The Role of Chest High Resolution CT and Rt-Pcr in Diagnosis of Different Stages of Coronavirus (Covid-19) Pneumonia

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RESEARCH ARTICLE

The Role of Chest High Resolution CT and RT-PCR in Diagnosis of Different Stages of Coronavirus (COVID-19) Pneumonia

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Abstract:
Purpose:
The purpose of this study is to investigate how RT-PCR (real time–polymerase-chain-reaction) and chest High-Resolution Computed Tomography (HRCT) can detect COVID-19 (Coronavirus Disease 2019) disease in the early, progressive and severe stages, as well as patient’s outcome.

Methods:
We perform a prospective study with chest HRCT on 206 patients with positive RT-PCR test. The patients were divided into three groups; early stage (100 patients), progressive stage (70 patients) and severe stage (36 patients).

Results:
The early stage involved typical category (COVID-19 Reporting and Data System, CO-RADS 5, 34 cases - 34%), indeterminate category (CO-RADS 3, six cases - 6%), atypical category (CO-RADS 4, ten cases - 10%) and normal chest HRCT imaging (CO-RADS 1, 50 cases - 50%). The progressive stage involved a typical category (CO-RADS 5, 70 cases, 100%), The severe stage involved a typical category (CO-RADS 5, 36 cases, 100%).

Conclusion:
RT-PCR is the gold standard and specific tool for confirming COVID-19 infection. Combination of RT-PCR and chest HRCT is used for the early diagnosis of COVID-19 pneumonia. Chest HRCT is positive in 50% of patients in the early stage of COVID-19. Chest HRCT is not only detecting pulmonary parenchymal changes but also determining patient’s outcome in the progressive and severe stages of COVID-19 (CO-RADS 5). Patients with progressive stage will not need ventilator and patients with severe stage should receive ventilator.

Keywords: HRCT, RT-PCR, COVID-19, Ground glass opacities, Consolidation, Pneumonia.

1. INTRODUCTION

COVID-19 pandemic started in Wuhan, China in December 2019 and spread all over the world. It is an infectious disease induced by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) [1, 2]. The SARS-CoV-2, similar to the Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS) coronaviruses, enter the cells via attachment of S1 subunit, which contains a receptor-binding domain, to the angiotensin converting enzyme related carboxypeptidase receptor [3].

Clinically, COVID-19 disease has three stages: i) early stage, asymptomatic infectious phase, which occurs in the first two days after infection during which the virus attaches to and replicates in the epithelial cells of the nose; ii) progressive stage, symptomatic phase, which appears from 5 to 14 days after infection during which the virus spread to the lung; iii) severe stage during which the immune system produces cytokine storm that attacks the virus and form pulmonary infiltrates, hypoxia with Adult Respiratory Distress Syndrome (ARDS) [4].

COVID-19 disease is diagnosed by taking the history of dry cough, fever and fatigue, and performing RT-PCR test to detect COVID-19 virus, a blood test to detect lymphopenia, IgM/IgG, and radiological examination to detect lung
parenchymal changes such as GGO and consolidation. RT-PCR is the gold standard test that confirms COVID-19 disease, but chest HRCT can be used for suspected patients with false-negative RT-PCR test [5]. Chest HRCT can detect different parenchymal patterns caused by COVID-19 infection [6]. The American college of radiology categorized the HRCT pulmonary changes that happen during COVID-19 disease into four groups; i) typical pattern: bilateral, peripheral, Ground Glass Pattern (GGO) or consolidation; ii) indeterminate pattern: few very small non-peripheral non-rounded GGO; iii) atypical pattern: segmental or isolated lobar consolidation with GGO, smooth interlobular septal thickening or pleural effusion; iv) negative pattern: no changes such as GGO and consolidation [7]. In addition, The COVID-19 Reporting and Data System (CO-RADS) is a categorical assessment scheme for pulmonary involvement of COVID-19 on non-enhanced chest HRCT for predicting COVID-19 in patients, especially for categories 1 and 5. Based on the CT findings, the level of suspicion of COVID-19 infection is graded from very low (CO-RADS 1) up to very high (CO-RADS 5). CO-RADS-1 has a normal CT appearance (high negative predictive value) in patients with early stages, CO-RADS 2 has no typical signs of COVID-19 (low suspicious), CO-RADS 3 has indeterminate signs of COVID-19 (indeterminate suspicious), CO-RADS 4 has atypical signs of COVID-19 (highly suspicious), and CO-RADS 5 has typical signs of COVID-19 (very high positive predictive value – very highly suspicious) [8].

