Original Article

Diagnostic Efficacy of Chest Computed Tomography for Coronavirus Disease 2019

Abstract

Background: A significant discrepancy between the results of previous studies is identified regarding the diagnostic efficacy of chest computed tomography (CT) for coronavirus disease 2019 (COVID-19). We aimed to evaluate the diagnostic efficacy of chest CT for COVID-19. **Methods:** Suspected cases of COVID-19 with fever, cough, dyspnea, and evidence of pneumonia on chest CT scan were enrolled in the study. The accuracy, sensitivity, and specificity of chest CT were determined according to real-time reverse transcriptase-polymerase chain reaction (RT-PCR) results as the gold standard method. **Results:** The study population comprised 356 suspected cases of COVID-19 (174 men and 182 women; age range 3–96 years; mean age ± standard deviation, 55.21 ± 18.38 years). COVID-19 patients were diagnosed using chest CT with 89.8% sensitivity, 78.1% accuracy, 21.3% specificity, 84.7% positive predictive value, and 30.23% negative predictive value. The odds ratio was 2.39 (95% confidence interval, 1.16–4.91). Typical CT manifestations of COVID-19 were observed in 48 (13.5%) patients with negative RT-PCR results and 30 (8.4%) patients with confirmed positive RT-PCR results had no radiological manifestations. Kappa coefficient of chest CT for diagnosis of COVID-19 was 0.78. **Conclusion:** The results show that when RT-PCR results are negative, chest CT could be considered as a complementary diagnostic method for the diagnosis of COVID-19 patients. A more comprehensive diagnostic method could be established by combining the chest CT examination, clinical symptoms, and RT-PCR assay.

Keywords: *Coronavirus disease 2019, pneumonia, severe acute respiratory syndrome coronavirus 2, X-ray computed tomography*

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Introduction

Coronavirus disease 2019 (COVID-19) is a new type of viral pneumonia caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)[1-3] that appeared in China in December 2019.[1,2,4] The rapidly growing numbers of affected people all around the world make this disease a public health emergency of international concern.[3,5]

Real-time reverse transcriptase-polymerase chain reaction (RT-PCR) test has routinely been used as the gold standard method for laboratory diagnosis of COVID-19 disease.[6] In addition to RT-PCR assay, other complementary diagnostic methods are used for accurate and in-time diagnosis of the disease.

The initial cases had fever, respiratory symptoms, and pneumonia of unknown etiology.[1,2,7-9] Chest computed tomography (CT) is a high sensitivity diagnostic tool for lung disease imaging.[10] Therefore, chest CT plays a critical role in detecting viral pneumonia and evaluation of the nature and extent of pulmonary lesions.[11-13]

Nevertheless, a significant discrepancy between the results of previous studies is identified regarding the diagnostic efficacy of chest CT for COVID-19. In Fang *et al.*'s study,[12] the sensitivity of the chest CT and RT-PCR were compared for 51 patients. Their results showed that the chest CT has higher sensitivity than RT-PCR (98% vs. 71%, respectively). Xie *et al.*'s study shows that RT-PCR and chest CT have approximately similar sensitivities (97% vs. 95.8%, respectively).[13] In other hand, a sensitivity of 82.6% has been also reported for CT examinations in comparison to RT-PCR.[4] This diagnostic approach has inherent strengths and limitations. For radiological manifestations of

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COVID-19 patients, false-negative results have been reported in several studies. The main reasons for these false-negative results are (1) pulmonary involvement may not be observed in the early course of the disease for symptomatic patients,[14,15] (2) pneumonia may not develop in symptomatic upper respiratory tract infections,[1,16] and (3) other viral types of pneumonia such as various forms of flu could also result in false-positive results[17] On the other hand, the radiologist's experience is one of the influential factors which may have affected the diagnostic performance of the chest CT method.

The study location is another influencing factor that could significantly modify the diagnostic performance of chest CT due to the heterogeneity in the severity of illness and epidemic, differences in sensitivity and accuracy of the commercially available kits (as the gold-standard method), the efficiency of the sample pooling in PCR test, hospital equipment, etc.

Therefore, cross-sectional studies regarding the diagnostic efficacy of chest CT must be first reported. Then, the results of these cross-sectional studies would be pooled to achieve comprehensive knowledge about the diagnostic performance of the chest CT approach. The present study aims to add evidence to this issue, by evaluating the diagnostic efficacy of chest CT for COVID-19.

