

The relationship between diagnostic value of chest computed tomography imaging and symptom duration in COVID infection

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Submission: 18-04-2020
Accepted: 06-05-2020
Published: 18-06-2020

Access this article online

Quick Response Code:



Website:

www.thoracicmedicine.org

DOI:

10.4103/atm.ATM_165_20

Abstract:

OBJECTIVES: Severe acute respiratory syndrome-coronavirus-2 is a global public health problem, in which early diagnosis is required to prevent the spread of infection. In this study, we aimed to reveal the diagnostic value of chest computed tomography (CT) imaging with respect to symptom duration.

METHODS: This retrospective study involved patients from five centers, who were admitted with typical COVID-19 symptoms and found to be positive for COVID-19 real-time reverse transcription-polymerase chain reaction (rtRT-PCR) test.

RESULTS: One hundred and five patients with positive COVID-19 rtRT-PCR test were involved in the study. Sixty percent of these patients had chest CT imaging findings consistent with COVID-19 pneumonia. The most common chest CT finding was bilateral and subpleural ground-glass opacity in middle-lower lobes of the lungs. Chest CT findings were detected in 85.1% of the patients with a symptom duration of more than 2 days. In receiver operating characteristic analysis of this parameter, area under the curve (AUC) was 0.869, while sensitivity and specificity were 90.5% and 76.2%, respectively. It was notable that chest CT findings were 7.17 times more common among the patients aged 60 years and older, with AUC, specificity, and positive predictive value of 0.768, 88.1%, and 84.8%, respectively.

CONCLUSION: Chest CT imaging is a quite valuable tool in patients with longer than 2 days' duration of symptoms, in whom clinical and epidemiological data support the diagnosis of COVID-19 infection. We suggest that the diagnosis of COVID-19 pneumonia should be made with chest CT imaging when rtRT-PCR test cannot be performed or gives a negative result, which is important for public health and to prevent the spread of infection.

Keywords:

Chest computed tomography, COVID-19, symptom duration

Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) is a global pandemic with a mortality rate of 1%–5%. Mortality is higher among older patients with comorbidities.^[1] Early detection of cases is essential for treatment, care, isolation, to decrease close contact and secondary infections among health-care

providers, and to limit person-to-person transmission. In patients with fever and respiratory symptoms, the diagnosis is made according to the history of exposure and detection of viral nucleic acid in respiratory tract samples using real-time reverse transcription-polymerase chain reaction (rtRT-PCR) technique.^[2] RT-PCR-based viral nucleic acid method is recently considered as a standard reference method to confirm the presence

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How to cite this article: Kant A, Kostakoğlu U, Atalar S, Erensoy Ş, Sevimli T, Ertunç B, *et al.* The relationship between diagnostic value of chest computed tomography imaging and symptom duration in COVID infection. *Ann Thorac Med* 2020;15:151-4.

of COVID-19 infection.^[3] Because rtRT-PCR method can give false-negative results in patients with typical clinical symptomatology for COVID-19, utilization of other diagnostic tools has become a current issue, and chest computed tomography (CT) imaging has been suggested as an important method in detecting patients with COVID-19 pneumonia.^[4] Incorrect sampling has been suggested as the main cause of false-negative test results.^[5] Taking into account the incrementally increasing number of cases infected with COVID-19 worldwide, these patients with initial negative results play an important role in the spread of infection.

In this study, we evaluated chest CT findings of the patients with typical clinical symptomatology for COVID-19 infection and positive rtRT-PCR test results and aimed to reveal the diagnostic value, timing, and eligibility criteria for chest CT examination.

Methods

This study was performed between March 20, 2020, and April 6, 2020. Patients who were admitted with typical symptoms for COVID-19 infection to Trabzon Vakfıkebir State Hospital, Recep Tayyip Erdogan University Hospital, Niksar State Hospital, Yavuz Selim Bone Diseases and Rehabilitation Hospital and Akçaabat Haçkalıbaşa State Hospital were involved. A total number of 105 patients with typical clinical symptoms and positive rtRT-PCR test results were retrospectively evaluated. A definitive diagnosis of COVID-19 infection was made according to positive rtRT-PCR test results, obtained either in first or sequential testing. Patients who did not undergo chest CT imaging were excluded. Chest CT examination and evaluation procedures were performed by the same center. Demographic data and clinical and laboratory findings of the patients were obtained from patient files and recorded.

Statistical analysis

Descriptive statistical analysis was performed for all the studied variables. Compatibility with normal distribution of data obtained by measurement was assessed using the Kolmogorov–Smirnov test. Student's *t*-test was used to analyze normally distributed data, and the Mann–Whitney U-test was used for nonnormally distributed data. The Chi-square test was used to compare categorical variables. Data obtained by measurement were expressed as mean \pm standard deviation. Data obtained by counting were expressed as numbers (%); analyses were performed using the Chi-square test. Correlation analysis was performed using Pearson's correlation test or Spearman's correlation test. Receiver operating characteristic (ROC) analysis was performed to calculate the sensitivity, specificity, and negative predictive value (NPV) and positive predictive

value (PPV) of statistically significant variables. $P < 0.05$ was considered statistically significant.

