Available online at www.medicinescience.org

ORIGINAL ARTICLE

Medicine Science International Medical Journal

Medicine Science 2022;11(3):1278-82

Chest computed tomography and COVID-19 RT-PCR: The tale of two diagnostic tests in a resource-limited setting

Reyhan Ozturk[1], Gokhan Tazegul[2]

[1]Ankara Polatlı Duatepe State Hospital, Department of Infectious Diseases, Ankara, Turkey
[2]Ankara Polatlı Duatepe State Hospital, Department of Internal Medicine, Ankara, Turkey

Received 02 July 2022; Accepted 20 July 2022
Available online 25.08.2022 with doi: 10.5455/medscience.2022.05.127

Abstract

Herein, we aimed to report the association between coronavirus disease 2019 (COVID-19) real-time polymerase chain reaction (RT-PCR) and computerized chest tomography (CT), along with hospitalization and mortality in rural secondary care, resource-limited hospital setting, without the capabilities to conduct RT-PCR or report chest CT results in-house. We included patients admitted to the COVID-19 outpatient clinic between August 2020 and January 2021. COVID-19 RT-PCR was the standard for diagnosis. Chest CT scans were categorized into negative, suspicious, or positive rather than using the COVID-19 Reporting and Data System (CO-RADS) system; and pneumonia was classified into mild, moderate, and severe, rather than using the global CT involvement score (CTIS), as provided by outsourcing. Of 954 outpatients admitted, 382 (40%) were RT-PCR positive, and 472 (49.5%) had pneumonia on chest CT. The sensitivity of the chest CT scans for RT-PCR positivity was 62.04%, and specificity was 58.92%. Cohen's kappa between the RT-PCR and chest CT results showed fair agreement (K=0.205, p=0.0001). Hospitalization and death rates were higher in the RT-PCR positive patient population (p=0.001 and 0.0001). In cases with negative CT scans for pneumonia, the death rates were higher in the RT-PCR positive population (p=0.025, chi-square test). RT-PCR and chest CT had a fair agreement, and the sensitivity and specificity of chest CT scans for RT-PCR positivity were low. Death rates were higher in RT-PCR positive, initial chest CTs negative patients, which underlines the importance of obtaining RT-PCR results in a resource-limited setting to identify patients with a higher risk for mortality.

Keywords: Coronavirus; COVID-19; Viral Pneumonia

Introduction

Early diagnosis and appropriate isolation of patients with coronavirus disease 2019 (COVID-19) can be complicated in centers with limited resources. In a resource-limited setting, computerized chest tomography (CT) can be a method for COVID-19 triage [1]; however, published literature on the correlation between chest CT and COVID-19 real-time polymerase chain reaction (RT-PCR) tests shows conflicting results. Patients with viral pneumonia may have a negative RT-PCR test [2,3], and conversely, patients with a COVID-19 infection may have a normal chest CT [4]. Moreover, previous literature reports a wide variety of results regarding the association between RT-PCR and chest CT results with hospitalization and mortality [5-9].

In this retrospective study, we aimed to report the association between COVID-19 RT-PCR assays and chest CT scan results, along with hospitalization and mortality outcomes, in rural secondary care, resource-limited hospital settings, without the capabilities to conduct RT-PCR tests or report chest CT results in house.

Material and Methods

This retrospective analysis was approved by the institutional review board of the Turkish Ministry of Health's COVID-19 Scientific Research Studies, and permission for data access was obtained from the hospital administration. The Ankara Research and Training Hospital Ethics Committee approved this study (Approval date: 29.07.2021, Approval number: 671). We conducted this study per the Declaration of Helsinki, and patient data were anonymized before analysis.

Study setting

This retrospective study was conducted in a 300-bed secondary

*Corresponding Author: Gokhan Tazegul, Ankara Polatlı Duatepe State Hospital, Department of Internal Medicine, Ankara, Turkey
E-mail: drgtazegul@gmail.com

care hospital in a rural part of Ankara, with no capability to perform the COVID-19 RT-PCR assay in-house. We included all patients admitted to the COVID-19 outpatient clinic between August 2020 and January 2021 during Turkey's second peak of transmission. Samples for RT-PCR assays were routinely transferred twice per day to a reference laboratory in a tertiary-care center. All patients admitted to the COVID-19 outpatient clinic regularly underwent RT-PCR assay tests. Chest CT scans were routinely carried out for all patients in the clinic; however, written reports were provided by a radiology outsourcing company with more than 20 different radiologists.

