MARMARA
MEDICAL JOURNAL

Original Article

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Diagnostic performance between RT-PCR and chest CT in outpatients with clinically suspected COVID-19

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Submitted: 09.06.2023 **Accepted:** 03.08.2023

ABSTRACT

Objective: To investigate the diagnostic performance between chest computed tomography (CT) and reverse transcription-polymerase chain reaction (RT-PCR) in outpatients with suspected coronavirus disease 2019 (COVID-19).

Patients and Methods: Between March and June 2020, a total of 812 patients with clinically suspected COVID-19 who underwent both chest CT and initial-single RT-PCR on admission to outpatient units were retrospectively enrolled. CT severity-score (CT-SS) was calculated and data were matched with PCR results.

Results: Of 812 patients, 54% (439/812) had positive RT-PCR results, and 47% (425/812) had a positive chest CT scan. With RT-PCR results as reference, the sensitivity, specificity, accuracy of chest CT in defining COVID-19 infection were 60%, (95% CI 56-65%, 265/439 patients), 57% (95% CI 52-62%, 213/373), 59% (95% CI 55-62%, 478/812), respectively. Three hundred eighty-seven (47%) patients had no CT findings, 380/812 (46.8%) had mild, 45/812 (5.5%) had moderate, and no patients in the severe group

Conclusion: Chest CT did not show high sensitivity for the diagnosis of COVID-19 for outpatients. We suggest RT-PCR should be the primary diagnostic tool. Chest CT might be considered if there is a strong clinical suspicion with repeatedly negative RT-PCR test results, ensuring infection prevention and control measures can be preserved.

Keywords: Chest CT, RT-PCR, COVID-19, Outpatient, Diagnosis

1. INTRODUCTION

Coronavirus disease 2019 (COVID-19) was first reported in China [1] and declared a pandemic on February 28, 2020. The best strategy for management of the pandemic had been a timely diagnosis of COVID-19 until a vaccine would be available for the population. The World Health Organization (WHO) has emphasized sampling for polymerase chain reaction (PCR) as a part of the assessment of suspected COVID-19 cases in primary care [2]. According to the guideline published by the Republic of Turkey Ministry of Health, all symptomatic patients and asymptomatic contacts are required to admit to hospitals for COVID-19 diagnostic testing. They do not have to apply to primary health care as the diagnostic tests are not available in the Family Health Centers in Turkey. However, outpatient COVID-19 patients are followed by their Family Physicians after the diagnosis.

Real-time-polymerase chain reaction (RT-PCR) is the reference standard test in COVID-19 diagnosis. However, RT-PCR positivity has changed between 0-60% at admission to the hospital [3]. False-negative RT-PCR results may be confusing. The major reason for a false-negative RT-PCR result is improper sampling. The low sensitivity of RT-PCR may result in a failure to diagnose on time, which may cause the transmission of the virus to a larger population. Therefore, alternative diagnostic tools have been researched. Chest CT examination seems to be an alternative diagnostic tool in patients, especially with false-negative RT-PCR results according to many studies [4-6]. Reported CT imaging findings include a bilateral distribution of ground-glass opacities (GGO), crazy paving patterns, reversed halo signs, and airway changes [7-9]. Yet, some small scaled studies have also documented limited RT-PCR sensitivity

How to cite this article: Tukenmez Tigen E, Sengel Erturk B, Cimsit C, Gurun Perk H, Kaya Apaydın C, Korten V. Diagnostic performance between RT-PCR and chest CT in outpatients with clinically suspected COVID-19. Marmara Med J 2024: 37(1):18-22. doi: 10.5472/marumj.1379916

ISSN: 1309-9469

http://doi.org/10.5472/marumj.1379916
Marmara Med J 2024;37(1): 18-22

despite having pulmonary abnormalities correlated with COVID-19 [4,5]. The discorrelations between chest CT and RT-PCR to diagnose COVID-19 infection have been reported in other studies as well [4-7]. Guan et al., did not document CT abnormalities in 2.9% of patients with severe and 17.9% of patients with non-severe disease at the time of admission [10]. Waller et al., reviewed that chest CT had limited clinical utility, especially in patients without symptoms at the beginning of the disease [11]. In this study, we investigated the diagnostic performance of RT-PCR tests and chest CT images of patients with suspected COVID-19 outpatients at the time of admission.

