Cumhuriyet Medical Journal, 44(4): 362-369, 2022
DOI: http://dx.doi.org/10.7197/cmj.1164858

Cumhuriyet Medical Journal

| cmj.cumhuriyet.edu.tr | Founded: 2004 Available online, ISSN:1305-0028 Publisher: Sivas Cumhuriyet Üniversitesi

Can Chest CT be The First-Line Diagnostic Test in COVID-19? A Cross-Sectional Study

Halil Çaylak[1,a*], Dilara Atasoy[1,b], Nazım Çetinkaya[1,c], İsmet Can[1,d], Rağıp Sariismailoğlu[2,e], Mehmet Haydar Atalar [3,f]

[1] Department of Radiology, Sivas Numune Hospital, Sivas, Turkey, [2] Department of Infectious Disease, Sivas Numune Hospital, Sivas, Turkey, [3] Department of Radiology, Faculty of Medicine, Sivas Cumhuriyet University, Sivas, Turkey

**Corresponding author*

Research Article

History

Received: 21/08/2022
Accepted: 21/12/2022

ABSTRACT

Background/aim: Early in the COVID-19 pandemic, chest computerized tomography (CCT) was shown to be more sensitive than real-time reverse transcription polymerase chain Reaction (rRT-PCR) in detecting the disease, especially in regions with high disease prevalence. In this study, we aimed to determine the sensitivity and specificity of chest CT in the diagnosis of COVID-19.

Materials and Methods: Between 17 March, 2020 and 25 April, 2020, 2170 patients who were admitted to the hospital for any reason and underwent chest CT scanning were retrospectively analyzed. Patients with a pre-diagnosis of COVID-19 and a positive rRT-PCR test, two consecutive negative rRT-PCR tests, or with a first negative rRT-PCR test and a positive follow-up rRT-PCR test were included. The day of the rRT-PCR test for these patients was counted as day "0," and 200 patients whose CCT was performed within +/- three days were included in the study.

Results: Of the 200 patients included in the study, 118 were rRT-PCR-positive, and 82 were rRT-PCR-negative. Of the 118 patients with positive rRT-PCR results, 62/118 (52.5%) had positive CCT scans. With the rRT-PCR results as the reference, the sensitivity, specificity, and accuracy of CCT in indicating COVID-19 infection were 52.5% (95% CI 43–61%), 67% (95% CI 56–77%), and 58.5% (95% CI 51-65%), respectively. The negative predictive value of CCT in diagnosing COVID-19 was greater for women than for men (p = 0.01).

Conclusions: In regions where the prevalence of COVID-19 is not high, the use of CCT in the diagnosis of the disease is not an alternative to the rRT-PCR test due to its low sensitivity.

Keywords: COVID-19, Chest computed tomography, rRT-PCR, Diagnostic test

Toraks BT, COVID-19'da ilk basamak tanı testi olabilir mi? Kesitsel bir çalışma

Süreç

Geliş: 21/08/2022
Kabul: 21/12/2022

ÖZ

Giriş ve Amaç: COVID-19 pandemisinin başlarında, Toraks Bilgisayarlı Tomografi (Toraks BT), hastalığın teşhisine özellikle hastalık prevalansının yüksek olduğu bölgelerde gerçek zamanlı- ters transkripsiyon polimeraz zincir reaksiyonundan (rRT-PCR) daha duyarlı olduğu gösterilmiştir. Bu çalışmada Toraks BT'nin COVID-19 tanısında duyarlılığını ve özgüllüğünü belirlemeyi amaçladık.

Gereç ve Yöntem: 17 Mart 2020 ile 25 Nisan 2020 tarihleri arasında herhangi bir nedenle merkezimize başvuran ve Toraks BT çekilen 2170 hasta retrospektif olarak incelendi. COVID-19 ön tanısı ile takip edilen hastalardan ilk rRT-PCR testi pozitif olan, ardışık iki rRT-PCR testi negatif olan veya ilk rRT-PCR testi negatif olan ve takip rRT-PCR testi pozitif olan hastalar çalışmaya dahil edildi. Bu hastalardan Toraks BT tarihi, hastanın ilk rRT-PCR testinin öncesinde veya sonrasında en fazla üç gün olan 200 hasta çalışmaya alındı.

Bulgular: Çalışmaya dahil edilen 200 hastanın 118'inin rRT-PCR testi pozitif ve 82'sinin rRT-PCR testi negatifti. rRT-PCR sonucu pozitif olan 118 hastanın sadece 62/118'i (%52,5) Toraks BT'de pozitif tanı alabildi. rRT-PCR testi sonuçları referans alındığında, Toraks BT'nin COVID-19 tanısındaki duyarlılığı, özgüllüğü ve doğruluğu sırası ile %52,5 (%95 Güven Aralığı (GA) %43–61), %67 (%95 GA %56–77), %58,5 (%95 GA %51-65)'dir. Toraks BT'nin COVID-19 teşhisindeki negatif öngörü değeri, kadınlarda erkeklerden daha yüksekti (p = 0.01).