Data acquisition

This study aimed to analyze the real-world data on the association between COVID-19 RT-PCR assays and chest CT scan results and hospitalization and mortality outcomes in a rural secondary care hospital. The patient's age, gender, outcomes (hospitalization and mortality), COVID-19 RT-PCR assay results, and chest CT scan results were obtained from patient charts. We included: (1) patients presenting to the COVID-19 outpatient clinic between August 2020 and January 2021 with suspected COVID-19; (2) patients with complete data. We excluded: (1) patients aged under 18 years; (2) scans that include motion artifacts; (3) interval between the initial RT-PCR assay and chest CT scan longer than 48 hours.

The COVID-19 RT-PCR test was used as the standard for diagnosis. The RT-PCR assay results were analyzed as either positive or negative. Repeat RT-PCR testing was routinely performed at intervals of 1 day or more for previous negative or indeterminate tests. Additionally, patients with a contact history with a confirmed COVID-19 case, clinical signs and symptoms consistent with COVID-19, and typical radiologic findings were considered clinically positive for the COVID-19 infection, even if repeat RT-PCR tests were negative.

The scanner was a 16-slice Toshiba Alexion (Toshiba Medical Systems, Japan). The chest CT scanning protocol was standard without intravenous contrast, with three mm slices for mediastinal and five mm for lung kernels. Reports of chest CT scan results were provided into three groups: negative [COVID-19 Reporting and Data System (CO-RADS) 1 equivalent)], suspicious (CO-RADS 2, 3, or 4 equivalent), and positive (CO-RADS 5 equivalent) for COVID-19 infection, as provided by the radiology outsourcing company [10]. The severity of COVID-19 pneumonia in patients with a positive or suspicious chest CT scan was quantified by the outsourcing company using a CT severity scoring [11,12], and the resulting global CT involvement score (CTIS), from 0 to 25, was categorized into three groups: mild, moderate, and severe COVID-19 pneumonia. However, reports provided by the radiology outsourcing company did not include CO-RADS classification or CTIS scores; they only included the data mentioned earlier. Additionally, radiologists were routinely blinded to patient data, as CT scans were reported before RT-PCR results.

Statistical Analysis

SPSS statistical software (SPSS for Windows 23.0, IBM Corp., Armonk, N.Y., USA) and MedCalc Diagnostic Test Evaluation Calculator were used for data analysis. Variables were presented as frequency and percentage; and mean and standard deviations. For comparisons, independent sample t- and chi-square tests were used. Fisher's exact test (two-tailed) was used for 2x2 tables. Diagnostic test statistics were expressed as percentages and confidence intervals, as described elsewhere [13-15]. Cohen's kappa statistic was performed to determine consistency between chest CT scans and RT-PCR results. Type I error was defined as less than 0.05.

Results

A summary of 954 outpatients admitted to the COVID-19 outpatient clinic in our hospital between August 2020 and January 2021 is presented in Table 1. Of all the patients admitted, one-third were hospitalized, and 6.5% died in hospital. Forty percent of the patients were RT-PCR positive, and 50% had suspicious (CO-RADS 2, 3, or 4 equivalent) or positive findings (CO-RADS 5 equivalent) for COVID-19 on chest CT scans. As classified by the CTIS score, 472 patients (49.4%) had pneumonia according to the chest CTs, 53.1% had mild, 38.1% had moderate, and 8.6% had severe pneumonia.