Subjects and Methods

The retrospective study was approved by the medical ethical committee (approved number. IR.MEDILAM.REC.1399.044). Informed consent was signed by patients or legally authorized representatives.

Patients

Suspected cases of COVID-19 with fever, cough, dyspnea, and evidence of pneumonia on chest CT scan were enrolled in the study. The histories of the patients were checked and the patients with radiological manifestations of COVID-19 were only included in the study. Patients with a confirmed positive result from RT-PCR assay of oropharyngeal and nasopharyngeal swab specimens were considered as COVID-19 patients. The RT-PCR assays were performed using Sansure Biotech Inc. kit (Changsha, China). For SARS-CoV-2 detection, the appropriate diagnostic performance of the Sansure Biotech kit has been approved.[18,19] For RT-quantitative PCR SARS-CoV-2 diagnosis using the Food and Drug Administration EUA 2019-nCoV CDC kit (IDT, Coralville, IA) as the gold standard method, the analytical sensitivity of the Sansure Biotech kit was 95.3% and its limit of detection has been estimated at about 1,000 copies/mL.[19] The medical records of suspected cases from February 15, 2020, to July 18, 2020, were reviewed at a referral hospital for COVID-19 patients.

Patient scanning was performed within 2 days or less from clinical onset. Chest CT examination has been confirmed as a complementary routine test in diagnosing the disease and no additional risk has been incurred as result of this study. All patients were admitted to a single referral center and all scanning procedures followed the same protocol with no variation.

Image acquisition

Nonenhanced chest computed tomographies were acquired using a 16-slice CT scanner (Brilliance 16; Philips Healthcare, Cleveland, OH, USA). Phantom calibration was performed on each scanning day using AAPM CT Performance Phantom Model CIRS 610. CT acquisition and reconstruction parameters are listed in Table 1. All patients were scanned in the supine position during end inspiration.

Image interpretation

Suspected cases of COVID-19 were reviewed to determine the diagnostic efficacy of chest CT in comparison to RT-PCR assay. All CT images were reviewed by two thoracic radiologists (with 4 and 6 years of experience in chest radiology), who were not aware of RT-PCR results or laboratory findings. The data were analyzed under the supervision of an attending radiologist with 23 years of experience in thoracic imaging. In the image interpretation, a subject with the presence of ground-glass opacities (GGOs), consolidation, and other manifestations in CT images (including crazy paving, spider web sign, reversed halo sign, vascular dilation, pleural fluid, subpleural bands and architectural distortion, enlarged lymph node, and traction bronchiectasis) was categorized as the COVID-19 patient. RSNA expert consensus statement on reporting chest CT findings related to COVID-19 was used as the diagnostic criteria for CT interpretation.[20] The disputes between the radiologists were resolved by consultation with the experienced attending radiologist.

Statistical analysis

Statistical analyses were performed using SPSS 16.0 (SPSS Inc., Chicago, IL, USA). Quantitative and counting data

Table 1: Computed tomography acquisition and reconstruction parameters

Scanning protocol	High-resolution CT (HRCT chest)
Tube voltage	120 kV
Tube current	Automatic tube current (180 mA–400 mA)
Detector configuration	12 mm
Slice thickness	1 mm
Detector collimation	5 mm
Detector width	0.75 mm
Pitch	1.2
Matrix	512×512
In-plane voxel size	1.05×1.05 mm^2
Reconstruction technique	Iterative
Convolutional kernel	Standard

CT: Computed tomography, HRCT: High-resolution CT were presented as mean ± standard deviation (SD) and count (percentage of total), respectively. The diagnostic performance of chest CT was determined according to the overall RT-PCR results as the gold standard method. An exemplary 2 × 2 contingency table for displaying the outcomes of a diagnostic method is presented in Table 2.

Sensitivity, specificity, accuracy, positive predictive value (PPV), negative predictive value (NPV), and odds ratio (OR) were calculated as follows:

$$\text{Sensitivity} = \frac{TP}{TP + FN}$$

$$\text{Specificity} = \frac{TN}{FP + TN}$$

$$\text{Accuracy} = \frac{TP + TN}{TP + FP + FN + TN}$$

$$\text{Positive predictive value (PPV)} = \frac{TP}{TP + FP}$$

$$\text{Negative predictive value (PPV)} = \frac{TN}{FN + TN}$$

$$\text{Odds ratio (OR)} = \frac{TP \times TN}{FP \times FN}$$

$$\text{Confidence interval (CI)} = \exp\left(\log(OR) \pm Z_{a/2} \times \sqrt{\frac{1}{TP} + \frac{1}{FP} + \frac{1}{FN} + \frac{1}{TN}}\right)$$

Where true positive, false positive, true negative, and false negative are true-positive, false-positive, true-negative, and false-negative values, respectively. In the last equation, $Z_{a/2}$ is 1.96 for a confidence level of 95%. In this study, COVID-19 patients were diagnosed based on the RT-PCR results and chest CT data. Kappa index was used to determine the agreement between these diagnosis methods.

