Screening COVID-19 with Chest CT in Preference to RT-PCR: Based on Mortality Analysis

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Abstract

Corona Virus Disease 2019 (COVID-19) became the outbreak of infectious diseases emergency worldwide. It remains unknown whether the RT-PCR test results was associated with the prognosis of COVID-19 patients or not. In this study, a total number of 495 patients with typical chest CT feature and symptom consistent with COVID-19 were retrospectively included from Jan 23, 2020 to Feb 26, 2020. 186 (37.58%), 32 (6.46%) and 277 (55.96%) COVID-19 patients had initial positive, suspected and negative RT-PCR results, respectively. The mean age was 58.55 years and 254(51.3%) were older than 60 years. 60.00% (297/495), 22.02% (109/495) and 17.98% (89/495) of COVID-19 patients were common, severe and critically type, respectively. There were no significant differences of age, gender, time from onset to hospitalization and severity classification in the patients with initial positive and negative RT-PCR result. The mortality rate of patients with positive and negative were 7.14% and 7.94%. Patients with initial negative or initial positive RT-PCR results had no significant difference of mortality rate (c2=4.079, p=0.130). The number of patients with lymphocyte ratios under the normal level was significantly larger in patients with initial negative RT-PCR results (59/92) compared with the patients with initial positive result (86/167), p=0.033. COVID-19 patients with positive or negative RT-PCR results had no significant difference in severity and mortality. Chest CT may be a more effective tool to screen COVID-19 in preference to RT-PCR.

Introduction

A cluster of new coronavirus pneumonia began to spread since December 2019, and then became the outbreak of infectious diseases emergency.[1] Even it is defined as Corona Virus Disease 2019 (COVID-19), but we still don’t fully understand this new coronavirus. The new coronavirus and SARS virus are similar in many ways, for example, the genetic sequence is 80% similar, both are transmitted through the respiratory tract, and can result in severe pneumonia even death.[2] However, since the incubation period of infection caused by the new coronavirus is significantly longer than SARS, besides the atypical symptoms, the COVID-19 is more likely to cause widespread transmission.[3] Therefore, early diagnosis and treatment of COVID-19 patients are very important.

The diagnostic criteria for COVID-19 has been controversial.[4–6] According to the sixth edition of guidelines for COVID-19, the reverse transcription-polymerase chain reaction (RT-PCR) for new coronavirus nucleic acid is the gold standard for diagnosis.[7] Only patients with positive RT-PCR result can be admitted to the hospital receiving appropriate treatment. However, the RT-PCR has limitations because of the low positive rate (30–40%), which leads to abound of COVID-19 patients with negative RT-PCR result stay untreated.[2] Some studies show that pulmonary computer tomography (CT) imaging should be used as the standard of clinical diagnosis, and suspected patients should be screened for isolation as well as be treated timely based on their clinical symptoms plus CT features.[8–11] Tao et al. [2] proposes that CT might be more sensitive and have the capacity to be an important tool for first-diagnosis screening by comparing the diagnostic efficacy of RT-PCR and CT.
The purpose of early diagnosis and treatment is to improve the prognosis of COVID-19 patients and reduce the severe illness rate and mortality rate. As a critical diagnosis factor, if the RP-PCR testing affect the prognosis of COVID-19 patients remains unknow. In this study, we compared the severity and mortality of patients with initial positive and negative RT-PCR results of COVID-19 in order to have patients been treated in time.

**Materials And Methods**

**Data Collection**

The institutional ethics board of Zhongnan Hospital of Wuhan University (NO. 2020067) approved this retrospective study and written informed consent was waived. A total of 529 suspected or conformed patients of COVID-19 pneumonia admitted to hospital from Jan 23, 2020 to Feb 26, 2020. The inclusion criteria are as followings: a, patients with typical chest CT features and clinical symptom according to the diagnosis and treatment announced by The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team.[12] We exclude 34 patients: 9 without symptom or chest CT, 15 without data-integrity of initial RT-PCR results, 4 with time-interval of CT and RT-PCR longer than 7 days, 6 with other viral pneumonia conformed by laboratory test. Figure 1 shows the flowchart of our study. The characteristics data of age, gender, time from onset of symptoms to admission, comorbid conditions, blood routine test results and PCT level results were retrospectively extracted from the patients’ electronic medical records in our hospital information system (HIS). The severity of symptoms variable was categorized as mild, severe, or critical following the the Novel Coronavirus Pneumonia Emergency Response Epidemiology Team.[12] Mild included non-pneumonia and mild pneumonia cases. Severe was characterized by dyspnea, respiratory frequency $\geq 30$/minute, blood oxygen saturation $\leq 93\%$, PaO2/FiO2 ratio $< 300$, and/or lung infiltrates $> 50\%$ within 24–48 hours. Critical cases were those that exhibited respiratory failure, septic shock, and/or multiple organ dysfunction/failure.

**Study Design**

Disease severity classification and mortality rate were analyzed in the patients with initial positive and negative RT-PCR result, for determining the correlation between RT-PCR results and prognosis. A total of 231 patients with PCT test in 3 days from admission were included for PCT level analysis and 259 patients with routine blood test in 3 days from admission were included for lymphocyte rate and monocyte rate analysis.