Sonuç: Torkas BT'nin, çalışmada gösterilen yetersiz duyarlılığı nedeniyle, başta COVID-19 prevalansının yüksek olmadığı bölgelerde olmak üzere rRT-PCR testine alternatif bir tanı testi olarak kullanımı uygun bulunmamıştır.

Anahtar sözcükler: COVID-19, Chest computed tomography, rRT-PCR, Diagnostic test

[a] drhalilcaylak@gmail.com https://orcid.org/0000-0001-8089-4822
[b] dilara.gungor@hotmail.com https://orcid.org/0000-0001-7924-1752
[c] drnazimcetinkaya@gmail.com https://orcid.org/0000-0001-9596-9057
[d] drismetcan@gmail.com https://orcid.org/0000-0002-5188-944X
[e] sariismailoglu58@gmail.com https://orcid.org/0000-0002-1859-6100
[f] mhatalar@gmail.com https://orcid.org/0000-0003-3076-8072

How to Cite: Çaylak H, Atasoy D, Çetinkaya N, Can İ, Sariismailoğlu R, Atalar MH (2022) Can Chest CT be The First-Line Diagnostic Test in COVID-19? A Cross-Sectional Study, Cumhuriyet Medical Journal, December 2022, 44 (4): 362-369

Introduction

In December 2019, several cases of unknown pneumonia were identified in Wuhan, China, and it was reported that the cause was the newly identified 2019 novel coronavirus belonging to the beta-coronavirus family [1]. Later, its name was updated to severe acute respiratory syndrome coronavirus 2 (SARS-CoV2), and the disease was named the novel coronavirus disease 2019 (COVID-19).[i] The clinical course of the disease covers a wide spectrum, from a simple common cold to severe acute respiratory disease. Although almost one and a half years have passed since the emergence of the disease, treatment options are still not fully effective.[ii] However, the vaccines introduced by different companies at the end of 2020 and the beginning of 2021 offer a chance to alleviate and end the pandemic [2]. Nevertheless, the pandemic is currently far from being controlled. Access to the vaccine and vaccination speed are not at the desired level in every country, and the emergence of different variants of the virus makes it difficult to control the pandemic. Thus far, 59.2% of the world population has received at least one dose of a COVID-19 vaccine.[iii] For this reason, rapid detection of possible COVID-19 cases and isolation of infected people and their contacts to prevent the spread of disease are very important factors in pursuit of controlling the pandemic. Since the beginning of the pandemic, the real-time reverse transcription polymerase chain reaction (rRT-PCR) test has been accepted and used as a reference diagnostic method in COVID-19 diagnosis [3]. However, the false-negative rate of the rRT-PCR test can be in the range of 1% to 30% [4-6]. The absence of a gold standard diagnostic test has revived other diagnostic methods, especially imaging, as alternatives to the rRT-PCR test. Chest computed tomography (CCT) is a rapid imaging method for detecting pneumonia. The typical radiological imaging findings in COVID-19 patients are peripheral distribution of patchy ground-glass areas, consolidations, and increased reticular density, which are seen in most CCT images [7]. CCT was shown to have high sensitivity in detecting COVID-19 in the beginning of the pandemic [8,9]. However, in recent studies, the sensitivity was not as high as previously thought, and the differences between the methodologies of the studies came to the fore [10,11]. In this study, we aimed to determine the sensitivity of CCT in the diagnosis of COVID-19.

Materials and Methods

This retrospective study was approved by the local ethics committee (Reference number: 2020-06/28 and date: 17 June 2020). Due to the nature of the retrospective study, the requirement to obtain patient consent was waived.

Patient selection

A total of 2170 non-contrast CCT examinations were taken on three different CT devices between March 17, 2020 (the date of the first COVID-19 case detected in the city where our hospital is located) and April 25, 2020, were examined. The patients were classified according to their preliminary diagnoses:

I. Pre-diagnosed as contact with or exposure to COVID-19 or under observation for suspected disease or condition (i.e., COVİD-19) or pneumonia or patients with respiratory system symptoms, such as cough, dyspnea, fever, etc.

II. Pre-diagnosed with other disease or condition except pre-diagnosed in section I; and

III. Pre-diagnosed with any kind of trauma.

Patients with pre-diagnoses in sections II and III were excluded from the study. The medical records of the patients who received pre-diagnoses in accordance with the first section were analyzed retrospectively. The patients who had an rRT-PCR test for the diagnosis of COVID-19 were included in the study. Among these patients, those who had a single rRT-PCR test with a negative result were excluded from the study to avoid high false-negative rates.