Table 1. Summary of Patient Characteristics

No. of patients		954
Age		52.9 ± 18.8
Gender		
	Female	462 (48.4%)
	Male	492 (51.6%)
RT-PCR assay result		
	Negative	572 (60%)
	Positive	382 (40%)
Chest CT reported as		
	Negative for COVID-19	482 (50.5%)
	Suspicious for COVID-19	86 (9%)
	Positive for COVID-19	386 (40.5%)
COVID-19 CTIS score group		
	No pneumonia	482 (50.5%)
	Mild	251 (26.3%)
	Moderate	180 (18.9%)
	Severe	41 (4.3%)
Outcomes		
	Outpatient care	638 (66.9%)
	Hospitalization	316 (33.1%)
	Death	62 (6.5%)

Data for categorical variables were presented as frequency and percentage; continuous variables were expressed as mean±standart deviations. RT-PCR: real time polymerase chain reaction, CT: computerized tomography, COVID-19: coronavirus disease 2019, CTIS: CT involvement score

The RT-PCR positive and negative patients were similar regarding gender distribution. However, RT-PCR positive patients were six years older than RT-PCR negative patients (p=0.0001, independent samples t-test). The RT-PCR positive patients had a higher rate of positive chest CT scans and a lower rate of negative scans; suspicious scan rates were similar between RT-PCR positive and negative patients (p=0.0001, chi-square tests). Among the patients with pneumonia, mild and moderate pneumonia was higher in RT-PCR positive patients, whereas severe pneumonia was similar in RT-PCR positive and negative patients (p=0.0001, chi-square tests). Hospitalization and death rates were higher in the RT-PCR positive patient population (p=0.001 and 0.0001, respectively, chi-square tests) (Table 2). Cohen's kappa between the RT-PCR

and chest CT results showed fair agreement (K: 0.205, p=0.0001). The sensitivity of the chest CT scans (including both positive and suspicious scans) for RT-PCR positivity was 62.04% (95% CI 56.97%–66.93%), specificity was 58.92% (95% CI 54.76%–62.98%), positive likelihood ratio was 1.73 (95% CI 1.50–2.01), and negative likelihood ratio was 0.62 (95% CI 0.54–0.71).

The chest CT results, pneumonia severity, and patient outcomes are presented for CT negative, suspicious, and positive cases in Figure 1. In cases with negative CT scans for pneumonia, the death rates were higher in the RT-PCR positive population (p=0.025, chi-square test). Similarly, in cases with positive CT scans for pneumonia, death rates were higher among the RT-PCR positive population (p=0.003, chi-square test). The death rates in the suspicious CT group, hospitalization rates in all three groups, and the CT pneumonia severity rates in the suspicious and positive CT scan groups were similar.

Table 2. Characteristics of PCR negative and positive patients included in the study

		RT-PCR negative (n=572)	RT-PCR positive (n=382)	p value
Age		50.5 ± 19	56.4 ±18	0.0001
Gender				
	Female	269 (47%)	193 (50.5%)	0.16
	Male	303 (53%)	189 (49.5%)	
Chest CT				
	Negative for COVID-19	337 (58.9%)	145 (38%)	
	Suspicious	60 (10.5%)	26 (6.8%)	0.0001
	Positive for COVID-19	175 (30.6%)	211 (55.2%)	
CTIS score				
	No pneumonia	337 (58.9%)	145 (38%)	
	Mild	126 (22.6%)	122 (31.9%)	
	Moderate	86 (15%)	94 (24.6%)	
	Severe	20 (3.5%)	21 (5.5%)	0.0001
Hospitalization		167 (29.2%)	149 (39%)	0.001
Death		20 (3.5%)	42 (11%)	0.0001

Data for categorical variables were presented as frequency and percentage; continuous variables were expressed as mean±standart deviations. For comparisons, independent sample t-tests and chi-square tests were used. Fisher's exact test (two-tailed) was used for 2x2 tables. RT-PCR: real time polymerase chain reaction, CT: computerized tomography, COVID-19: coronavirus disease 2019, CTIS: CT involvement score