Results

In this study, a total of 105 patients with positive rtRT-PCR test for COVID-19 were included. The mean age of the patients was 49.3 ± 18.4 (9–88) years, 67 (63.8%) were male and 38 (36.2%) were female. Forty-three (41.0%) patients had a history of contact with a COVID-19 patient. Forty-nine (46.7%) patients had comorbidity, with the most common being hypertension ($n = 27$). When evaluated according to the symptoms, 51 (48.6%) had fever, 64 (61.0%) had cough, 26 (24.8%) had sore throat, 25 (23.8%) had dyspnea, 22 (21.0%) had myalgia, 51 (48.6%) had fatigue, 17 (16.2%) had headache, and 6 (5.7%) had diarrhea. The time period between the initiation of symptoms and hospital admission was 3.8 ± 3.2 days. Chest CT examination was performed on the $4.2 \pm 3.5^{\text{th}}$ day after the initiation of symptoms. Sixty-three (60%) patients had chest CT findings consistent with COVID-19 pneumonia. Chest CT findings were subpleural ground-glass opacities in 53 (50.5%), consolidation in 12 (11.4%), air bronchograms in 9 (8.6%), pleural effusion in 5 (4.8%), cobblestone appearance in 4 (3.8%), vascular enlargement in 4 (3.8%), air cysts in 2 (1.9%), reverse halo sign in 1, mediastinal lymphadenopathy in 1, and tree in bud appearance in 1 patient. These CT findings were bilateral in 69.8%, subpleural in 92.1%, and were located in middle and lower lobes in 76.2% of the patients. There was a positive correlation between age and the presence of chest CT findings ($r = 0.440$; $P < 0.001$). Thirty-six (34.3%) patients were 60 years of age or older. Thirty-one (86.1%) patients aged older than 60 years had CT findings, while 32 (46.4%) patients younger than 60 years had abnormal chest CT imaging (odds ratio = 7.17; $P < 0.001$). The duration of symptoms was 5.5 ± 3.9 and 3.5 ± 3.1 days for patients older and younger than 60 years, respectively ($P = 0.002$). A positive correlation was detected between the presence of chest CT findings and symptom duration ($r = 0.631$; $P < 0.001$). CT findings were present in 57 (85.1%) patients in whom the imaging was performed after the 2nd day of the symptoms, while only 6 (15.8%) cases who underwent imaging within 2 days of the initiation of symptoms had CT findings ($P < 0.001$). There was a positive correlation between the presence of fever ($r = 0.249$; $P = 0.01$), dyspnea ($r = 0.228$; $P = 0.019$), fatigue ($r = 0.366$; $P < 0.001$), and CT findings. In ROC analysis performed to determine the relationship between the duration of symptoms and diagnostic efficacy of CT imaging, area under the curve (AUC) was 0.869, while sensitivity, specificity, PPV, and NPV were 90.5%, 76.2%, 85.1%, and 84.2%, respectively, in case of symptom duration of longer than 2 days [Figure 1]. ROC analysis data

utilized to determine the relationship between symptom duration, symptoms, age, and diagnostic efficacy of chest CT imaging are presented in Table 1.

CT findings were detected in 81.6% of the cases with comorbidity. The number of patients who required intensive care unit follow-up was 13 (12.3%), all of which had comorbid conditions. Three patients died, 59 patients were discharged, while 43 patients are still receiving treatment.

Discussion

SARS-CoV-2 pandemic is an urgent public health problem. Its incubation period range is 2–14 days. The virus can be transmitted from person to person via droplets, contaminated hands, and surfaces, which makes transmission very easy. Early diagnosis is quite important to prevent the spread of the disease.^[6] rtRT-PCR test positivity is the gold standard in the diagnosis, while negative test result does not exclude COVID-19 diagnosis in the presence of clinical and epidemiological features consistent with COVID-19 infection. Poor sample quality,

