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Original Article

Chest CT Diagnostic Potential as a Tool for Early Detection of Suspected COVID-19 Cases in Pandemic Peaks

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Abstract

Introduction: The emergence of severe acute respiratory syndrome coronavirus disease (COVID-19) in China at the end of 2019 caused a massive global outbreak that has become a major public health issue.

Aim: Our aim was to investigate the diagnostic potential of chest CT in screening patients suspected of having COVID-19 in high-prevalence settings.

Materials and methods: This is a real-life, prospective, observational study involving 260 patients. All patients received chest CT scan at the emergency department (ED) of Kaspela University Hospital, Plovdiv, Bulgaria and RT-PCR testing for suspected COVID-19 from March 27 to December 31, 2020. COVID-19 likelihood was assessed by assigning each CT scan to a particular category of the COVID-19 Reporting and Data System (CO-RADS). IBM SPSS v. 26 was used to process the data.

Results: The male-to-female distribution ratio was 1.4:1 – 150 (57.7%) males vs. 110 (42.3%) females (p=0.014). The median age was 55 yrs (range 46–65 yrs). Discharged patients were 247 (95.0%), the rest died in the COVID-19 intensive care unit. Males were 4.13 times more likely to be diagnosed with CO-RADS≥3 score than females. Increasing age was associated with an increased likelihood of being classified with higher CO-RADS scores. The ROC curves analysis demonstrated that CO-RADS ≥3 was the optimal cutoff for discriminating between a positive and negative PCR (Youden's index J=0.67), with an AUC of 0.825 (95% CI 0.72-0.93), sensitivity of 91.9% (95% CI 87.7%-95.1%), specificity of 75.0% (95% CI 53.3%-90.2%) and accuracy of 76.4% (95% CI 70.7%-81.4%).

Conclusions: The results of this study reveal that a CT examination can provide a quick and accurate diagnosis of patients with suspected COVID-19 infection, whereas the PCR test is time-consuming, and the delay in receiving results can be substantial when the incidence curve begins to grow rapidly.

Keywords

CO-RADS, RT-PCR, SARS-CoV-2, sensitivity, specificity

INTRODUCTION

The emergence in China, at the end of 2019, of severe acute respiratory syndrome coronavirus 2 disease (SARS-CoV-2, formerly known as the 2019 new coronavirus or 2019-nCoV) triggered a massive global outbreak which is now a major public health issue.[1] In the absence of a specific therapeutic treatment, it is essential to detect the disease as early as possible so that we can reduce the risk of severe complications and stop the further transmission of the infection to the healthy population. The diagnosis of COVID-19 currently relies on the reverse transcription-polymerase chain reaction (RT-PCR) assay of oropharyngeal and/or nasopharyngeal swabs. However, while false positives are conceivably rare, false negatives can occur, even in patients with pneumonia, who may have negative nasal/oropharyngeal samples but positive lower airway samples. The true clinical sensitivity of RT-PCR is thus unknown.[2,3]

Previous small-scale studies have found that the RT-PCR testing currently in use has limited sensitivity, whereas the chest CT examination may identify pulmonary abnormalities consistent with COVID-19 in patients with initial negative RT-PCR results.[4,5] Moreover, 15-30% of the people hospitalized with COVID-19 will go on to develop COVID-19-associated acute respiratory distress syndrome (CARDS).[6] Thus, timeliness and diagnostic accuracy are crucial especially in high-prevalence settings.

Using an imaging method to assess the severity and duration of changes in COVID-19 patients is extremely important. Chest CT is a conventional, non-invasive imaging modality characterized by high accuracy and speed. Computed tomography (CT) often shows some typical findings in COVID-19 pneumonia, especially bilateral, patchy ground-glass opacities and consolidations with predominantly peripheral distribution; the crazy-paving pattern, peripheral vessel enlargement, and findings of organizing pneumonia such as reverse halo sign have also been described.[7-11] High-resolution computed tomography (HRCT) with its modern available software techniques is the method of choice for initial examination, staging, and follow-up for patients with suspected COVID-19 infection.

AIM

The aim of our study was to investigate the diagnostic potential of chest CT in screening patients suspected of COVID-19 in high-prevalence settings.

MATERIALS AND METHODS

Time and setting

This is a real-life, prospective, observational study involving 260 patients. All patients received chest CT examination at the emergency department (ED) of Kaspela University Hospital, Plovdiv, Bulgaria and RT-PCR testing for suspected COVID-19 from March 27 to December 31, 2020. Additionally, the overall sample size was split in two: 1st wave of COVID-19 (n=28) starting from March 13, 2020[12] to May 26 2020[13] and 2nd wave of COVID-19 (n=232) starting from October 27, 2020[14] to January 4, 2021[15]. The timeframe for both waves is based on the official lockdown measures introduced by COVID-19 State of Emergency Measures Act originally announced on March 13, 2020 by a decision of the National Assembly as an Emergency Measures Act.

Study participants, inclusion and exclusion criteria

This study included patients with clinical-epidemiological suspicion of COVID-19 infection based on the manifestation of at least one of the following features: a) fever – temperature >37.8°C; b) one or more clinical findings of lower respiratory illness (e.g., cough, shortness of breath, difficulty breathing)[16] with or without a history implying exposure to SARSCoV-2 including: (1) close contact with a confirmed case of SARS-CoV-2 disease, (2) close contact with a person with mild, moderate, or severe respiratory illness for whom a chain of transmission can be linked to a confirmed case of SARS-CoV-2 disease in the 10 days preceding the onset of symptoms, (3) travel or residential history in locations with a documented high prevalence of disease, or (4) close contact with individuals with mild-to-moderate symptoms and with a history of travel to a location with documented high prevalence of disease within 14 days prior to the CT scan. Exclusion criteria were set as follows: (a) lack of RT-PCR testing results or "gray-zone" results, (b) a time interval between the CT scan and RT-PCR testing greater than 5 days, and (c) poor/unreadable image quality of the CT scans due to motion artefacts or incomplete data image. The final outcome was expressed as hospital discharge or died.