The inclusion criteria were as follows: 1. No more than three days between the date of the CCT scan and the first rRT-PCR test (the CCT scan could be before or after the rRT-PCR test); 2. Patients with a first rRT-PCR test with a positive or negative result and a second RT-PCR test that was positive (the maximum time between two RT-PCR tests was three days); 3. Patients with two consecutive negative rRT-PCR tests (the maximum time between the two tests was three days); and 4. The earliest CCT scans of patients who had more than one CCT scan were included in the study.

As a result, 200 patients with CCT scans from 2170 CT scans that met these criteria were included in the study and evaluated retrospectively.

rRT-PCR testing for the Sars-CoV2 virus

We accepted rRT-PCR as the reference test for diagnosing COVID-19. Samples were collected via nasopharyngeal and oropharyngeal swabs. Patients with a positive initial rRT-PCR test (n = 109) and patients

[i] World Health Organization (WHO) (2020). Naming the Coronavirus Disease (COVID-19) and the Virus that Causes it [online]. Website https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-(covid-2019)-and-the-virus-that-causes-it [accessed 07 January 2021].

[ii] WHO (2021). Therapeutics and COVID-19: Living Guideline. Website https://apps.who.int/iris/bitstream/handle/10665/340374/WHO-2019-nCoV- therapeutics-2021.1-eng.pdf [accessed 31 March 2021].

[iii] Coronavirus (COVID-19) Vaccinations [online]. Website: https://ourworldindata.org/covid-vaccinations [accessed 12 January 2022].

with a negative initial rRT-PCR test (n = 9) but positive for a second rRT-PCR test (n = 9) were accepted as rRT-PCR-positive; patients with two negative rRT-PCR tests were considered rRT-PCR-negative (n = 82).

Chest CT protocols

CCT imaging was acquired using 16-detector CT scanners (Alexion and Aquillion; Toshiba, Tokyo, Japan). CT images were obtained during a single inspiratory phase in the supine position without contrast medium injection. The CT scan parameters were tube voltage 120 KVp with automatic tube current modulation, rotation times of 0.5 (Aquillion; Toshiba) and 0.75 seconds (Alexion; Toshiba), and pitch factor 0.938. The 3 mm-thick images were reconstructed and stored in the picture archiving and communication system (PACS).

Chest CT image analysis

The 200 CCT images were evaluated by two board-certified radiologists with 10 and 8 years of experience. The images were divided into three categories: typical findings for COVID-19, atypical findings for COVID-19, and no findings on CCT (Table 1) [12]. In cases where the two radiologists could not agree, consensus was reached with a third board-certified radiologist with 8 years' experience. All three radiologists were blinded to the patients' rRT-PCR results. Typical CCT findings for COVID-19 were considered a positive diagnosis; atypical CT findings and no findings were accepted as negative diagnoses for COVID-19 (Figures 1 and 2).