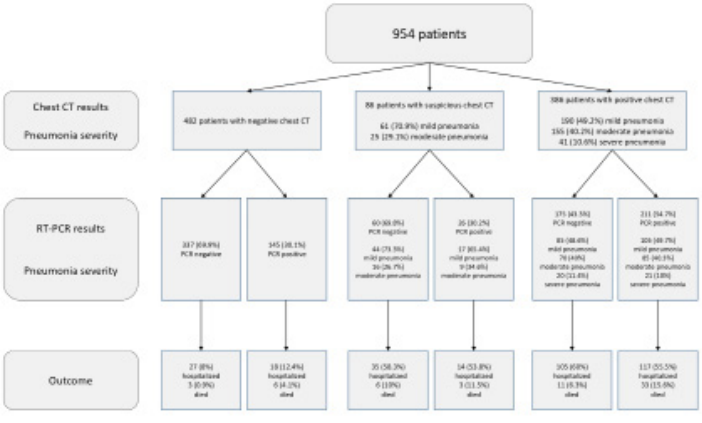

Figure 1. A flowchart of the patient population demonstrating chest computerized tomography (CT) and real-time polymerase chain reaction (RT-PCR) results along with patient outcomes

Discussion

In the current pandemic, early diagnosis and appropriate isolation of patients with COVID-19 are vital. However, this process can become complicated in centers with limited resources. In this study, we reported our real-world data of COVID-19 RT-PCR assay and chest CT scan association, along with hospitalization and mortality outcomes, in rural secondary care, and resource-limited hospital setting. Our samples for RT-PCR assays had to be transferred to another location, and chest CT scans were routinely reported by a radiology outsourcing company with more than 20 different radiologists. Our results show that RT-PCR and chest CT results had a fair agreement; however, the chest CT scans' sensitivity and specificity for RT-PCR positivity were low (62.04% and 58.92%, respectively). Although RT-PCR positive patients had a higher rate of positive chest CT findings and a lower rate of negative chest CT results, the proportions of patients with suspicious CT findings were similar between RT-PCR positive and negative patients. When considering hospitalization, we routinely took into consideration the chest CT results, since these were available within a few hours and clinical findings. However, the hospitalization rates were similar in all three groups. Therefore, chest CT results did not affect hospitalization decisions. Although we did not have the RT-PCR results readily available at hospitalization, this retrospective data shows higher hospitalization rates in RT-PCR positive cases. Moreover, death rates were also higher in the RT-PCR positive, chest CT negative, and chest CT positive populations. In contrast, the death rates in the suspicious CT group were not statistically different between the two RT-PCR groups.

The literature suggests that in a resource-limited setting, such as our center, where immediate decision-making is of utmost importance, imaging can be used as a method for COVID-19 triage [1]. However, the published literature regarding the association between chest CT and COVID-19 RT-PCR tests shows a variety of results since patients with COVID-19 pneumonia may have findings on the chest CT, with an initial negative RT-PCR test: a study from Wuhan reported that sixty to ninety percent of the patients had a positive chest CT before the having a confirmed diagnosis with a positive RT-PCR test [2,3]. Furthermore, patients with a confirmed infection may have no findings on CT at presentation, as Bernheim et al. [4] reported more than half of the patients within 48 hours of onset had no CT findings. Moreover, a retrospective study comparing pre-pandemic and pandemic periods regarding the diagnostic role of CT imaging for viral pneumonia in transplant patients revealed that CT showed no difference in terms of CT findings caused by different viral pathogens causing viral pneumonia [16]. A previous study from Wuhan on the correlation of chest CT and RT-PCR reported that 59% of the patients had positive RT-PCR results, and 88% had positive chest CT scans, with a sensitivity of chest CT of 97% for positive RT-PCR and a specificity of 25%. In the remaining patients with a negative RT-PCR, 75% had positive chest CT findings, of which 48% had highly likely cases, and 33% had probable findings [3]. Moreover, Wang et al. reported that the sensitivity of the RT-PCR test was 65% and the specificity 83% when a chest CT was used as the diagnostic criterion [17]; and Waller et al. reported that chest CT has insufficient sensitivity and specificity than RT-PCR testing for COVID-19 [18]. In their study, Kovács et al. reported that CT provides additional value in the diagnosis, specifically in patients

with typical symptoms, and negative RT-PCR test results in high prevalence areas with typical clinical symptoms or contact with COVID-19 infected patients [19]. This hypothesis was further supported by a systematic review, in which the authors concluded that chest CT is not to be used as a primary screening tool but to be used for symptomatic and hospitalized patients [20]. Therefore, chest CT and RT-PCR tests should be used together to diagnose COVID-19 infection.