2. PATIENTS and METHOD

The study protocol was approved by the Institutional Review Board and the Clinical Research Ethics Committee of Marmara University School of Medicine (approval number: 09.2020.578).

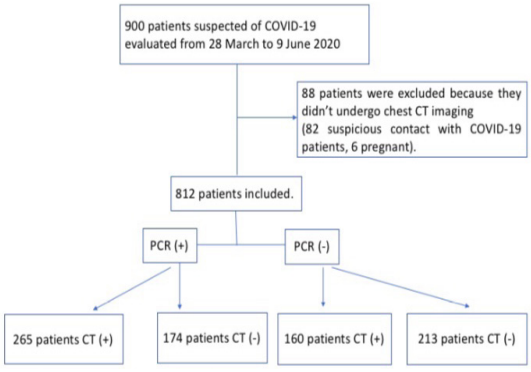

Figure 1. *The flowchart of the study*

Study population

At the beginning of the novel coronavirus pandemic, the Turkish Ministry of Health made an algorithm to take care of patients to offer quality healthcare services to the public in our country. From March 28 to June 9, 2020, a total of 900 outpatients suspected of COVID-19 disease were retrospectively recorded (Figure 1). Patients with mild symptoms of COVID-19, according to the WHO scale <4 who did not need oxygen support [11] were organized as outpatients. After the exclusion of 88 patients (82 patients had suspicious contact with COVID-19-infected patients, and 6 women were pregnant) due to lack of chest CT imaging, the remaining 812 patients who underwent both chest CT imaging and RT-PCR assay were included in the study. Chest CT and RT-PCR tests were done on the same day.

Viral RNA was taken out by using Bio-speedy1 (Bioexen LTD, Turkey)

Chest CT protocol and image analysis

Chest CT imaging was examined on a picture archiving and communication system (PACS) independently by two radiologists who were blinded to RT-PCR results of the patients. Their data were then cross-matched and if there were any conflicts, the images were reevaluated, and an agreement was provided to resolve the inconsistencies. CT-severity score (CT-SS) was used for evaluating infection burden at admission to the hospital [12]. CT-SS was counted up by enumerating the infected lobe. Lung lobes were scored ranging between 0-4 and, categorized as none, minimal, moderate, or severe, (0%), (1-25%), (26-50%), (51-75%), (76-100%) respectively. CT-SS was calculated by summing these affected lung lobes and ranged from 0-20. According to this count, CT-SS score analysis was grouped into four levels none (0), mild (1-5), moderate (6-10), and severe (11-20) [7,13,14].

Statistical Analysis

Statistical Package for Social Sciences (SPSS) software model 22.0 was performed for statistical analyses. Categorical variables were shown as percentages/counts while continuous variables were shown as mean +/-standard deviation. The RT-PCR was evaluated as a reference test to compare the diagnostic performance of chest CT. The CT-SS categories were analyzed to predict the presence of PCR positivity according to Receiver Operating Characteristics (ROC) curve analysis. The 5% type-1 error limit was utilized to approve the test variables' statistically significant predictive value. P<0.05 was considered statistically significant.

Table I. *The yield of chest CT for COVID-19 infection with RT-PCR results as reference*

	Results (n)				Test performance (%)				
	TP	TN	FP	FN	Sensitivity	Specificity	PPV	NPV	Accuracy
Overall	265	213	160	174	60% (265/439)	57% (213/373)	62% (265/425)	55% (213/387)	59% (478/812)
Age									
>50 years	54	21	35	28	65% (54/82)	37% (21/56)	61% (54/89)	43% (21/49)	54% (75/138)
<50 years	211	192	125	146	59% (211/357)	60% (192/317)	62% (211/336)	56% (192/338)	59% (403/674)
Sex									
Male	145	115	95	85	63% (145/230)	55% (115/210)	60% (145/240)	57% (115/200)	59% (260/440)
Female	120	98	65	89	57% (120/209)	60% (98/163)	69% (120/185)	52% (98/187)	58% (218/371)