**Statistical Analysis**

The statistical analysis was performed using GraphPad Prism version 6.01. Continuous variables were displayed as mean with SEM. Shapiro-Wilk normality test was applied to test the normality of continuous variables. Mann Whitney U test was applied if the data didn’t pass the normality test. Categorical variables were reported as counts and percentages and Chi square test.
A total number of 495 patients with typical chest CT feature and symptom consistent with the feature of COVID-19 were included in the study. Figure 1 shows the flowchart of our study. 37.58% (186/495), 6.46% (32/495) and 55.96% (277/495) of these patients had initial positive, suspected and negative RT-PCR results, respectively. Table 1 showed the characteristics of included COVID-19 patients with initial positive or negative RT-PCR result. The mean age was 58.55 years (SEM 0.67) and 254(51.3%) were older than 60 years. There was no significant in gender between the initial positive and negative RT-PCR results group(p>0.05). And no significant difference of time from onset to hospitalization was observed in patients with initial negative (10.08 ± 0.32 days) and positive (9.64 ± 0.37 days) RT-PCR results, (p>0.05). 303(61.2%) patients had various comorbid conditions.

Table 1
Characteristics of the included COVID-19 patients

|                      | Positive (n = 186) | Suspicious (n = 32) | Negative (n = 277) | All patients (n = 495) |
|----------------------|-------------------|---------------------|--------------------|------------------------|
| Age, years (means ± SEM) | 58.34 ± 0.94      | 60.94 ± 2.66        | 57.75 ± 0.67       | 58.55 ± 0.67           |
| Age range, years     |                   |                     |                    |                        |
| ≥ 60                 | 94(39.00%)        | 12(4.98%)           | 135(56.02%)        | 241                    |
| < 60                 | 92(36.22%)        | 20(7.87%)           | 142(55.91%)        | 254                    |
| Sex                  |                   |                     |                    |                        |
| male                 | 85(35.12%)        | 11(4.55%)           | 146(60.33%)        | 242                    |
| female               | 101(39.92%)       | 21(8.30%)           | 131(51.78%)        | 253                    |
| Mean from onset of symptoms to admission | 10.08 ± 0.32 | 8.09 ± 0.56 | 9.64 ± 0.37 | 9.79 ± 0.23 |
| Comorbid conditions  |                   |                     |                    |                        |
| Yes                  | 109(35.97%)       | 17(5.61%)           | 177(58.42%)        | 303                    |
| No                   | 77(40.10%)        | 15(7.81%)           | 100(52.09%)        | 192                    |
Table 2
Mortality rate of COVID-19 patients with initial negative and positive RT-PCR results

| Initial RT-PCR results | n   | Common (%) | Severe (%) | Critically (%) | Mortality rate (%) |
|------------------------|-----|------------|------------|---------------|-------------------|
| Positive               | 186 | 115(61.83) | 41(22.04)  | 30(16.13)     | 19(7.14)          |
| Suspicious             | 32  | 21(65.63)  | 4(12.50)   | 7(21.88)      | 6(18.75)          |
| Negative               | 277 | 161(58.12)| 62(22.39)  | 54(19.49)     | 22(7.94)          |

Mortality rate of COVID-19 patients with initial positive or negative RT-PCR results.

According to the diagnosis standard announced by the Chinese Health Commissioner, 60.00% (297/495), 22.02% (109/495) and 17.98% (89/495) of COVID-19 patients were common, severe and critically type, respectively. No significant difference of disease severity classification was found between the patients with initial positive and negative RT-PCR result, (χ² = 1.414, p = 0.841). Total mortality rate was 9.49% (47/495). The mortality rate of patients with positive and negative were 7.14% and 7.94%. Patients with initial negative or initial positive RT-PCR results had no significant difference of mortality rate (χ² = 4.079, p = 0.130).

Table 3
Lymphocyte rate and monocyte rate of COVID-19 patients with initial RT-PCR results

| Results          | Positive (n = 167) | Negative (92) | p     |
|------------------|--------------------|---------------|-------|
| Lymphocyte rate (% | 19.50(0.62-48.0)  | 15.05(2.30–40.80) | 0.0381|
| Monocyte rate (%)  | 7.47 ± 0.26        | 6.53 ± 0.34   | 0.0155|
Discussion

In the outbreak of COVID-19, the sensitivity of widely applied RT-PCR detection may determine the effectiveness of identifying COVID-19 patients in time.[13] Patients with delayed diagnosis may not be treated promptly and constitute a risk for infecting the others.[14] It is reported that COVID-19 patients with positive chest CT findings may present with negative RT-PCR results. Thus, determining the value of RT-PCR detection on COVID-19 came to a particularly urgent task.

In this retrospective study, all included COVID-19 patients were conformed with chest CT and clinical symptom. The patients with initial negative or positive RT-PCR results had no significant difference in disease severity classification and mortality. Therefore, whatever the RT-PCR test results, patients with positive chest CT scan result and symptom consistent with the feature of COVID-19 should accept equal attention and treatment. Chest CT, as a routine imaging tool, is more convenient for fast diagnosis and screen of COVID-19 patients, especially in the underdeveloped area and the areas with insufficient nucleic acid detection capability.

The rate of low lymphocyte of COVID-19 patients with negative RT-PCR test results was higher than that of the patients with positive RT-PCR test result. Delayed admission from the onset of symptom may be one of the reasons, but there is no statistical difference between the two groups in the median time from onset to admission. Further study is needed to determine whether the length of time from onset to admission is correlated with the incidence of low lymphocyte. Another reason may be the worse immunity in COVID-19 patients with negative RT-PCR test result. It is reported that the number of peripheral CD4 and CD8 T cells decreased significantly in COVID-19 patients, and the cell status was more active.[15] However, low lymphocyte ratio may also result in high false negative in nucleic acid detection. Whatever, it further indicates that patients with positive chest CT scan result and symptom consistent with the feature of COVID-19 should accept equal attention and treatment. It is urgent to develop more effective standard diagnosis of COVID-19.

Declarations

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Conflict of interest

No potential conflict of interest was reported by the authors.
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Figures

Figure 1

Inclusion flow chart