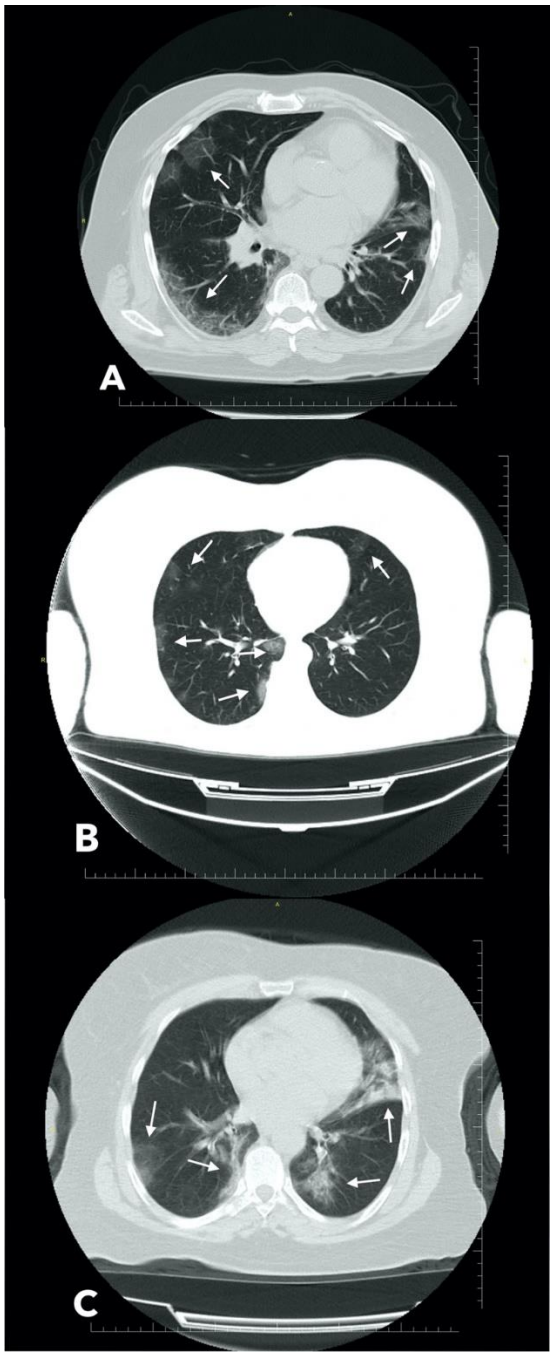

Figure 1. Typical CCT manifestations (pure bilateral subpleural patchy GGO) of COVID-19 with different rRT-PCR results. A) 65-year-old male patient's CCT two days after COVID-19 diagnosis with positive rRT-PCR, (arrows show GGO's); B) 55-year-old female patient's CCT two days after COVID-19 diagnosis with initial rRT-PCR was negative and consequent rRT-PCR was positive, (arrows show GGO's); C) 58-year-old female patient's CCT at one day before initial rRT-PCR and consequent rRT-PCR were both negative, (arrows show GGO's).
CCT: chest computerized tomography; GGO: ground-glass opacity; rRT-PCR: real-time reverse transcription polymerase chain reaction.

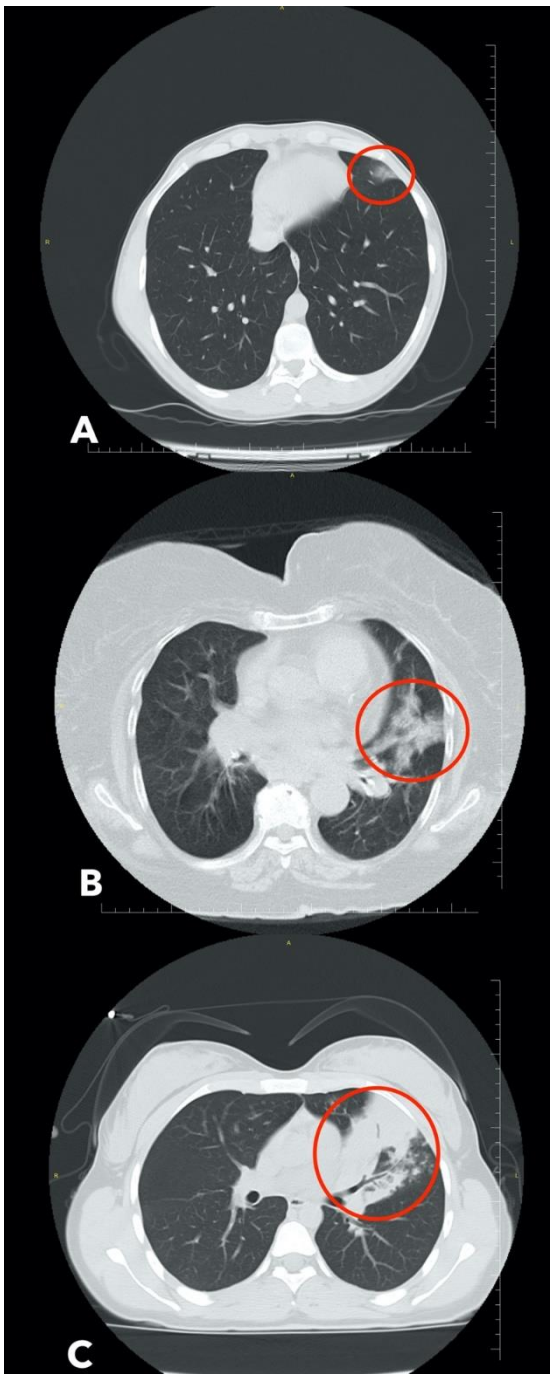

Figure 2. Atypical CCT manifestations of COVID-19 with different rRT-PCR results. A) 23-year-old male patient's CCT on same day that COVID-19 diagnosis with rRT-PCR was positive. The only finding on CCT (red circle) was small patchy GGO in the left upper lobe lingular segment; B) 87-year-old female patient's CCT one day before COVID-19 diagnosis with initial rRT-PCR was negative and consequent rRT-PCR was positive. The only finding on CCT (red circle) was patchy GGO with consolidation in the left upper lobe lingular segment; C) 19-year-old female patient's CCT on the same day as initial rRT-PCR and consequent rRT-PCR were both negative. The only finding on CCT (red circle) was a consolidation with air bronchogram in the left upper lobe lingular segment.
CCT: chest computerized tomography; GGO: ground-glass opacity; rRT-PCR: real-time reverse transcription polymerase chain reaction.

Table 1. Classification of chest CT findings.

Typical COVID-19 findings on chest CT: Bilateral or unilateral multilobe pure GGO with peripheral distribution, with/without side findings (e.g., interlobular septal thickness, consolidation, crazy paving, air bronchograms, vascular enlargement, curvilinear densities, etc.), without mediastinal lymphadenopathy (short axis of node larger than 10 mm) and uni-/bilateral pleural effusion.
Atypical COVID-19 finding on chest CT: Findings that do not meet typical COVID-19 chest CT criteria (e.g., unilateral single lobe GGO, nodular clustered GGO, etc.)
No findings on chest CT: Bilateral normal lung parenchyma

Note: adapted from reference 12.
CT: computerized tomography. GGO: ground-glass opacity.