Results

The study population comprised 356 suspected cases of COVID-19 (174 men and 182 women; age range 3–96 years; mean age ± SD, 55.21 ± 18.375 years). From suspected cases of COVID-19, 295 subjects have a confirmed positive result from RT-PCR assay. The study flowchart is shown in Figure 1.

Evidence of abnormal CT manifestations compatible with viral pneumonia was observed in 313 (87.9%) subjects, while 43 (12.1%) patients had normal CT. Demographic information, symptoms, and chest CT manifestations of suspected cases of COVID-19 are summarized in Table 3.

The most common lung lesions were patchy GGO (68.3%), consolidation (26.7%), pleural fluid (15.7%), and crazy paving (9.3%). Other manifestations were no frequent.

Table 4 shows demographic information and symptoms of COVID-19 patients diagnosed by CT and RT-PCR methods. There were no significant differences in demographic information and symptoms between the groups.

Table 2: An exemplary 2×2 contingency table for displaying the outcomes of a diagnostic method

Test outcome	Infection status (as determined by the gold standard method)	
	Positive	**Negative**
Positive	TP	FP
Negative	FN	TN

TP: True positive, FP: False positive, FN: False negative, TN: True negative

Table 3: Demographic information, symptoms, and computed tomography manifestations of suspected cases of coronavirus disease 2019

Demographic information	*n* (%)
Sex	
Male/female	174 (48.9)/182 (51.1)
Age (years)	
Mean±SD	55.21±18.38
Minimum–maximum	3–96
Height (cm)	
Mean±SD	167.96±9.49
Minimum–maximum	92–186
Weight (kg)	
Mean±SD	73.62±12.18
Minimum–maximum	13–115
BMI (kg/m^2)	
Mean±SD	26.00±3.36
Minimum–maximum	10.97–37.02
Symptoms	
Fever (°C)	152 (42.7)
Mean±SD	37.76±0.50
Minimum–maximum	36.20–39.00
Muscle soreness	175 (49.2)
Cough	242 (68.0)
Trembling	155 (43.5)
Dyspnea	253 (71.1)
Olfactory loss	59 (16.6)
Taste loss	62 (17.4)
Nausea	96 (27.0)
Vomiting	83 (23.3)
CT findings	
GGOs and consolidation	
GGO (round)	10 (2.8)
GGO (Patchy)	243 (68.3)
Consolidation	95 (26.7)
Crazy paving	33 (9.3)
Spider web sign	4 (1.1)
Reversed halo sign	7 (2.0)
Vascular dilation	12 (3.4)
Pleural fluid	56 (15.7)
Enlarged lymph node	4 (1.1)
Traction bronchiectasis	9 (2.5)
Sub pleural bands and architectural distortion	8 (2.2)

CT: Computed tomography, GGOs: Ground-glass opacities, BMI: Body mass index, SD: Standard deviation

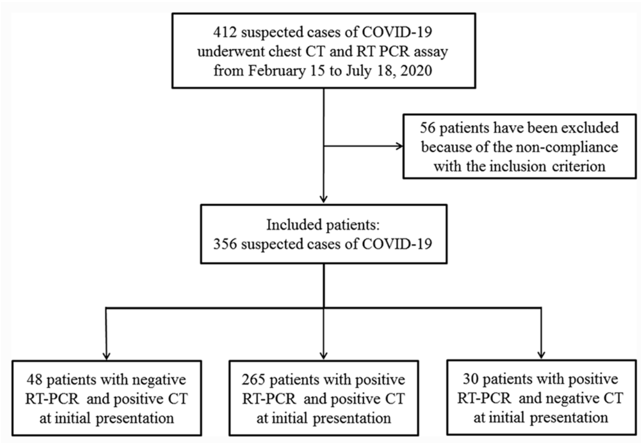

Figure 1: Study flowchart. COVID-19: Coronavirus disease 2019, RT-PCR: Reverse-transcription polymerase chain reaction

COVID-19 patients were diagnosed using chest CT with 89.8% sensitivity, 78.1% accuracy, 21.3% specificity, 84.7% PPV, and 30.23% NPV. The OR was 2.39 (95% CI, 1.16–4.91). The OR shows that subjects with positive PCR results are more likely to have typical CT manifestations of COVID-19. These subjects have CT manifestations 2.39 times more likely than subjects with negative PCR results.