However, this was not the immediate solution in our situation, where only clinical findings and chest CT were the readily available tools to diagnose COVID-19; and we reported that chest CT had a sensitivity for RT-PCR positivity of 62.04% and a specificity of 58.92%, similar to the rates reported in the literature. Nevertheless, hospitalization rates were similar in the CT positive, negative, or suspected CT groups. Therefore, CT findings did not have a major role in hospitalization decisions. More importantly, 30.1% of the patients whose chest CT findings were negative at the first admission (145 of 482) were found to have positive RT-PCR tests. This indicates that approximately one-third of patients with normal CT findings are positive for COVID-19 RT-PCR and may be overlooked based on the chest CT alone, which would be an important point to consider in a resource-limited setting without internal capabilities to conduct RT-PCR tests.

RT-PCR positivity is still the hallmark of the COVID-19 diagnosis. However, studies on the relationship between RT-PCR positivity and mortality report different results. In the first study evaluating mortality from the Central Asia and Eurasia regions, Gaipov et al. [5] reported that positive RT-PCR cases had a twofold higher risk of mortality than negative counterparts. In contrast, in a study from Turkey, Ozcan et al. [6] reported that among patients with suspected COVID-19 and positive CT findings, mortality rates were not statistically different between RT-PCR positive and RT-PCR negative patients. Moreover, the literature suggests that chest CT severity is correlated with disease severity and mortality in COVID-19 [7-9]. In the present study, we also demonstrated that mortality was higher in RT-PCR-positive patients (11% vs. 3.5%). Interestingly, death rates were higher in the RT-PCR positive-chest CT negative and RT-PCR positive-chest CT positive subgroups. In contrast, the death rates in the suspicious CT group were similar to RT-PCR positive and negative groups. Because we have also demonstrated that one-third of patients with normal CT are positive for RT-PCR and may be overlooked based on a chest CT alone, and mortality rates were also higher in the RT-PCR positive-chest CT negative patient subgroup (4.1% vs. 0.9%), we underline the need to obtain RT-PCR results as fast as possible in a resource-limited setting to identify patients with a higher risk for mortality.

There are certain limitations to our study. First, due to the retrospective nature of our study, only the included data were available without data loss. Second, due to the radiology outsourcing company's reporting standards, we could not analyze data using all subclasses of CO-RADS (from 1 to 5) and CTIS scores. Instead, we routinely received negative, suspicious, and positive reports for COVID-19 and mild, moderate, and severe COVID-19 pneumonia subclasses. Although this situation adds to the limited resources of our center, the results of this study should be considered accordingly.

Conclusion

In this study, we reported our real-world data of COVID-19 RT-PCR assay and chest CT scan association, along with hospitalization and mortality outcomes, in rural secondary care, and resource-limited hospital setting. We demonstrated that RT-PCR and chest CT results had a fair agreement; however, chest CT scans' sensitivity and specificity for RT-PCR positivity were low. Although we routinely considered chest CT results in addition to clinical findings when considering hospitalization, since it was readily available, hospitalization rates were unaffected by CT results. Hospitalization rates were higher in RT-PCR positive cases, even though we did not have the RT-PCR results available at hospitalization. Moreover, death rates were also higher in RT-PCR positive patients, especially in patients with initial chest CTs negative for COVID-19, which underlines the need to obtain an RT-PCR result as fast as possible in a resource-limited setting to identify patients with a higher risk for mortality.

Conflict of interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical approval
This retrospective analysis was approved by the institutional review board of the Turkish Ministry of Health COVID-19 Scientific Research Studies, and permission for data access was obtained from the hospital administration. The Ankara Research and Training Hospital Ethics Committee approved this study (Approval date: 29.07.2021, Approval number: 671). The study was conducted according to the Declaration of Helsinki, and patient data was anonymized before analysis.