Statistical analysis

For statistical analysis, IBM SPSS Statistics 20 (IBM Corp., Armonk, NY, USA) was used. Categorical variables were expressed as numbers (%), and quantitative variables were expressed as mean (standard deviation [SD]) or median (interquartile range [IQR]) values. Using the RT-PCR results as a reference, the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of the CCT imaging were calculated. The

confidence intervals for sensitivity, specificity, and accuracy are "exact" Clopper-Pearson confidence intervals, and for the predictive values they are the standard logit confidence intervals. The performance of CCT for identifying COVID-19 in different age groups (< 65 years and ≥ 65 years) and by gender was compared by the Chi-square test and McNemar's test. A p-value of less than 0.05 was considered statistically significant.

Results

In this cross-sectional retrospective study, 200 patients (114 [57%] male and 86 [43%] female) were included. The median age was 51 years (IQR 32–65 years). Figure 3 shows the flowchart of the study.

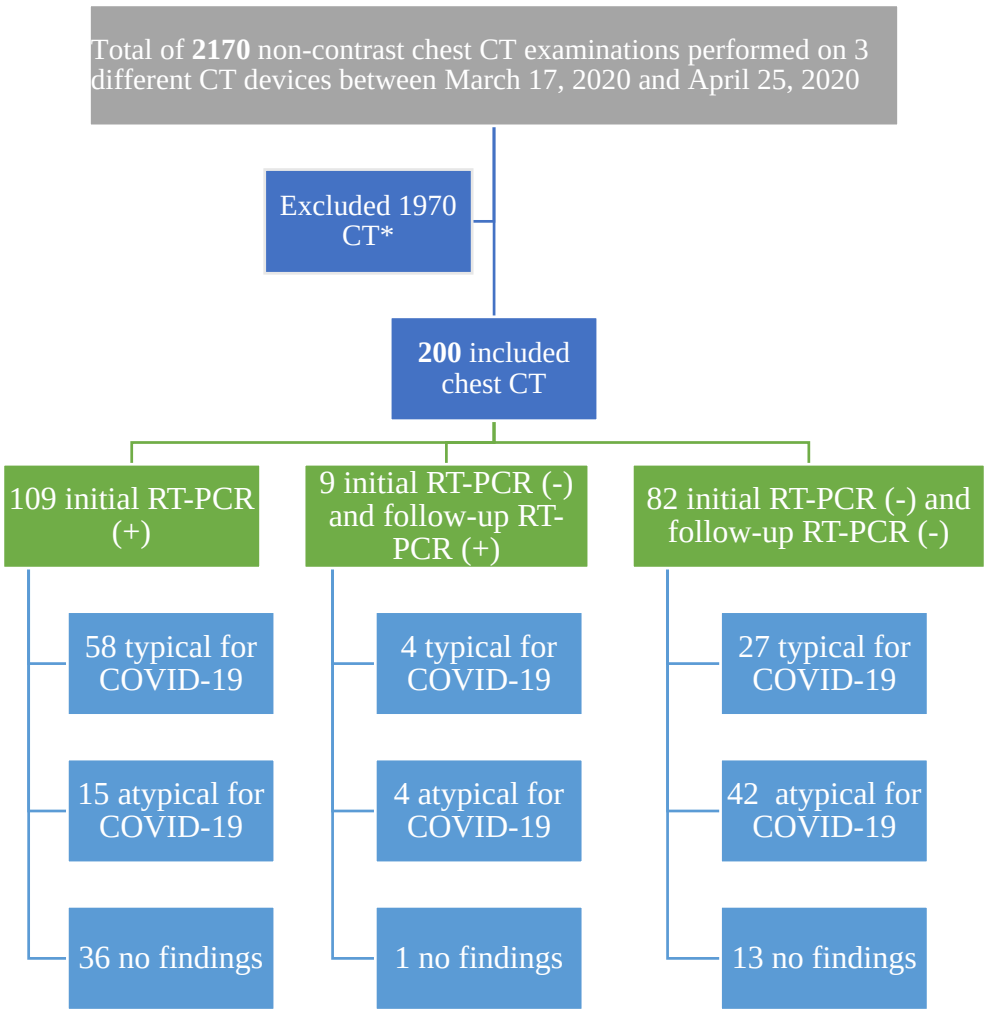

Figure 3. Study flowchart.
CT: computerized tomography; RT-PCR: Reverse transcription polymerase chain reaction.