Reference standard

All patients received RT-PCR laboratory tests before or after the chest CT as a reference standard for the diagnosis of COVID-19. The naso- or oropharynx specimens were obtained according to WHO recommendation.[17] A patient with CT findings suggestive of COVID-19 and positive RT-PCR results was considered to be infected with COVID-19. A patient with negative CT findings and negative RT-PCR test was considered to be negative if no symptoms worsening or laboratory findings consistent with COVID-19 occurred.

CT protocol

All patients were examined with a multidetector 32-channel CT scanner (Siemens Go Up). The parameters of CT acquisition are: tube voltage 130 kV, quality ref. mAs 54, Eff. mAs 73 with CARE Dose4D dose optimization. Acquisition (mm) 32×0.7; pitch 1.5; rot. time (s) 0.80. All exams were performed in a supine position, at full inspiration without contrast medium. Two reconstructions were made – the first was with 1.5 mm slice thickness with 1.5 mm increment, Br60 Kernel, Lung window, Narrow FAST Planning Width and FAST 3D with Matrix Size 512, and the second was with 1.5 mm slice thickness with 1.5 mm increment, Br40 Kernel, Mediastinum window, SAFIRE strength 3, Narrow FAST Planning Width and FAST 3D with Matrix Size 512. The scans were observed in axial, sagittal, and coronal plane.

CT chest findings: image analysis

All patients admitted to Kaspela University Hospital underwent chest CT examination. Because there were not enough PCR facilities in Bulgaria at the start of the pandemic, samples from Plovdiv were analyzed in the city of Stara Zagora. The result from the CT examination was crucial because this was the only way to confirm the COVID-19 pneumonia suspicions. Patient's CT scans were interpreted by the radiologist on duty and staged according to the CORADS classification.[18] Our hospital ward employs five radiologists; three of them (P.S., M.S., and M.G.) has more than 30 years of experience and the other two (L.C. and K.D.) have more than 7 years of experience in the field of radiology; all of them are assistant professors at the Department of Diagnostic Imaging of the Medical University of Plovdiv. The CT readers were not blinded to clinical information, but the RT-PCR results were never available at the time of reading. Apart from the CORADS staging, all patients were classified according to the changes in the parenchyma as mild, intermediate, or severe. Moreover, with the accumulation of knowledge, we were able to determine the duration of the process. The patients with 25% or less affected parenchyma are classified as mild, patients with 25%–75% of affected parenchyma are classified as intermediate, and patients with 75% and higher are classified as severe. In the first wave of the pandemic, it was found that there were patients classified as CORADS 2 or patients with other than COVID-19 pneumonia, probably due to the fact that COVID-19 pneumonia was a new disease and some of the patients were initially misdiagnosed. During the second wave in autumn/winter, almost all the patients had certain changes.

CT scans scored by CO-RADS classification

COVID-19 likelihood was assessed by assigning each CT scan to a particular category of the COVID-19 Reporting and Data System (CO-RADS).[19] The CO-RADS classification is a standardized reporting system for patients with suspected COVID-19 infection developed for a moderate to high prevalence setting based on a 6-point scale of suspicion for pulmonary involvement of COVID-19 on chest CT: CO-RADS 0 – not interpretable (scan technically insufficient for assigning a score); CO-RADS 1 – very low (normal or noninfectious); CO-RADS 2 – low (typical for other infections but not COVID-19); CO-RADS 3 – equivocal/unsure (features compatible with COVID-19 but also other diseases); CO-RADS 4 – high (suspicious for COVID-19); CO-RADS 5 – very high (typical for COVID-19); CO-RADS 6 – proven (RT-PCR positive for SARS-CoV-2).[19]

Statistical analysis

Quantitative variables were summarized by mean and standard deviation (mean±SD) or median (25th percentile; 75th percentile), based on the sample distribution. Qualitative variables are presented as numbers/totals and percentages (n, %). The Kolmogorov-Smirnov test was applied to inform about the distribution of the patients sampled. Differences between groups were tested using the independent samples t test, Fisher exact test and z-test as appropriate. A 2-sided *p*-value of <0.05 was considered statistically significant. Statistical analyses were performed using SPSS Statistics v. 26 software (IBM Corp., Chicago, IL, USA).

The discriminatory power of CO-RADS was estimated by the area under the receiver operating characteristic (ROC) curve. Youden's index was calculated to indicate the optimal cutoff value, followed by diagnostic measures estimate.

Binary logistic regression analysis was performed to test whether the severity of disease CO-RADS score was associated with age and sex. Associations were quantified by odds ratios (OR).