In this study, we investigate how chest RT-PCR and HRCT can diagnose COVID-19 disease in its early, progressive, and severe stages, as well as patient’s outcome.

1.1. Patients and Methods

1.1.1. Patients

206 patients were enrolled in this prospective study. The patients were categorized into three stages; i) early stage (number=100 patients with mild symptoms (fever or dry cough) and positive RT-PCR), ii) progressive stage (number=70 with severe symptoms (fever > 37.5°C, dry cough, or shortness of breath) and positive RT-PCR who did not receive ventilator) and iii) severe stage (number=36 with severe symptoms (fever > 37.5°C, dry cough, or shortness of breath) and positive RT-PCR who received ventilator). Another 120 patients with a negative RT-PCR for SARS-COV2 were enrolled in this study to test the sensitivity and the specificity of chest HRCT.

1.1.2. Chest HRCT Imaging Procurement

Chest HRCT was performed on all patients for detection of pulmonary-change patterns, using a Siemens 16-channel scanner without contrast injection. The images were acquired at the end inspiration while the patient lying supine on CT table, with choosing slice thickness 0.7 mm and 120 kilo volt helical tube. The images were processed on the workstation using (lung window level, −700 H and width, 1,500 H) and (mediastinal window level, 40 H and width, 350 H).

1.1.3. HRCT Image Interpretation

Chest HRCT images acquired were assessed by two radiologists. The Chest HRCT images were interpreted according to the American college of radiology and CO-RADS for detection of parenchymal-change patterns such as bilateral peripheral GGO, consolidation, and septal thickening, or pleural effusion.

1.1.4. Statistical Analysis

Statistical analysis was conducted using all continuous variables that are expressed as ranges, mean with standard deviation, and categorical variables that expressed as counts and percentages by using SPSS version 21.0 (SPSS Inc. Chicago, IL). By using RT-PCR as the reference gold standard, the diagnostic efficiency of chest HRCT for detection of pulmonary changes was assessed using sensitivity, specificity, Negative Predictive Value (NPV), Positive Predictive Value (PPV). The different pulmonary patterns between groups were evaluated using Odds ratio with 95% confidence interval and level of significance P < 0.05.

2. RESULTS

COVID-19 risk factors are shown in Table 1. 206 patients, 140 men and 66 women aged 30-61 years old, mean 52.49 ± 8.27 years were involved in this study (early stage 50.18±8.85 vs. progressive and severe stages 54.66±7.02). The viral concentration (±SD) among patients with early stage was significantly lower than in those with progressive and severe stages (3.61±1.35 vs. 5.28±1.51, P<0.001). All patients above age 50 years old, bad social situations, and with chronic disease showed odd ratio 2.75, 1.52, 1.41, respectively, with significant P values (0.002, 0.14, 0.36, respectively), indicating high risk of getting progressive and severe stages of COVID-19 disease. The smoker group showed non-significant odd ratio (0.97) and P values (0.93). Eight patients in the control group (6.7%) had abnormal chest HRCT compatible with atypical viral pneumonia.

2.1. Chest HRCT Findings in COVID-19 Early Stage

Four categories were detected in the early stage: typical category, the most prominent chest HRCT finding, accounted for (CO-RADS 5, 34 cases - 34%), indeterminate category (CO-RADS 3, six cases - 6%), atypical category (CO-RADS 4, ten cases - 10%) and 50% were negative for pneumonia (CO-RADS 1, 50 cases – 50%) and showed normal chest HRCT imaging (Table 2).