Of the 200 patients, 109 had positive and 91 had negative results after their initial rRT-PCR tests. Of the 91 patients with negative initial RT-PCR results, 9 had positive and the remainder had negative results after the second rRT-PCR test.

Of the 118 patients with positive rRT-PCR results, 62/118 (52.5%) had positive CCT scans. The median time interval between the paired CCT scan and the rRT-PCR test was 0 days (range: -3 to +3 days) (Figure 4). With the rRT-PCR results as the reference, the sensitivity, specificity, and accuracy of CCT in indicating COVID-19 infection were 52.5% (95% CI 43–61%), 67% (95% CI 56–77%), and 58.5% (95% CI 51–65%), respectively.

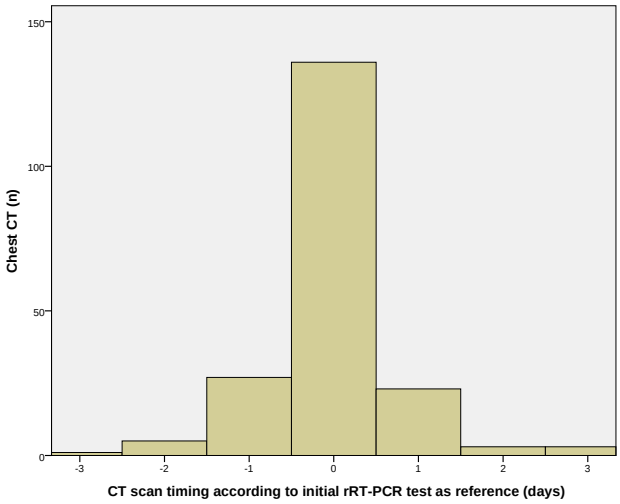

Figure 4. Distribution of chest CT acquisition time (days) when patients' initial rRT-PCR test accepted as reference (day "0")

The performance of CCT in diagnosing COVID-19 in different age and sex groups is reported in Table 2. There was no significant difference in diagnosing COVID-19 between patients ≥ 65 years and <65 years for sensitivity, specificity, PPV, NPV, and accuracy (p = 0.09, 0.84, 0.38, 0.32, and 0.27, respectively). The NPV of CCT in diagnosing COVID-19 was greater for women than for men (p = 0.01), and no difference existed for sensitivity, specificity, PPV, and accuracy (p = 0.82, 0.53, 0.14, and 0.50, respectively).

There were some incompatible results between the CCT findings and the rRT-PCR results. Nineteen atypical COVID-19 CCT findings with positive rRT-PCR results are detailed in Table 3.

Medical records of patient cases with two consequent rRT-PCR negative (-) results diagnosed with COVID-19 on chest CT as follows: Seven cases had close contact with rRT-PCR (+) patients; 8 cases had suspicious contact (e.g., travel from cities with high daily COVID-19 cases); 12 cases had no contact with any suspicious COVID-19 cases.

Table 2. Performance of chest CT for COVID-19 diagnosis with RT-PCR result as the reference.

	Results (n)				Test Performance (%)				
	TP	TN	FP	FN	Sensitivity [95% CI]	Specificity [95% CI]	PPV [95% CI]	NPV [95% CI]	Accuracy [95% CI]
Overall	62	55	27	56	52.5 [43–62]	67 [56– 77]	69.6 [62 –76]	49.5 [43 – 55]	58.5 [51–65]
Sex									
Male	32	37	17	28	53 [40 – 66]	68.5 [54 – 80]	65 [54 – 74]	57 [48– 64]	60.5 [51– 69]
Female	30	18	10	28	52 [38–65]	64 [44–81]	75 [63–84]	39 [30–48]	56 [30–48]
Age									
< 65 years	42	40	20	44	49 [37–59]	66 [53–78]	68 [58–76]	47 [40–54]	56 [47–64]
≥ 65 years	20	15	7	12	62.5 [43–78]	68 [45–86]	74 [59–84]	55.5 [42–68]	65 [50–77]

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

Table 3. Chest CT findings of patients with RT-PCR (+) and diagnosed as atypical chest CT category.

Initial PCR positive (+) but atypical chest CT findings (n = 15)	Initial PCR negative (-), second RT-PCR (+) but atypical chest CT findings (n = 4)
7 single lobe pure GGO	2 single lobe pure GGO
2 bilateral diffuse GGO + mediastinal LAP	1 single lob pure consolidation
2 single lobe GGO + consolidation	1bilateral peripheral patchy GGO + consolidation + unilateral pleural effusion
1 single lobe patchy GGO	
1 reticular opacities + bilateral pleural effusion	
1 peripheral multilobar GGO + mediastinal LAP	
1 diffuse acinar-nodular like infiltrations+mediastinal LAP	

RT-PCR: reverse transcription polymerase chain reaction; CT: computerized tomography; GGO: ground-glass opacity; LAP: lymphadenopathy.