TP: true positive, TN. true negative, FP: false positive, FN: false negative, PPV: positive predictive value, NPV: negative predictive value, RT-PCR: reverse transcription polymerase chain reaction

http://doi.org/10.5472/marumj.1379916
Marmara Med J 2024;37(1): 18-22

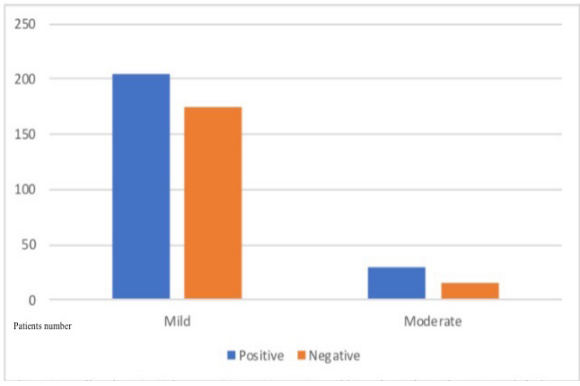

Figure 2. *Baseline chest CT-SS between COVID-19 RT-PCR positive and negative patients. No statistical difference (P:0.75).*

3. RESULTS

Nine hundred outpatients' (mean age 37.8; male 53.9%) data were evaluated at the beginning of the study. Eighty-eight patients were excluded due to a lack of chest CT scans. Eight hundred and twelve patients (mean age, 38; male 54%) were included in the analysis. Figure 1 demonstrates the flowchart of the study. The clinical symptoms were cough (68%), dyspnea (44%), myalgia (14%), and sore throat (13%). One hundred and forty-eight patients had comorbidity; such as 67 patients (7.4%) had hypertension, while 65 patients (7.2%) had asthma and bronchitis and 38 patients (4.2%) had diabetes.

Two hundred and sixty-five patients (mean age: 39,9±12,1 years; 112 males) had positive RT-PCR and positive chest CT while 213 patients (mean age: 38,5±11,9 years, 103 males) had negative RT-PCR and negative chest CT. On the other hand, 174 patients (mean age: 36.8±12.4 years; 85 male) had positive RT-PCR without a pathological finding at the chest CT and 160 patients (mean age: 39.6±11.8 years; 95 males) had suspicious findings for COVID-19 with negative RT-PCR assays.

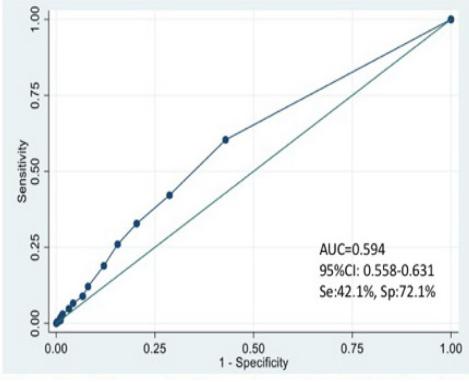

Figure 3. *ROC test for the diagnostic utility of CT-SS in COVID-19. ROC analysis showed the area under the curve (AUC) of CT-SS for diagnosing COVID-19 was 0.594 (95%CI 0.553–0.631). The CT-SS cutoff of 2 had 42.1% sensitivity and 72.1% specificity*

The accuracy, sensitivity, and specificity of chest CT in identifying COVID-19 infection diagnosed by RT-PCR results were 59% (95% CI 55-62%, 478/812), 60%, (95% CI 56-65%, 265/439), 57% (95% CI 52-62%, 213/373) retrospectively. The chest CT performances to diagnose COVID-19 were also assessed according to age and gender (Table I). No significant difference was detected.

Three hundred eighty-seven (47.7%) patients had no pathological CT findings while 425 patients had positive chest CT. CT-SS is categorized into three-part; mild, moderate, and severe. With reference to this score, most of the patients cumulated in the mild group 380/812 (46.8%) while 45/812 patients (5.5%) were in the moderate group, and no patients were in the severe group. According to the CT-SS, the positive RT-PCR rates were 54% in the mild group and 64% in the moderate groups (P=0.75) (Figure 2).

ROC analysis was performed to explore the diagnostic utility of CT-SS to predict RT-PCR positivity (Figure 3). ROC analysis revealed that a cut-off of 2 CT-SS predicted a positive RT-PCR with a sensitivity of 42.1% and a specificity of 71.3% (area under the ROC curve (AUC) was 0.594 (95%CI 0.558–0.631).

4. DISCUSSION

In this study, we investigated whether there was a correlation between RT-PCR results and chest CT images in COVID-19 suspected outpatients and we detected a low sensitivity for chest CT.