RESULTS

Study participants: demographic and clinical results

From March 27 to December 31, 2020, after initial symptom evaluation in the triage of Kaspela University Hospital, Plovdiv, Bulgaria, 260 patients with suspected COVID-19 were referred for chest CT. The male-to-female distribution was 1.4:1 – 150 (57.7%) males vs. 110 (42.3%) females ($z=3.5$; $p=0.0004$). The median age was 55 yrs (range 46-65 yrs). We set a CO-RADS score ≥4 as the optimal threshold to discern between patients with PCR+ from those with PCR– results.[20] We classified 212 (81.5%) patients to CO-RADS –≥4 and the number of false-positive chest CT findings in patients without COVID-19 was 6 (2.8%), confirmed by negative RT-PCR test. PCR-positive patients were 236 (90.8%) and 30 (12.7%) of them had CO-RADS ≤3. Discharged from the hospital were 247 (95.0%) patients, the rest died in the COVID-19 intensive care unit (ICU).

Reference standard

The distribution of patients' characteristics by RT-PCR results is presented in **Table 1**. No differences were found in the mean age between RT-PCR positive and negative patients (t=1.4, p=0.164) as such were not observed after split by sex neither between negative vs. positive males (t=0.67, p=0.507), nor between females (t=0.92, p=0.380). RT-PCR positive patients who were reported dead (n=13) had a higher mean age (64.69±12.07 yrs) than the mean age of discharged patients (54.86±14.81 yrs.) (t=2.34, p=0.020).

Diagnostic approach in patients with COVID-19: CT imaging findings

In the first wave of the pandemic, it was found that there were patients classified as CO-RADS 2 or patients with other than COVID-19 pneumonia, probably due to the fact that COVID-19 pneumonia was a new disease and some of the patients were initially misdiagnosed. In the second wave, almost all patients had certain changes.

The most common finding was ground-glass opacities, which were mostly present in both lungs and were only seen in a few cases in only one lung. In the early stage of the disease, the opacities had low-to-intermediate density while in the later stages, they had higher density. Interlobular septal thickening, crazy-paving patterns, and dilatation of the distal small pulmonary vessels were also observed as the disease progressed. Most often, the changes affected the middle and lower parts of the lungs. Enlarged lymph nodes and pleural effusions were not observed in our patients.

In **Fig. 1A**, we show a patient with typical COVID symptoms – loss of smell and taste, no fever or cough. The exam was performed 4 days after the onset of symptoms. The CT scan showed no pathological findings. **Fig. 1B** shows the CT examination of a patient with positive PCR, fever, cough, and shortness of breath. The imaging finding was ground-glass opacity in the left lung. The CT examination in **Fig. 1C** shows typical COVID-19 changes – ground-glass opacity in the right lung, the lung parenchyma is affected around 10%. **Figs 1D** through **1I** show the CT scans of patients with the typical changes of ground-glass opacities, interstitial thickening, crazy-paving patterns, and dilated distal pulmonary vessels. Depending on the stage of the disease, initially, the ground-glass opacities have low density, and then, after the acute stage, the opacities have mainly two types of progression – the density of the opacities can decrease or get higher but affect less of the parenchyma. Patients who had a severe disease needed at least 6 months to completely recover from the COVID pneumonia. Some patients do not fully recover and have permanent fibrotic changes in the lung parenchyma.

Figs 2 and **3** show the scans of a 49-year-old patient with COVID-19 with thrombosis of the cavernous sinus that developed as a complication. The patient was hospitalized with positive PCR and CT examination showing typical changes. After a week in the hospital, the patient complained of severe headache and underwent an emergency native CT examination, which showed no changes. This patient lost his vision in the right eye the next day, with exophthalmos and swelling of the soft tissues around the right eye. CT angiography was performed showing a hyperdense structure in the right cavernous sinus thrombosis. On the arterial and venous series, thrombosis of the right sinus cavernosus is presented. The internal carotid arteries and other cerebral arteries were normal.

Table 1. Distribution of patients' characteristics by RT-PCR results

Characteristic	RT-PCR – n=24	RT-PCR + n=236	p-value
Age, yrs (mean±SD)	50.88±17.55	55.40±14.875	0.164*
Sex			
Male, n (%)	15 (62.5)	135 (57.2)	0.670**
Female, n (%)	9 (37.5)	101 (42.8)	
CO-RADS, n (%)			
No	12 (50.0)	19 (8.1)	N/A
Low	6 (25.0)	0 (0.0)	
Indeterminate	0 (0.0)	11 (4.7)	
High	1 (4.2)	23 (9.7)	
Very high	5 (20.8)	183 (77.5)	
CO-RADS ≥4, n (%)	6 (25.5)	206 (87.3)	<0.001**
Outcome			
Discharged, n (%)	24 (100)	223 (94.5)	N/A
Died, n (%)	0 (0.0)	13 (5.5)	