The typical category group (CO-RADS 5) included; i. bilateral peripheral GGO, (Fig. 1); ii. bilateral peripheral GGO with consolidation (Fig. 2). The Indeterminate category group (CO-RADS 3) included a few small non-rounded and non-peripheral GGO. The Atypical category group (CO-RADS 4) included; i. bilateral focal segmental consolidation without GGO, (Fig. 3) ii. bilateral peripheral parenchymal venous infarction in connection with the draining vein that appears as focal peripheral consolidation (Fig. 4). Finally, negative for pneumonia with absent GGO and consolidation (CO-RADS 1).
2.2. Chest HRCT Findings in COVID-19 Progressive Stage

The progressive stage of COVID-19 pneumonia included typical pattern (CO-RADS 5) in all 70 cases - 100% (Table 2). This group included: i. bilateral peripheral lower lobes GGO (Fig. 5); ii. bilateral diffuse GGO with reverse halo (atoll) sign (Fig. 6); iii. peripheral bilateral GGO and mediastinal lymphadenopathy with short axis of more than 1 cm.

2.3. Chest HRCT Findings in COVID-19 Severe Stage

The severe stage of COVID-19 pneumonia included typical pattern (CO-RADS 5) in all 36 cases - 100% (Table 2). This group included: i. bilateral crazy paving appearance with GGO (Fig. 7) and ii. bilateral diffuse GGO (Fig. 8) or consolidation (Fig. 9) with bronchiolar and vascular dilatation.
The Role of Chest High Resolution CT and RT-PCR

**Table 1. Risk factors associated with early, progressive and severe stages of COVID-19.**

| Risk Factors                                      | Early Stage N=100 | Progressive and Severe Stages N=106 | Odd Ratio & 95% Confidence Interval | P Value |
|--------------------------------------------------|-------------------|-------------------------------------|-------------------------------------|---------|
| Age ≥ 50                                          | 64                | 64                                  | 88                                  | 83      | 2.75 (1.43 to 5.27) | 0.002   |
| Medical disease (asthma, liver, cardiac, renal, cancer) | 80                | 80                                  | 90                                  | 85      | 1.41 (0.68 to 2.9) | 0.36    |
| Crowding (>2 people/room)                        | 54                | 54                                  | 68                                  | 64      | 1.52 (0.87 to 2.67) | 0.14    |
| Smoking                                          | 76                | 76                                  | 80                                  | 75.5    | 0.97 (0.51 to 1.83) | 0.93    |

**Table 2. Chest HRCT findings in early, progressive and severe stages of COVID-19. No; Patients' number, GGO; ground glass opacity, LN; lymph node.**

| COVID-19 Stage | No. | HRCT Categories | No. | % | HRCT Findings | CO-RADS Category |
|----------------|-----|-----------------|-----|---|---------------|-----------------|
| Early stage    | 100 | Typical         | 34  | 34 | Bilateral peripheral GGO | CORADS 5       |
|                |     |                 |     |    | Bilateral peripheral GGO + consolidation |           |
|                |     | Indeterminate   | 6   | 6  | few small non-rounded and non-peripheral GGO | CORADS 3      |
|                |     | Atypical        | 10  | 10 | bilateral focal segmental consolidation without GGO | CORADS 4      |
|                |     |                 |     |    | bilateral parenchymal venous infarction |           |
|                |     | Negative        | 50  | 50 | no GGO and no consolidation | CORADS 1      |
| Progressive stage | 70 | Typical        | 70  | 100 | Bilateral peripheral GGO | CORADS 5      |
|                |     |                 |     |    | Bilateral diffuse GGO + reverse halo sign |           |
|                |     |                 |     |    | Bilateral peripheral GGO + mediastinal LN |           |
| Severe stage   | 36  | Typical        | 36  | 100 | Bilateral Crazy Paving with GGO | CORADS 5      |
|                |     |                 |     |    | Diffuse consolidation, GGO with bronchial and vascular dilatation |           |