early or delayed sampling, inappropriate deposition and handling of samples, and viral mutations have been reported to cause false-negative results.^[7] Considering that these false-negative results play an important role in the dissemination of the infection, it is reasonable to suggest that alternative diagnostic tools are required. At the beginning of COVID-19 outbreak, the diagnosis was based on clinical features and thoracic imaging.^[8] Because the sensitivity of conventional chest X-ray imaging is about 30%–60%, a normal posteroanterior chest X-ray examination does not exclude the diagnosis.^[9] Thorax CT, another method in thoracic imaging, is more sensitive than chest X-ray examination. Therefore, it was suggested that chest CT imaging might be used as an initial diagnostic tool in patients with high clinical suspicion for COVID-19 infection.^[10] In this study, we aimed to determine the timing and eligibility criteria for chest CT examination and reveal diagnostic efficiency of this technique. For this purpose, patients with rtRT-PCR test positivity were enrolled in this study, and a positive correlation was detected between patients' age, symptom duration, and CT findings. We demonstrated that the presence of chest CT findings was 7.17 times more common among the cases older than 60 years of age, who had clinical and epidemiological features consistent with COVID-19 infection. When the presence of CT imaging findings in the patients aged 60 years or older was evaluated by ROC analysis, AUC was 0.768 and high specificity and PPV were detected (88.1% and 84.8%, respectively). The symptom duration of patients under the age of 60 is significantly lower than those over the age of 60. This may be because younger patients are able to use the means of communication more widely and effectively than older ones and have previously COVID-19 knowledge. The most common CT finding was bilateral and subpleural ground-glass opacities, which were mostly located in the middle and lower lung lobes. Typical radiological findings of COVID-19 infection may differ depending on the stage of disease.^[10] The main initial radiological finding is ground-glass opacity, whereas other patterns such as pulmonary consolidation and cubblestone appearance may be observed in the latter stages of the disease.^[11,12] In our study, 85.1% of the patients with a symptom duration of longer than 2 days had chest CT findings. When this parameter was evaluated by ROC analysis, AUC, sensitivity, and specificity were found

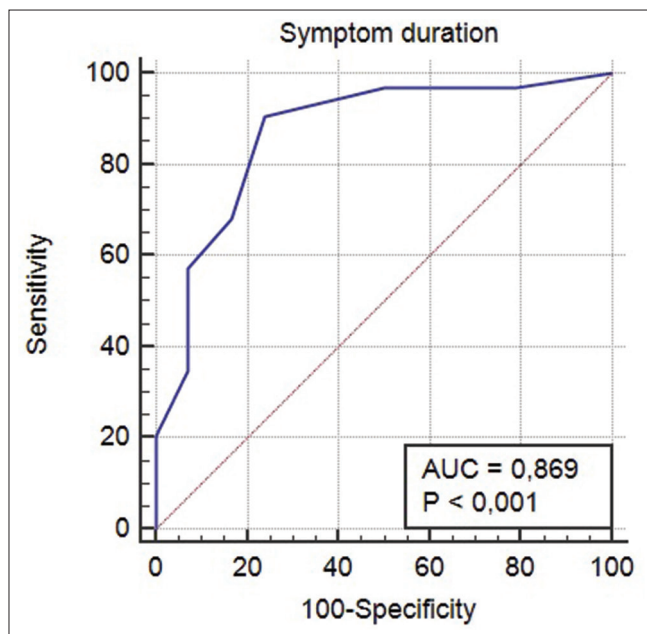


Figure 1: Receiver operating characteristic curve showing the relationship between symptom duration and the presence of computed tomography findings

Table 1: Receiver operating characteristic analysis data obtained to determine the diagnostic efficacy of chest computed tomography imaging

Parameters	Cut off	AUC	AUC 95% CI	Sensitivity	Specificity	PPV	NPV	P
Age	≥60	0.768	0.675-0.844	44.4	88.1	84.8	51.4	<0.001
Symptom duration	>2	0.869	0.789-0.927	90.5	76.2	85.1	84.2	<0.001
Fever	1	0.627	0.527-0.719	58.7	66.7	72.5	51.9	0.009
Dyspnea	1	0.599	0.499-0.694	31.7	88.1	80.0	46.3	0.011
Fatigue	1	0.687	0.589-0.774	63.5	73.8	78.4	57.4	<0.001

AUC=Area under the curve, CI=Confidence interval, PPV=Positive predictive value, NPV=Negative predictive value

to be 0.869, 90.5%, and 76.2%, respectively. Literature data also indicate a relationship between the frequency of chest CT findings and symptom duration.^[12,13] In their study, Pan *et al.* also reported ground-glass opacity to be the most common initial radiological finding.^[12] Bernheim *et al.* demonstrated that CT findings during the first 2 days of the disease were not sufficient to make the diagnosis, while it might have a diagnostic value in the upcoming days.^[13]

Conclusion

Literature data strongly suggest that chest CT imaging plays an important role in the diagnosis of COVID-19 pulmonary involvement. Chest CT imaging is considerably valuable in patients with a symptom duration of longer than 2 days in whom clinical and epidemiological findings are consistent with COVID-19 infection. It is important for public health to utilize thoracic CT imaging in the diagnosis to prevent the spread of the disease, especially when rtRT-PCR test is not available or gives a negative result.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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