*Independent samples t-test; **Fisher's exact test

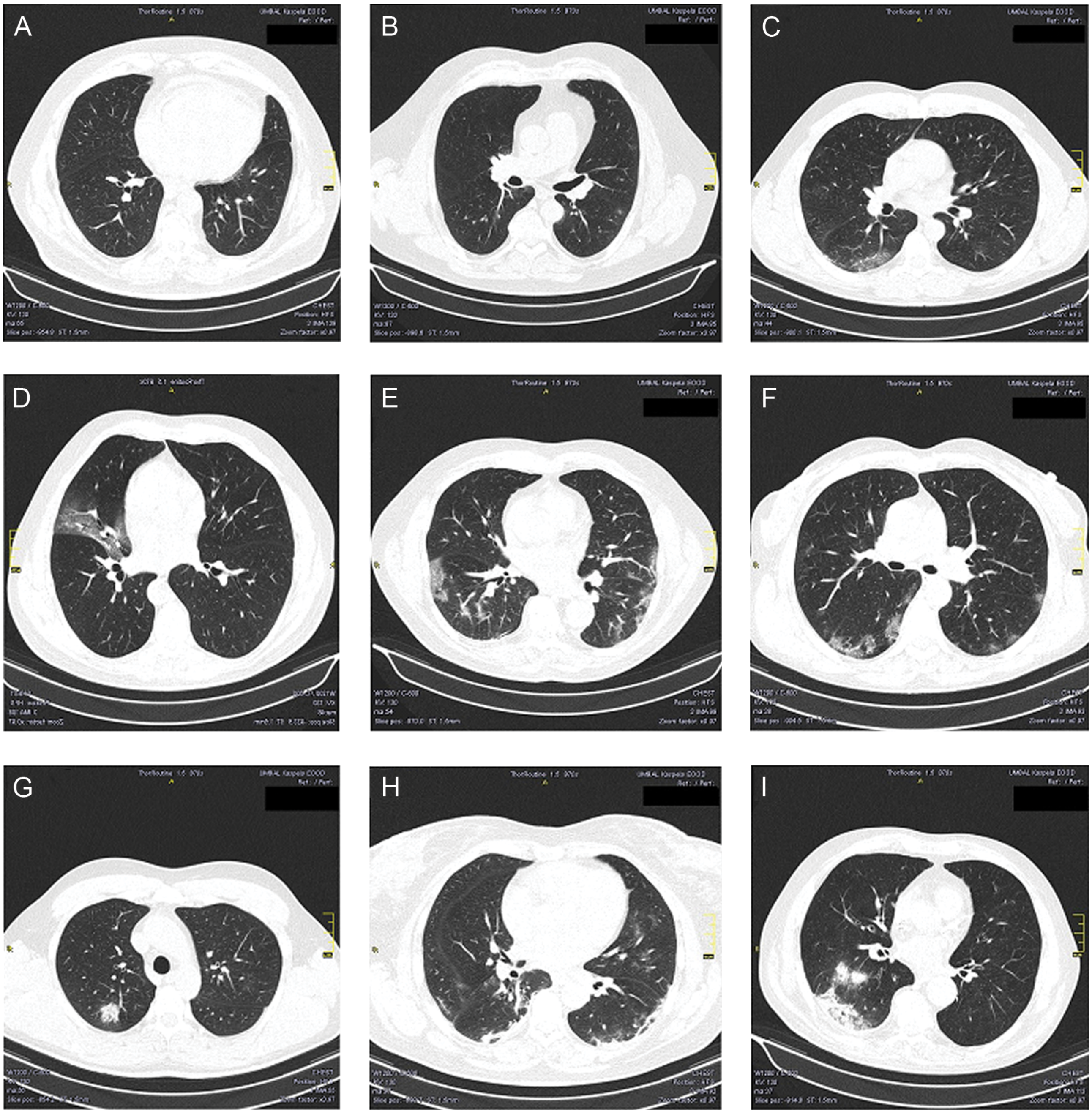

Figure 1. CT slices of the lung window in different cases with COVID-19 pneumonia. **A**. Patient with no imaging findings; **B**. A small ground-glass opacity is seen in the left lung - CO-RADS 3 changes, later confirmed with PCR test; **C**. Low density ground-glass opacity in the right lung – COVID-19 pneumonia, initial stage; **D**. Ground-glass opacity in the left lung - mild COVID-19 pneumonia; **E**. Ground-glass opacities in the periphery of both lungs - COVID-19 pneumonia, 7 days; **F**. Ground-glass opacities in the periphery of both lungs - mild COVID-19 pneumonia, duration 10 days; **G**. Oval dense ground-glass opacity in the right lung - COVID-19 pneumonia, 14 days; **H**. Diffuse interstitial thickening in the periphery of both lungs - COVID-19 pneumonia, duration 14 days; **I**. Diffuse infiltrate in the 6th segment of the right lung - COVID-19 pneumonia, duration >14 days.

Diagnostic approach in patients with COVID-19: Patients follow-ups

In the second wave of the pandemic, there were patients that had already been cured of COVID-19 infection and such patients received control CT scans. We found that patients were healing generally in two ways: some patients had low-density ground-glass opacities that looked like those in acute COVID-19 pneumonia – such patients were clinically examined and their anamneses were taken, while in other patients, the changes became denser and affected less lung volume compared to the first CT examination. We

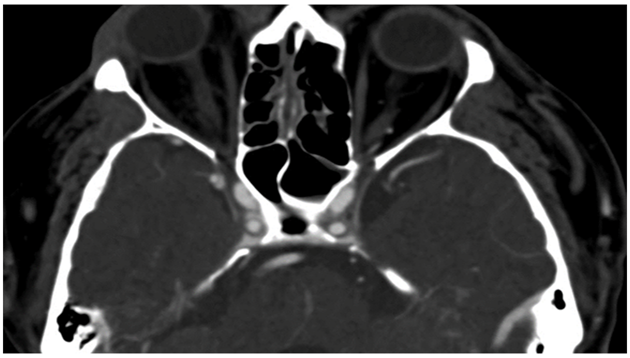

Figure 2. CT with contrast enhancement, axial slice. Thrombosis of the right sinus cavernosus.