Discussion

The role of CCT has evolved during the pandemic as an alternative and possibly superior test compared to rRT-PCR, especially in epidemic areas [13]. In our study, 200 patients with suspected COVID-19 were included, and when the rRT-PCR test was taken as the reference, CCT achieved 52.5% sensitivity, 67% specificity, 70% PPV, 49% NPV, and 58.5% accuracy. The data obtained in this study show that the use of CCT in the diagnosis of COVID-19 has low sensitivity but moderate specificity.

To control the COVID-19 pandemic, patients with suspected COVID-19 should be quickly identified with a highly sensitive diagnostic test. If the patients test positive, they should start treatment and be placed under quarantine, and close contacts should be informed. For this purpose, rRT-PCR nucleic acid tests are used globally. However, it has been reported that the sensitivity of the rRT-PCR test is relatively high in the first few days of the onset of COVID-19 symptoms, and false negative rates may be relatively high before and after this time interval [14-16]. High false-negative rates have been reported for the rRT-PCR test, which results in tests being administered to the same patient several times, delays in diagnosis, and the spread of the disease by non-diagnosed infected patients [4,6].

In several articles published in 2020, the authors asserted that the sensitivity of CCT is higher than rRT-PCR tests and that it could be used as the first-line diagnostic test. In two meta-analyses by Islam et al. and by Khatemi et al., the overall sensitivity of CCT in suspected COVID-19 patients was 89.9% (95% CI 85.7–92.9) and 87% (95% CI 85–90%), respectively, and the pooled specificity was 61.1% (95% CI 42.3–77.1) and 46% (95% CI 29–63%), respectively [11,10]. However, the authors of both noted the poor quality and the heterogeneity of the studies included in the meta-analyses.

The typical CCT findings for COVID-19 are well described [17]. However, the most confusing part about CCT is how to evaluate and categorize atypical findings. Some studies have accepted atypical findings detected in CCT as a positive diagnosis [8,9,18], but the design of these studies can lead to an overestimate of sensitivity [19]. Where the disease's prevalence is high, most atypical findings are associated with COVID-19, and in such cases, CCT may be more sensitive than rRT-PCR testing. Of course, differences in patient selection criteria also have a significant effect on the high sensitivity and accuracy of CCT [11].

There are some concerns that CCT is difficult to use in patients with suspected COVID-19. CCT is not practical to apply to a large population because of radiation. There could be many patients with suspected COVID-19 in the CT waiting rooms, which could turn into a transmission source. Also, numerous CCT exams will obviously cause great responsibility and increased workload for radiologists and technicians, which is very difficult to handle.

We acknowledge that our study had some limitations. Since many patients who presented with suspected COVID-19 and had a single negative rRT-PCR result were not included in the study, the study population was restricted. There were 27 patients with typical COVID-19 findings on CCT for whom two consecutive rRT-PCR tests were negative. These patients were considered COVID-19 positive and received treatment, and some of them lost their lives. If these patients had a third or fourth rRT-PCR or other laboratory test, such as an antibody test, they could have been diagnosed with COVID-19. This may have underestimated the sensitivity and specificity of CCT. The classification of lesions detected in CCT differs in similar sensitivity studies. Although a definite finding specific to COVID-19 has not been described, typical appearances have been mentioned in previous studies [12,17]. However, it has been shown that viral infections other than Sars-CoV-2 overlap with CT findings in COVID-19 [20]. Therefore, we found it more appropriate to put the atypical CT findings we mentioned in the methods section into the negative category for diagnosis unlike as in some other similar studies. If we had accepted the atypical findings as positive in the diagnosis of COVID-19, perhaps the sensitivity would have increased, but the number of false positives would also have increased significantly.

Conclusion

CCT has a role in the COVID-19 pandemic as it can determine the severity of the disease, identify complications, and support the diagnosis in cases where highly suspicious COVID-19 with multiple

negative rRT-PCR, rather than to be the independent diagnostic tool.

Sivas Cumhuriyet University Non-Interventional Clinical Research Ethical Committee Approval Number: 2020-06/28, date: 17 June 2020

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

This article was accepted and presented as an oral presentation at the 42nd National Radiology Congress (SS-013, TURKRAD-2021, 26-31 October 2021 Belek/Antalya/Turkey).