Strategies for COVID-19 encircle and management heavily depend on disease diagnosis. RT-PCR test has many limitations such as sampling error, staff experience, quality differences of kits, the detection sensitivity of COVID-19, changing test protocols between countries, and long waiting time to get results. Serial RT-PCR tests should be done to deal with these problems, but it prolongs the diagnostic time. Chest CT imaging is faster and easier than RT-PCR to diagnose COVID-19. Thin-section chest CT imaging is more precise in demonstrating pathological findings even in the early stages of COVID-19 [15,16]. According to two diagnostic accuracy studies, the sensitivity of the RT-PCR test varies between 50% to 83% [17,18]. In a study, 100% of symptomatic COVID-19-infected patients had positive RT-PCR, while 56% of them had no signs of chest CT at the beginning of symptoms [9]. A review evaluating 641 studies has shown that chest CT has limited utility in patients with early disease and those who show no symptoms [19]. Investigators have claimed that chest CT has low sensitivity and specificity and may be used as a supportive tool to diagnose COVID-19, especially for symptomatic patients. Pan et al., showed that chest CT demonstrates high specificity but low sensitivity, in the initial period [20]. Similar to other studies, we found positive lung CT findings in 60% of 439 patients with positive RT-PCR results.

Li et al., showed that among 78 cases, 31% had positive RT-PCR, despite a normal chest CT [13]. The use of lung CT alone as a diagnostic tool in cases with suspected COVID-19 may result in missing positive cases and may also pose a potential infection risk transmission. Still, RT-PCR is a better tool for diagnosing

http://doi.org/10.5472/marumj.1379916
Marmara Med J 2024;37(1): 18-22

COVID-19 infection, while chest CT may be used to support the diagnosis.

In many cases, despite the first RT-PCR test being negative, it has been reported that subsequent tests develop positivity [21]. Repeated RT-PCR tests can be performed to avoid these limitations, but this may prolong the diagnostic process.

In a study by Ai et al., when the RT-PCR test was taken as the reference test, the accuracy, sensitivity, and specificity of lung CT were found to be 68%, 97%, and 25%, respectively [22]. We found chest CT specificity, sensitivity, and accuracy at 57%, 60%, and 59%, respectively. In our study, the sensitivity of chest CT was not high compared to this study.

Our study has certain limitations. First of all, we only analyzed outpatients who were relatively younger with less comorbidities compared to inpatients. This may be a reason of lower CT-SS in our study. Secondly, we did not perform the COVID-19 antibody test in patients with significant findings on lung CT, although, the RT-PCR test was negative. Therefore, we could not check false RT-PCR negativities by testing for COVID-19 antibodies in the blood. Despite this, we tried to emphasize the importance of RT-PCR and lung CT in controlling the COVID-19 pandemic in our study.

Conclusion

We have explored the diagnostic performance between RT-PCR and chest CT in outpatients with clinically suspected COVID-19 infection. We have detected that chest CT does not show high sensitivity for the diagnosis of COVID-19 for outpatients. RT-PCR seems as a first-choice diagnostic tool to be used. In case of high clinical suspicion, despite repeated negative RT-PCR results lung CT may be appropriate. In addition, the over-screening of patients with suspected COVID-19 may also put an unnecessary financial burden on the health system.

In conclusion, our study supports the use of RT-PCR as a first-line test due to the low sensitivity of lung CT in the diagnosis of COVID-19. We recommend RT-PCR as the first choice in the diagnosis of COVID-19 and that chest CT should be used in clinically highly suspicious cases where RT-PCR is negative. It will be important to prioritize RT-PCR testing in primary healthcare centers and outpatient clinics because these centers play an important role in the COVID-19 pandemic.

Compliance with the Ethical Standards

Ethics Committee approval: The study protocol was approved by the Institutional Review Board and the Clinical Research Ethics Committee of Marmara University School of Medicine (approval number: 09.2020.578).

Financial disclosure: The authors declared that this study has received no financial support.

Conflict of interest: The authors report that they have no conflict of interest.

Authors' contributions: ETT and BB: Study conception and design, ETT, BB, CC and CAK: Data collection, ETT, HPG and VK: Analysis and interpretation of results, ETT, BB, CC and CAK: Draft manuscript preparation. All authors reviewed the results and approved the final version of the manuscript.

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