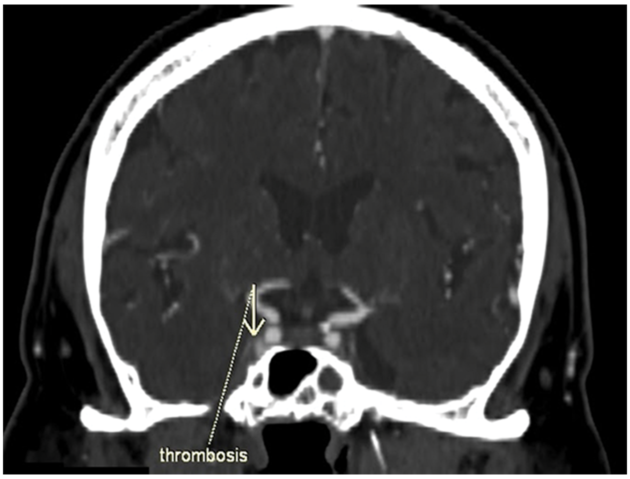

Figure 3. CT with contrast enhancement, coronal reconstruction. Thrombosis of the right sinus cavernosus.

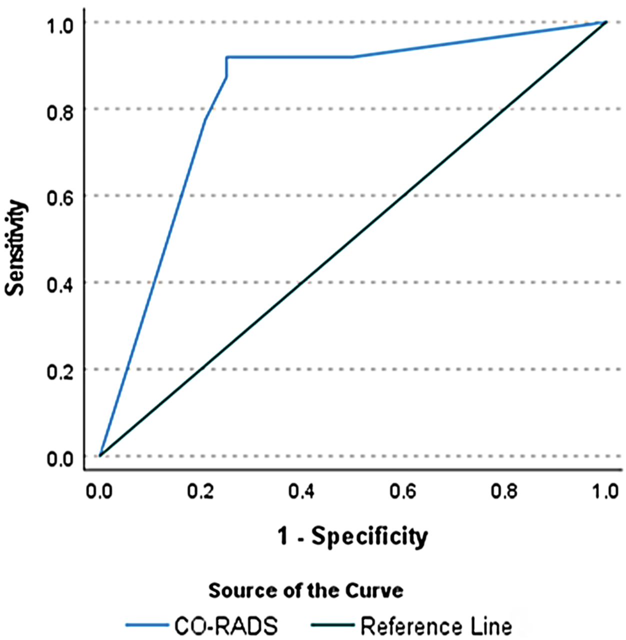

Figure 4. ROC curve for predicting lung involvement by SARS-CoV-2 disease using the COVID-19 Reporting and Data System (CO-RADS). AUC: area under the curve; ROC: receiver operating characteristic.

recommended that such patients should have a control CT scan in no less than 6 months to observe the changes and find whether the changes persisted and if there was pneumonia. It was found that the less volume was affected, the faster the healing process was.

CO-RADS

The ROC curves analysis **(Fig. 4)** demonstrated that CO-RADS ≥3 was the optimal cutoff for discriminating between a positive and negative PCR (Youden's index J=0.67), with an AUC of 0.825 (95% CI 0.72-0.93), a sensitivity of 91.9% (95% CI 87.7%-95.1%), specificity of 75.0% (95% CI 53.3%-90.2%), negative predictive value of 99.1% (95% CI 98.5%-99.4%), positive predictive value of 24.2% (95% CI 13.8%-39.0%), and an accuracy of 76.4% (95% CI 70.7% to 81.4%). The positive likelihood ratio was 3.78 (95% CI 1.84-7.36), and the negative likelihood ratio was 0.11 (95% CI 0.07-0.18). The interval likelihood ratio was 2.34 (95% CI 0.3-16.6) for CO-RADS 4 and 3.72 (95% CI 1.7-8.1) for CO-RADS 5. The overall model quality was 72%.

Detailed patients' characteristics split by the established CO-RADS optimal cutoff are reported in **Table 2**. Additionally, we explored the difference in the mean age between males (n=133) and females (n=90) by the CO-RADS split and proved that although younger approximately by 5 yrs than females (54.70±14.57 vs. 59.43±13.97; t=2.24, p=0.016), males had higher dead rate 76.9% (n=10). The mean age of dead males was 11 yrs higher than that of the discharged males (64.60±11.29 vs. 53.89±14.55; t=2.27, p=0.025). Statistically significant differences were found between the age groups listed in **Table 2** and the CO-RADS categories. A difference existed also between the severity (CO-RADS ≥3) of those patients below (31.8%) and above (68.2%) 50 years of age (z=7.7; p<0.0001). The same result about severity (CO-RADS ≥3) was observed for the patients below (68.2%) and above (31.8%) 65 years of age (z=7.7; p<0.0001), but in the opposite direction – a significantly smaller proportion of patients ≥60 yrs experienced severe symptoms of the disease.

COVID-19 incidence waves

The overall sample size was split in two, regarding the peaks of the epidemic curve of COVID-19 incidence in Bulgaria. Overall, four Ministerial Ordinances determined the beginning, length, and end of the two COVID-19 lockdowns.[12-15] They basically defined the two incidence waves. The first lockdown measures were introduced on 13 March 2020 after the registration of the first cases of COVID-19. Due to the strict measures during the first wave between 13 March and 26 May 2020, there were very few cases of COVID-19 registered with 2443 cumulative cases for the period of which 106 for the Plovdiv region.[21] The beginning of the second wave was on 27 October 2020 and it finished approximately by the beginning of 2021. During this period, the increase of registered COVID-19 cases was