Typical CT manifestations of COVID-19 were observed in 48 (13.5%) patients with negative RT-PCR results and 30 (8.4%) patients with confirmed positive RT-PCR results had no radiological manifestations. Frequencies of COVID-19 patients diagnosed by CT and RT-PCR methods are listed in Table 5. RT-PCR and CT results were positive in 295 and 313 subjects, respectively.

Kappa coefficient of chest CT for diagnosis of COVID-19 was 0.78. Radiological manifestations of COVID-19 patients with positive and negative RT-PCR results are shown in Figures 2-4.

Table 4: Demographic information and symptoms of coronavirus disease 2019 patients diagnosed by computed tomography and real-time reverse transcriptase-polymerase chain reaction methods

Demographic information	CT, *n* (%)	RT-PCR, *n* (%)
Sex		
Male/female	153 (48.9)/160 (51.1)	137 (46.4)/158 (53.6)
Age (years)		
Mean±SD	57.50±17.58	55.23±18.35
Minimum–maximum	3–96	3–92
Height (cm)		
Mean±SD	168.11±9.59	167.95±9.88
Minimum–maximum	92–186	92–186
Weight (kg)		
Mean±SD	73.80±12.19	73.42±12.51
Minimum–maximum	13–115	13–115
BMI (kg/m^2)		
Mean±SD	26.02±3.37	25.91±3.40
Minimum–maximum	10.97–37.02	10.97–37.02
Symptoms		
Fever (°C)	148 (47.3)	132 (44.7)
Mean±SD	37.76±0.50	37.78±0.51
Minimum–maximum	36.20–39.00	36.20–39.00
Muscle soreness	170 (54.3)	146 (49.5)
Cough	228 (72.8)	210 (71.2)
Trembling	148 (47.3)	129 (43.7)
Dyspnea	240 (76.7)	214 (72.5)
Olfactory loss	54 (17.3)	50 (16.9)
Taste loss	57 (18.2)	52 (17.6)
Nausea	91 (29.1)	79 (26.8)
Vomiting	78 (24.9)	68 (23.1)

RT-PCR: Real-time reverse transcriptase-polymerase chain reaction, CT: Computed tomography, BMI: Body mass index, SD: Standard deviation

Table 5: Frequencies of coronavirus disease 2019 patients diagnosed by computed tomography and real-time reverse transcriptase-polymerase chain reaction methods

	COVID-19 patient diagnosis by RT-PCR=Yes	COVID-19 patient diagnosis by RT-PCR=No
COVID-19 patient diagnosis by CT=Yes	265	48
COVID-19 patient diagnosis by CT=No	30	13

COVID-19: Coronavirus disease 2019, CT: Computed tomography, RT-PCR: Real-time reverse transcriptase-polymerase chain reaction

Discussion

The corona pandemic is spreading rapidly all around the world and no treatment has been provided to date. The accurate diagnosis of COVID-19 is the most important step in providing clinical services. The improvement of patient management and better allocation of human and medical resources could be performed based on the early and accurate diagnosis of patients. The real-time PCR assay is the most common molecular diagnostic test that is used for the detection of viral nucleic acids.[21] COVID-19 patients had characteristic radiological manifestations. CT is a more reliable and rapid imaging approach for diagnosis of COVID-19 which has a comparable sensitivity with RT-PCR results.

In this retrospective study, sensitivity, accuracy, and specificity of chest CT for diagnosis of COVID-19 were 89.8%, 78.1%, and 21.3%, respectively. In Ai *et al.*'s study,[17] the correlation of chest CT and RT-PCR testing was evaluated. In their study, the diagnostic value and consistency of chest CT were investigated in 1014 patients. The sensitivity, specificity, and accuracy of chest CT were 97%, 25%, and 68%, respectively. Our results are in close agreement with these results.