References

1. Zhu N, Zhang D, Wang W, Li X, Yang B et al. (2020) A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med 382 (8):727-733. doi:10.1056/NEJMoa2001017

2. Golob JL, Lugogo N, Lauring AS, Lok AS (2021) SARS-CoV-2 vaccines: a triumph of science and collaboration. JCI Insight. doi:10.1172/jci.insight.149187

3. Corman VM, Landt O, Kaiser M, Molenkamp R, Meijer A et al. (2020) Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Euro Surveill 25 (3). doi:10.2807/1560-7917.ES.2020.25.3.2000045

4. Arevalo-Rodriguez I, Buitrago-Garcia D, Simancas-Racines D, Zambrano-Achig P, Del Campo R et al. (2020) False-negative results of initial RT-PCR assays for COVID-19: A systematic review. PLoS One 15 (12):e0242958. doi:10.1371/journal.pone.0242958

5. Green DA, Zucker J, Westblade LF, Whittier S, Rennert H et al. (2020) Clinical Performance of SARS-CoV-2 Molecular Tests. J Clin Microbiol 58 (8). doi:10.1128/JCM.00995-20

6. Kanji JN, Zelyas N, MacDonald C, Pabbaraju K, Khan MN et al. (2021) False negative rate of COVID-19 PCR testing: a discordant testing analysis. Virol J 18 (1):13. doi:10.1186/s12985-021-01489-0

7. Ye Z, Zhang Y, Wang Y, Huang Z, Song B (2020) Chest CT manifestations of new coronavirus disease 2019 (COVID-19): a pictorial review. Eur Radiol 30 (8):4381-4389. doi:10.1007/s00330-020-06801-0

8. Fang Y, Zhang H, Xie J, Lin M, Ying L et al. (2020) Sensitivity of Chest CT for COVID-19: Comparison to RT-PCR. Radiology 296 (2):E115-E117. doi:10.1148/radiol.2020200432

9. Ai T, Yang Z, Hou H, Zhan C, Chen C et al. (2020) Correlation of Chest CT and RT-PCR Testing for Coronavirus Disease 2019 (COVID-19) in China: A Report of 1014 Cases. Radiology 296 (2):E32-E40. doi:10.1148/radiol.2020200642

10. Khatami F, Saatchi M, Zadeh SST, Aghamir ZS, Shabestari AN et al. (2020) A meta-analysis of accuracy and sensitivity of chest CT and RT-PCR in COVID-19 diagnosis. Sci Rep 10 (1):22402. doi:10.1038/s41598-020-80061-2

11. Islam N, Salameh JP, Leeflang MM, Hooft L, McGrath TA et al. (2020) Thoracic imaging tests for the diagnosis of COVID-19. Cochrane Database Syst Rev 11:CD013639. doi:10.1002/14651858.CD013639.pub3

12. Simpson S, Kay FU, Abbara S, Bhalla S, Chung JH et al. (2020) Radiological Society of North America Expert Consensus Statement on Reporting Chest CT Findings Related to COVID-19. Endorsed by the Society of Thoracic Radiology, the American College of Radiology, and RSNA - Secondary Publication. J Thorac Imaging 35 (4):219-227. doi:10.1097/RTI.0000000000000524

13. Kanne JP, Bai H, Bernheim A, Chung M, Haramati LB et al. (2021) COVID-19 Imaging: What We Know Now and What Remains Unknown. Radiology:204522. doi:10.1148/radiol.2021204522

14. He X, Lau EHY, Wu P, Deng X, Wang J et al. (2020) Temporal dynamics in viral shedding and transmissibility of COVID-19. Nat Med 26 (5):672-675. doi:10.1038/s41591-020-0869-5

15. Kucirka LM, Lauer SA, Laeyendecker O, Boon D, Lessler J (2020) Variation in False-Negative Rate of Reverse Transcriptase Polymerase Chain Reaction-Based SARS-CoV-2 Tests by Time Since Exposure. Ann Intern Med 173 (4):262-267. doi:10.7326/M20-1495

16. Zhang Z, Bi Q, Fang S, Wei L, Wang X et al. (2021) Insight into the practical performance of RT-PCR testing for SARS-CoV-2 using serological data: a cohort study. Lancet Microbe 2 (2):e79-e87. doi:10.1016/S2666-5247(20)30200-7

17. Kwee TC, Kwee RM (2020) Chest CT in COVID-19: What the Radiologist Needs to Know. Radiographics 40 (7):1848-1865. doi:10.1148/rg.2020200159

18. Ravikanth R (2021) Diagnostic accuracy and false-positive rate of chest CT as compared to RT-PCR in coronavirus disease 2019 (COVID-19) pneumonia: A prospective cohort of 612 cases from India and review of literature. Indian J Radiol Imaging 31 (Suppl 1):S161-S169. doi:10.4103/ijri.IJRI_377_20

19. Waller JV, Kaur P, Tucker A, Lin KK, Diaz MJ et al. (2020) Diagnostic Tools for Coronavirus Disease (COVID-19): Comparing CT and RT-PCR Viral Nucleic Acid Testing. AJR Am J Roentgenol 215 (4):834-838. doi:10.2214/AJR.20.23418

20. Elmokadem AH, Batouty NM, Bayoumi D, Gadelhak BN, Abdel-Wahab RM et al. (2021) Mimickers of novel coronavirus disease 2019 (COVID-19) on chest CT: spectrum of CT and clinical features. Insights Imaging 12 (1):12. doi:10.1186/s13244-020-00956-6