Table 2. Patients' characteristics split by CO-RADS cutoff

Characteristic	CO-RADS <3 n=37	CO-RADS ≥3 n=223	*p*-value
Age, yrs (mean±SD)	45.19±15.63	56.61±14.49	<0.001*
Age-groups, n (%)			
<50 yrs	22 (59.5)	71 (31.8)	0.001**
≥50 yrs	15 (40.5)	152 (68.2)	
<65 yrs	32 (86.5)	152 (68.2)	0.015**
≥65 yrs	5 (13.5)	71 (31.8)	
Sex			
Male, n (%)	17 (45.9)	133 (59.6)	0.150**
Female, n (%)	20 (54.1)	90 (40.4)	
Outcome			
Discharged, n (%)	37 (100.0)	210 (94.2)	-
Died, n (%)	0 (0.0)	13 (5.8)	

*Independent samples t-test; **Fisher's exact test

very distinctive, with 197384 cumulative number of cases of which 18474 cases were in the Plovdiv region. The incidence in this period peaked in November with the highest registered incidence in our country from the beginning of the pandemic – 660.33/100 000.[21] The sample size for the first wave was 28 patients and 232 patients for the second wave. **Table 3** summarizes patient characteristics measured throughout the two waves.

Fig. 5 illustrates the CO-RADS categories distributed by age and RT-PCR results in each wave. The mean age (57.95±13.82) of the second wave RT-PCR positive patients assigned to CO-RADS 5 was approximately 7 yrs less than the one measured in the first wave RT-PCR positive patients with CO-RADS 5 score (65.80±7.60), although the difference failed to reach statistical significance (p=0.081).

Table 3. Distribution of patients' characteristics by waves

Characteristic	First wave n=28	Second wave n=232	*p*-value
Age, yrs (mean±SD)	51.43±17.28	55.41±14.87	0.189*
Sex			
Male, n (%)	15 (62.5)	135 (57.2)	0.840**
Female, n (%)	9 (37.5)	101 (42.8)	
PCR			
Positive, n (%)	8 (28.6)	228 (98.3)	<0.001
Negative, n (%)	20 (71.4)	4 (1.7)	
CO-RADS, n (%)			
No	11 (39.3)	20 (8.6)	N/A
Low	5 (17.9)	1 (0.4)	
Indeterminate	0 (0.0)	11 (4.7)	
High	3 (10.7)	21 (9.1)	
Very high	9 (32.1)	179 (77.2)	
CO-RADS ≥3, n (%)	12 (42.9)	211 (90.9)	<0.001**
Outcome			
Discharged, n (%)	27 (96.4)	220 (94.8)	1.000**
Died, n (%)	1 (3.6)	12 (5.2)	

*Independent samples t-test; **Fisher's exact test

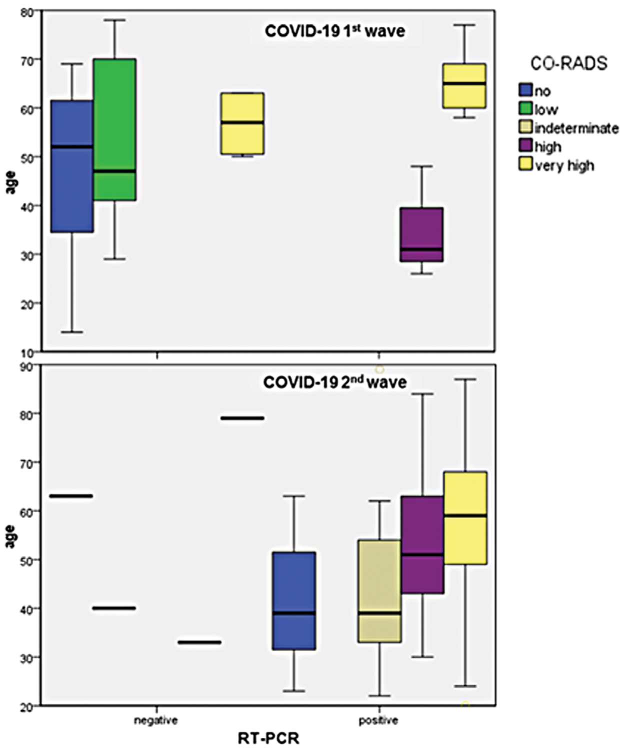

Figure 5. CO-RADS categories distributed by age and RT-PCR results.

Binary logistic regression

The second wave logistic regression model was statistically significant: $\chi^2(2)=26.04$, $p=0.000$, explained 23.0% (Nagelkerke R2) of the variance in disease severity (measured by binary outcome variable of CO-RADS <4 or CO-RADS ≥4) and correctly classified 90.9% of cases. Males were 4.13 times more likely to be diagnosed with CO-RADS ≥3 score than females. Increasing age was associated with increased likelihood of being classified with higher CO-RADS scores. The results of the logistic regression are shown in **Table 4**.

DISCUSSION

The current practice of COVID-19 diagnosis relies mainly on reverse transcriptase polymerase chain reaction (RT-PCR) testing of samples collected from the respiratory tract, most commonly through oro- or nasopharyngeal swabs. The advantages offered are associated with low costs, safety, and the relative simplicity of collection. The initial shortages in RT-PCR testing kits supply now have been largely overcome and this is the standard available technique in use. However, the sensitivity of this diagnostic tool varies in terms of the location of collected biological samples (broncho-alveolar lavage for sputum, throat, or nasopharyngeal swabs) and is not suitable to assess disease severity.[22-25] Thus, the chance of false-negative results increases, initiating diagnostic uncertainty and the need for additional diagnostic tools to confirm a suspected diagnosis.[26] An additional advantage would be to accurately differentiate between patients with mild and severe SARS-CoV-2 infection.