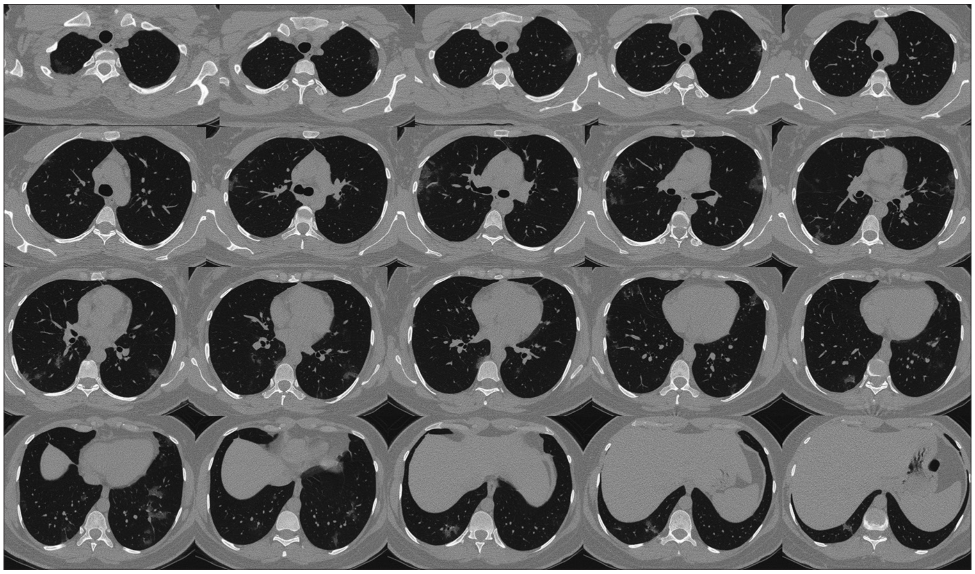

Figure 2: CT images of a 39-year-old female with clinical symptoms and a negative RT-PCR result. Pneumonia was distributed in both lungs and there were five affected lobes. CT manifestations were peripheral and peribronchovascular GGO (Patchy). CT: Computed tomography, RT-PCR: Reverse-transcription polymerase chain reaction, GGO: Ground-glass opacities

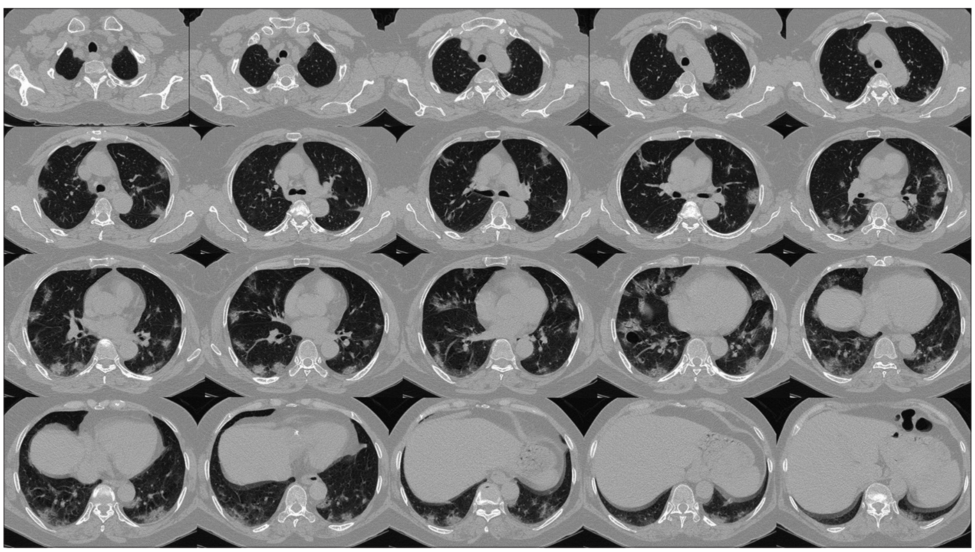

Figure 3: CT images of a 62-year-old female with clinical symptoms and a positive RT-PCR result. Pneumonia was distributed in both lungs and there were five affected lobes. Pulmonary lesions have predominant bilateral peripheral distributions. CT manifestations were GGO and consolidation. CT: Computed tomography, RT-PCR: Reverse-transcription polymerase chain reaction, GGO: Ground-glass opacities

There are high sensitivities and low specificities for chest CT. This could be because when asked a radiologist to search for signs of COVID-19 disease, a bias occurs that all changes might be considered as COVID-19 disease-related changes. Therefore, the sensitivity increased and specificity would decrease.[22]