**Table 3. Sensitivity and specificity of chest HRCT in early, progressive and severe stages of COVID-19 when the RT-PCR is a gold standard test, PPV; Positive Predictive Value, NPV; Negative Predictive Value.**

| HRCT               | Early Stage | Progressive Stage | Severe Stage | Total       |
|--------------------|-------------|-------------------|--------------|-------------|
| **Sensitivity 95% CI** | 50.00%      | 100.00%           | 100.00%      | 75.73%      |
|                    | 39.38% to 60.17% | 94.87% to 100.00% | 90.26% to 100.00% | 69.28% to 81.42% |
| **Specificity 95% CI** | 93.33%      | 93.33%            | 93.33%       | 93.33%      |
|                    | 83.80% to 98.15% | 83.80% to 98.15% | 83.80% to 98.15% | 83.80% to 98.15% |
| **PPV 95% CI**     | 92.59%      | 94.59%            | 90.00%       | 97.50%      |
|                    | 82.62% to 97.05% | 87.16% to 97.83% | 77.74% to 95.87% | 93.78% to 99.02% |
| **NPV 95% CI**     | 52.83%      | 100.00%           | 100.00%      | 52.83%      |
|                    | 47.65% to 57.95% | 94.76% to 96.32% | 89.67% to 98.85% | 46.58% to 59.00% |
| **Accuracy 95% CI** | 66.25%      | 96.92%            | 95.83%       | 79.70%      |
|                    | 58.36% to 73.52% | 92.31% to 99.16% | 89.67% to 98.85% | 74.36% to 84.37% |
2.4. Comparison of Sensitivity and Specificity Between Gold Standard RT-PCR and Chest HRCT

The early stage of COVID-19 disease showed low sensitivity and high specificity of chest HRCT (50, and 93.33%, respectively), contrary to the high sensitivity and specificity in the progressive and severe stages of COVID-19 (100 and 93.33%, respectively). Similarly, the NPVs and PPVs showed discrepancy among early, progressive, and severe stages of COVID-19 (NPVs; 52.83, 100, 100% and PPVs; 92.59, 94.59, 90.00% respectively). Chest HRCT accuracy was 66.25% in the early stages, 96.92 in the progressive stage and 95.83% in the diagnosis of the severe stage (Table 3).

3. DISCUSSION

3.1. RT-PCR and HRCT Comparison

The gold standard RT-PCR is a rapid screening test for detection of early COVID-19 pneumonia, even if imaging is normal; however, 2% and 29% of patients show false negative results with sensitivity (71-98%), indicating negative PCR results does not exclude COVID-19 pneumonia [9]. In contrast, Chest HRCT plays an important role in detection and evaluation the progression and severity of COVID-19 pneumonia and patient’s outcome [10]. The combination of RT-PCR and chest HRCT can be used for the early detection of COVID-19 pneumonia. Our study shows promising diagnostic accuracy of chest HRCT and in agreement with most of COVID-19 disease published studies [11 - 18].

3.2. Chest HRCT Findings in COVID-19 Early Stage

The typical feature (34%) of early stage COVID-19 disease (CO-RADS 5) with positive RT-PCR show the characteristic bilateral peripheral posterior lower lobes GGO, which was in concordance with the studies conducted by Salehi et al. [19]. Contrarily, GGO appearance was shown in 47% by Zhu et al. [20]. Furthermore, our study showed a promising finding of bilateral peripheral lobes GGO with consolidation. The chest HRCT features of a few small GGO with a non-rounded and non-peripheral distribution (6%) were seen in the indeterminate category (CO-RADS 3) of the early stage, which was in concordance with many previous studies [21]. Our study showed two atypical patterns (CO-RADS 4) in the early stage of COVID-19 pneumonia; the first was the bilateral focal segmental consolidation, which was consistent with studies conducted by Wu et al. [22] who showed the same findings and the second was an interesting observation as bilateral lower lobes Peripheral parenchymal venous infarction secondary to peripheral venous thrombosis. This finding agreed with Middeldorp et al. [23] who reported Venous thromboembolism (VTE) in COVID-19 in 13% of patients. In addition, this interesting venous infarction observation was reported by Tal et al. [24] who stated that Venous Thromboembolism Complicates COVID-19.