Chest computed tomography (CT) is described as one such diagnostic tool in numerous recently published scientific articles.[27] For symptomatic patients suspected of having COVID-19, WHO suggests using chest imaging for the diagnostic work-up of COVID-19 when: (1) RT-PCR testing is not available; (2) RT-PCR testing is available, but results are delayed, and (3) initial RT-PCR testing is negative, but with high clinical suspicion of COVID-19; (4) for patients with confirmed COVID-19 or patients suspected of having COVID-19 not currently hospitalized and (a) with mild symptoms in addition to clinical and laboratory assessment to decide on hospital admission versus home discharge or (b) with moderate to severe symptoms in addition to clinical and laboratory assessment to decide on regular ward admission versus intensive care unit admission, or (c) with moderate to severe symptoms in addition to clinical and laboratory assessment to inform the therapeutic management.[28] Based on WHO recommendations, in our setting CT scan procedure was performed when RT-PCR testing was available, but results were delayed.[29] Moreover, chest CT scan is associated with easy accessibility, lower radiation dose and the possibility of carrying out a portable examination, reducing the probability of contagion from health personnel.[30] Use of a standardized chest CT scan reporting system as CO-RADS, based on consensus appearances of typical and atypical findings have been shown to aid in the triage of ED patients. In the acute care setting, chest CT imaging also may be used to stratify the severity of lung involvement; to assist in the determination of the need for hospitalization, ICU admission, or both; and to

Table 4. Results of logistic regression, with binary outcome variable of CO-RADS <3 or CO-RADS ≥3

Wave		B	S.E.	Wald	df	Sig.	Exp(B)	95% CI for EXP(B)	
								Lower	Upper
COVID-19 first wave	Sex (male)	−0.260	0.802	0.105	1	0.746	0.771	0.160	3.714
	Age	0.024	0.024	1.003	1	0.317	1.024	0.977	1.073
	Constant	−1.368	1.355	1.019	1	0.313	0.255		
COVID-19 second wave	Sex (male)	1.417	0.522	7.364	1	0.007	4.125	1.482	11.477
	Age	0.078	0.019	16.709	1	0.000	1.081	1.041	1.122
	Constant	−2.189	0.944	5.373	1	0.020	0.112		

predict outcomes in COVID-19.[31] In our study, the ROC analysis identified the CORADS score ≥3 as the optimal threshold to distinguish between patients with PCR positive and PCR negative results. The threshold is below the one reported in a multi-reader validation study (CORADS score ≥4), which evaluates the interobserver variability and the diagnostic accuracy for the lung involvement by COVID-19 of COVID-19 Reporting and Data System (CO-RADS) score and in one prospective, multi-center, observational study.[20,32] One of the possible explanations is that most of the patients were admitted during the peak of the second COVID-19 wave in a high-prevalence setting. The threshold of CO-RADS 3 or greater incidentally detected in asymptomatic individuals should trigger testing for respiratory pathogens, according to a study investigating the value of chest CT with CO-RADS classification to screen for asymptomatic SARS-CoV-2 infections and to determine its diagnostic performance in individuals with COVID-19 symptoms during the exponential phase of viral spread.[33]

Our results demonstrate that when a threshold of CO-RADS ≥3 was applied, and readers with different levels of expertise were able to discriminate between patients with positive and negative RT-PCR testing results, with a sensitivity of 91.9% (95% CI 87.7%-95.1%), specificity of 75.0% (95% CI 53.3%-90.2%), negative predictive value of 99.1% (95% CI 98.5%-99.4%), positive predictive value of 24.2% (95% CI 13.8%-39.0%), accuracy of 76.4% (95% CI 70.7% to 81.4%), positive likelihood ratio of 3.78 (95% CI 1.84-7.36), and negative likelihood ratio of 0.11 (95% CI 0.07-0.18). The sensitivity result matches the pooled sensitivity calculated in a meta-analysis of six trials that reported data on CT of the chest – 91.9% (95% CI 89.8%-93.7%)[34]; the summary of sensitivity (n=16 studies) presented in a systematic review and meta-analysis of diagnostic accuracy – 92.0% (95% CI 86%-96%)[35] and the result presented in a systematic review and meta-analysis of comparative studies (n=13 studies) on chest CT versus RT-PCR for the detection of COVID-19 – 91.0% (95% CI 82.0%-98.0%) [27]. However, the sensitivity demonstrated by our results is slightly lower than the pooled sensitivity calculated in a meta-analysis of 68 studies – 94% (95% CI 91%-96%)[36] and higher compared to the summarized sensitivity reported in a meta-analysis of the accuracy and sensitivity of chest CT and RT-PCR in COVID-19 diagnosis – 87% (95% CI 85%-90%) [37]. The specificity result of 75.0% in our study is in contrast with the pooled specificity summarized by the four meta-analyses – 25.1% (95% CI 21.0%-29.5%)[34]; 31.0% (95% CI 22.0%-42.0%)[35]; 37.0% (95% CI 26.0%-50.0%) [36]; 46.0% (95% CI 29%-63%[37]. However, in a recently published systematic review and meta-analysis, the specificity results [77.5% (95% CI 25.0%-100%)] are closer to the one presented here.[27] The substantially higher specificity value was explained by the authors with the design of their study, which synthesized comparative studies only and also included additional recently published studies and those in preprint, so the results may more accurately represent how the investigations can be expected to perform and compare to RT-PCR in routine clinical practice and as the pandemic progresses.[27] The positive predictive value (PPV) calculated by us (24.2%) is close to the upper boundary reported by Kim et al. (1.5% to 30.7%)[36] and lower compared to the result of Khatami et al. (96%, 95% CI 56%-82%)[37]. The negative predictive value (NPV) estimated by us (99.1%) matches the upper limit of the range reported by Kim et al. (95.4% to 99.8%)[36] and is slightly higher than the result summarized by Khatami et al. (89%; 95% CI 82%-96%)[37]. Our results for positive [3.78 (95% CI 1.84-7.36)] and negative [0.11 (95% CI 0.07-0.18)] likelihood ratios are similar to the medians reported by Karam et al. – PLR: 3.185 (range 1.29-18.35) and NLR: 0.13 (range 0.03-0.25).[2]