In Guan *et al*.'s study,[1] clinical characteristics of COVID-19 disease 2019 were evaluated in Chinese patients. Their results show that chest CT has 86.2% sensitivity for the diagnosis of COVID-19, similar to our findings. Typical CT manifestations of COVID-19 were observed in 265 (89.8%) patients before or parallel to the initial positive RT-PCR results that indicate the considerable role of the chest CT in the early detection of suspected cases. There were clinical symptoms and typical CT manifestations of COVID-19 in 48 (13.5%) patients with negative RT-PCR results. In Fang *et al*.'s study,[12] the sensitivities of chest CT and RT-PCR assay for diagnosis of COVID-19 were evaluated. There were radiological manifestations for 15 (29.4%) patients with negative RT-PCR results.

These results indicate the high diagnostic power of chest CT for COVID-19 patients. Some studies have reported poor performance of RT-PCR assay for diagnosis of COVID-19.[23-25] Low efficiency of viral nucleic acid detection may be the result of improper sampling operations, the difference in sampling location (e.g., upper

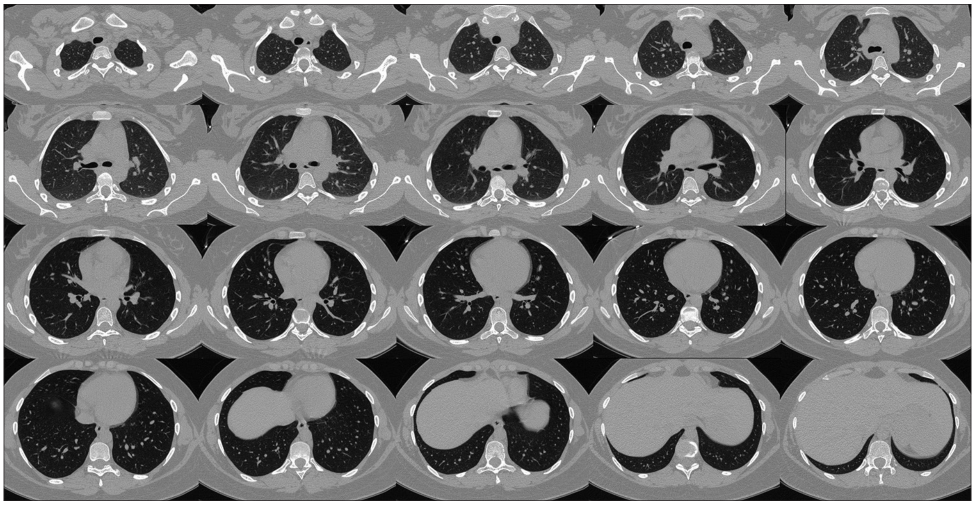

Figure 4: CT images of a 19-year-old female with fever and positive RT-PCR result. There was no radiological manifestation. CT: Computed tomography, RT-PCR: Reverse-transcription polymerase chain reaction

or lower respiratory tract), difference in sampling time (different phase of the disease development), low viral load of the patient, and low efficiency of detection kits.[12,26] Therefore, RT-PCR tests must interpret with caution.

For the diagnosis of COVID-19, chest CT has an acceptable Kappa coefficient (0.78). It means that CT could discriminate patients and healthy subjects with a considerable agreement with the RT-PCR assay.

These results show that when RT-PCR results are negative, chest CT could be considered as a complementary diagnostic method for the diagnosis of COVID-19 patients. A more comprehensive diagnostic method could be established by combining the chest CT examination, clinical symptoms, and RT-PCR assay.

Our study has some limitations. First, this is a single-center retrospective study and the results require further confirmation by multicenter studies. Second, the time of the initial CT after admission was not unified. We only used the initial chest CT on the day of hospital admission. Thus, further studies are recommended to consider these limitations.

Conclusion

In addition to the real-time PCR assay as the most commonly used molecular diagnostic test for the detection of viral nucleic acids, other complementary diagnostic methods are also used for diagnosis of COVID-19. CT is a more reliable and rapid imaging approach for diagnosis of COVID-19 which has a comparable sensitivity with RT-PCR results. In this study, the diagnostic efficacy of chest CT was evaluated. These results show that when RT-PCR results are negative, chest CT could be considered as a complementary diagnostic method for the diagnosis of COVID-19 patients. A more comprehensive diagnostic method could be established by combining the chest CT examination, clinical symptoms, and RT-PCR assay.

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Conflicts of interest

There are no conflicts of interest.

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