In the current study, 50% of the patients showed normal chest HRCT (no GG or consolidation) in the early stage of COVID-19 disease with positive RT-PCR. Compared with the gold standard RT-PCR, the chest HRCT sensitivity was 50% and the specificity was 93.33%, corresponding to CO-RADS 1. He et al. showed higher sensitivity 77% and a specificity 96.33% [25]. The normal chest HRCT images (CO-RADS 1) detected in our study was due to early stage during which no lung parenchymal changes started because the virus was still in the nose and did not spread to the lung, indicating that lung changes at least take one week after inflammatory changes occur in the lung [6]. Our study showed PPVs and NPVs were (92.59% and 52.83%, respectively). In contrast, different values of PPV and NPV (92% and 42%, respectively), were reported in other published COVID-19 patients having high pretest probability (e.g., 85% prevalence by RT-PCR) [26]. Accordingly, chest HRCT may not be performed as a screening test in earlier stages of COVID-19 disease due to the low NPVs.

3.3. Chest HRCT Findings in COVID-19 Progressive Stage

In the present study, all patients in the progressive stage with positive RT-PCR had chest HRCT findings of the typical category of COVID-19 pneumonia (CO-RADS 5). By comparison with the gold standard RT-PCR test, the chest HRCT sensitivity was 100% and specificity was 93.33%. The high NPV of chest HRCT shown in progressive stage patients in our results agreed with He et al., who reported comparable diagnostic performance of RT-PCR and chest HRCT in the diagnosis of COVID-19 disease [25]. Our findings of bilateral diffuse GGO with reverse halo sign in COVID-19 disease in concordance with diffuse GGO seen in the progressive stage of COVID-19 disease reported by Yang et al. [27]. In addition, our findings of bilateral peripheral GGO with mediastinal lymphadenopathy were not frequent and were in parallel with Valette et al. findings [28].

3.4. Chest HRCT Findings in COVID-19 Severe Stage

Our study confirmed that diffuse consolidation, crazy-paving pattern, bronchiolar and/or vascular dilatation were associated with the severe stage of COVID-19 pneumonia. All patients with severe stage had positive RT-PCR and chest HRCT findings of the typical category of COVID-19 pneumonia (CO-RADS 5). By employing RT-PCR as a reference, the chest HRCT sensitivity was 100% and specificity was 93.33%. Our results with high NPV in severe stage establish the diagnostic efficacy of chest HRCT, which agreed with Zhang et al. [29]. Furthermore, our results reported a higher frequency of crazy paving patterns compared to studies conducted by Chung et al. [17]. Our findings of diffuse consolidation with bronchiolar and vascular dilatation in the severe stage of COVID-19 disease agreed with Yang et al. who reported diffuse consolidation of the lung parenchyma seen in the severe stage of COVID-19 disease [27]. SARS-CoV-2 infection causes subsegmental vascular dilatation and hyperemia more than that induced by other viruses such as MERS and SARS [30].

Our study was conducted on small population size for statistical measurement and time constraint to follow-up producing limitation. A follow-up study will be conducted with more patients with post COVID-19 disease. Our current study confirmed that chest HRCT exam is more accurate and efficient in the diagnosis of pulmonary parenchymal changes in the progressive and severe stages of COVID-19 disease.
CONCLUSION

In conclusion, RT-PCR is the gold standard and specific test for confirming COVID-19 infection. However, it should not be the sole test for the diagnosis of the COVID-19 infection. Chest HRCT is negative in 50% of patients in the early stage of COVID-19 (CO-RADS 1). Neither negative RT-PCR nor negative chest HRCT excludes the COVID-19 infection. Combination of RT-PCR and chest HRCT is used for the early detection of COVID-19 pneumonia. Chest HRCT is positive in 50% of patients in the early stage of COVID-19. Chest HRCT is not only detecting pulmonary parenchymal changes but also determining patient’s outcome in the progressive and severe stages of COVID-19 (CO-RADS 5). Patients with progressive stage will not need ventilator and patients with severe stage should receive ventilator.

ETHICAL STATEMENT

No Animals were used in this research. All human research procedures were followed in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2013.

CONSENT FOR PUBLICATION

Written informed consent was obtained from the patients.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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