References

1. Rubin GD, Ryerson CJ, Haramati LB, et al. The Role of Chest Imaging in Patient Management during the COVID-19 Pandemic: A Multinational Consensus Statement from the Fleischner Society. Chest. 2020;158:106-116.
2. Kanne JP, Little BP, Chung JH, et al. Essentials for Radiologists on COVID-19: An Update-Radiology Scientific Expert Panel. Radiology. 2020;296:E113-E114.
3. Ai T, Yang Z, Hou H, et al. Correlation of Chest CT and RT-PCR Testing for Coronavirus Disease 2019 (COVID-19) in China: A Report of 1014 Cases. Radiology. 2020;296:E32-E40.
4. Bernheim A, Mei X, Huang M, et al. Chest CT findings in coronavirus disease-19 (COVID-19): relationship to duration of infection. Radiology. 2020;295:200463.
5. Gaipov A, Gusmanov A, Abbay A, et al. SARS-CoV-2 PCR-positive and PCR-negative cases of pneumonia admitted to the hospital during the peak of COVID-19 pandemic: analysis of in-hospital and post-hospital mortality. BMC Infect Dis. 2021;21:458.
6. Ozcan E, Yavuzer S, Borku Uysal B, et al. The relationship between positivity for COVID-19 RT-PCR and symptoms, clinical findings, and mortality in Turkey. Expert Rev Mol Diagn. 2021;21:245-50.
7. Francone M, Iafrate F, Masci GM, et al. Chest CT score in COVID-19 patients: correlation with disease severity and short-term prognosis. Eur Radiol. 2020;30:6808-17.
8. Tabatabaei SMH, Rahimi H, Moghaddas F, Rajebi H. Predictive value of CT in the short-term mortality of Coronavirus Disease 2019 (COVID-19) pneumonia in nonelderly patients: A case-control study. Eur J Radiol. 2020;132:109298.
9. Ruch Y, Kaeuffer C, Ohana M, et al. CT lung lesions as predictors of early death or ICU admission in COVID-19 patients. Clin Microbiol Infect. 2020;26:1417.e5-1417.e8.

10. Prokop M, van Everdingen W, van Rees Vellinga T, et al. CO-RADS: A Categorical CT Assessment Scheme for Patients Suspected of Having COVID-19-Definition and Evaluation. Radiology. 2020;296:E97-E104.

11. Yang R, Li X, Liu H, et al. Chest CT Severity Score: An Imaging Tool for Assessing Severe COVID-19. Radiol Cardiothorac Imaging. 2020;2:e200047.

12. Pan F, Ye T, Sun P, et al. Time Course of Lung Changes at Chest CT during Recovery from Coronavirus Disease 2019 (COVID-19). Radiology. 2020;295:715-21.

13. Altman DG, Machin D, Bryant TN, et al. Statistics with confidence. BMJ Books Bristol. 2000

14. Mercaldo ND, Lau KF, Zhou XH. Confidence intervals for predictive values with an emphasis on case-control studies. Stat Med. 2007;26:2170-83.

15. MedCalc Software Ltd. Diagnostic test evaluation calculator (Version 20). Available from: https://www.medcalc.org/calc/diagnostic_test.php. Access date: 31.05.2021.

16. Altunisik Toplu S, Bayindir Y, Yilmaz S, et al. Short-term experiences of a liver transplant centre before and after the COVID-19 pandemic. Int J Clin Pract. 2021;75:e14668.

17. Wang Y, Hou H, Wang W, Wang W. Combination of CT and RT-PCR in the screening or diagnosis of COVID-19. J Glob Health. 2020;10:010347.

18. Waller JV, Kaur P, Tucker A, et al. Diagnostic Tools for Coronavirus Disease (COVID-19): Comparing CT and RT-PCR Viral Nucleic Acid Testing. AJR Am J Roentgenol. 2020;215:834-8.

19. Kovács A, Palásti P, Veréb D, et al. The sensitivity and specificity of chest CT in the diagnosis of COVID-19. Eur Radiol. 2021;31:2819-24.

20. Poortahmasebi V, Zandi M, Soltani S, Jazayeri SM. Clinical Performance of RT-PCR and Chest CT Scan for Covid-19 Diagnosis; a Systematic Review. Adv J Emerg Med. 2020;4:e57.