-19 lung infection had given a result that is not described and diagnosed in the literature. The greatest contribution of our study to the literature is to emphasize the importance and value of early detection of lung infection in early-stage patients. The disease progressed without complications and for a short period of time in all of our patients who were diagnosed at an early stage and began early the treatment. Considering the complication risks of patients with chronic diseases over 40 years old showed that our study is meaningful and in terms of disease follow-up. This study
showed that staging is shortness the recovery time and reduces aggravation.

It is also important to note some limitations about the sample size in this study. In Stage IV, only 2 patients were included. Thus, the statistical significance was not carried out by Stage IV patients’ clinical features. We could not collect some information from patients like the duration of symptoms and so the p-value was not meaningful. Also, some patients did not clearly tell their COVID-19 symptoms, duration of symptoms, and ongoing symptoms. Therefore, these parameters’ significance could not be analyzed very well.

5. Conclusion

We reached the following conclusions from our study, which included 130 patients in 4 different stages; the lung HRCT examinations were performed simultaneously with RT-PCR scans of patients who do not have clinically significant symptoms but have a history of contact. In this study, we showed that the determination of COVID-19 patients’ HRCT findings in early stages may increase the response to treatment, and also reduce the hospitalization of patients. It is seen that the need for hospitalization is very low but significant early treatment response is high in patients with early-stage involvement of COVID-19 pneumonia. These findings could be helpful for an early diagnosis and a key for future research as well.

Author contributions

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