Regarding the effect of sex on disease severity, we found males (59.6%) to be more than females (40.4%) in severe cases, whereas the males were 45.9%, and 54.1% were females in non-severe cases. An outcome in accordance with the findings reported in a meta-analysis of 55 studies and 10014 cases about the impact of age, sex, comorbidities, and clinical symptoms on the severity of COVID-19 cases.[38]

The effect of age on severity also was analyzed and the results similar to the reported by Barek et al.[38] show that 68.2% of the severe cases were registered in patients ≥50 years and 31.8% in patients ≥65 years of age.

The binary logistic regression performed demonstrated that the second wave model was statistically significant with males being 4.13 times more likely to be diagnosed with CO-RADS ≥3 score than females, which is a higher odds ratio (OR) compared to 2.41 times reported by Barek et al.[38] Increasing age was associated with an increased likelihood of being classified with higher CO-RADS scores as this is also confirmed by Barek et al.[38] results of the risk ratio of 3.36 (age ≥50 yrs vs. age<50 yrs).

The first cases of COVID-19 detected in the WHO European Region were reported in France on 24 January 2020. From late February, the pandemic evolved rapidly across the region, with Europe taking just 3 months to reach the first 1 million cases and 8 months to reach the first 10 million cases.[39] Compared to the very few numbers of cases in our country in the period March 13 – May 26, 2020 with 2443 cumulative cases, other countries across Europe were hit hard by the pandemic – UK: 261188 cases, Spain: 235400 cases, Italy: 230158 cases, Romania: 18283, Serbia: 11193 cases as of May 26, 2020.[40] This difference might be explained by the very strict measures imposed by the Bulgarian government at a very early stage, which helped to limit the spread of the COVID-19 infection. During the first wave, the Bulgarian incidence data did not show a distinctive peak in the cases and this can be explained by the small number of cases included in the first period of our study. During the summer months, the cases in our country started to increase gradually to reach 17050 cases by the beginning of September. The second wave of the pandemic in our country started around 27 October 2020 and it ended at the beginning of 2021. This coincided with the imposed new lockdown measures on 27 October 2020. The increase in the cases for the period matched the data of other European countries – UK: 1,574,562; Italy: 1,509,875; Romania: 449,349.[41] The differences in the measures applied and as a consequence the increased incidence rate explain the contrast between results obtained during the first and second wave of the pandemic.

Limitations of the study

Our study has some limitations. First, it was conducted in one of the hospitals with the newly established COVID-19 ICU. Second, in the beginning, the radiologists on duty were not experienced in assessing chest CT in COVID-19 and there may be a learning curve, which combined with the small number of patients during the first wave could lead to bias in CT scan interpretation. Third, our study was conducted in a high-prevalence setting with the majority of patients admitted during the second peak of the COVID-19 pandemic. Thus, in the future, when pandemics subside, and other respiratory diseases symptoms would be observed the CO-RADS classification might not be able to successfully discriminate between them, and presumably, the false-positive results will increase.

CONCLUSIONS

Based on the findings in our study, the CT examination provides quick and accurate diagnosis of patients with suspected COVID-19 infection, as the PCR testing is time-consuming and the delay of obtaining results could be substantial when the incidence curve starts to grow rapidly. Moreover, chest CT scan is associated with easy accessibility, lower radiation dose and the possibility of carrying out a portable examination, reducing the probability of contagion from health personnel. However, further knowledge should be gained about how to differentiate COVID-19 findings from those of other viral pneumonia in times with decreasing COVID-19 infection prevalence, especially in the context of low positive predictive value results.

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Диагностические возможности компьютерной томографии органов грудной клетки как инструмента раннего выявления случаев подозрения на COVID-19 в пик пандемии

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Резюме

Введение: Появление тяжёлого острого респираторного синдрома коронавирусной болезни (COVID-19) в Китае в конце 2019 года вызвало массовую глобальную вспышку, которая стала серьёзной проблемой общественного здравоохранения. Нашей целью было изучить диагностический потенциал компьютерной томографии органов грудной клетки при скрининге пациентов с подозрением на COVID-19 в условиях высокой распространённости.

Материалы и методы: Это реальное проспективное обсервационное исследование с участием 260 пациентов. С 27 марта по 31 декабря 2020 г. всем пациентам была проведена компьютерная томография грудной клетки в отделении неотложной помощи Университетской больницы Каспела, Пловдив, Болгария, и RT-PCR -тестирование на подозрение на COVID-19. Вероятность заражения COVID-19 оценивалась путём распределения каждого случая компьютерной томографии в соответствующую категорию Системы отчётности и данных по COVID-19 (CO-RADS). Для обработки данных использовалась IBM SPSS v. 26.

Результаты: Соотношение распределения мужчин и женщин составило 1.4:1 – 150 (57.7%) мужчин против 110 (42.3%) женщин (p=0.014). Средний возраст составил 55 лет (диапазон 46–65 лет). Выписанных больных было 247 (95.0%), остальные умерли в реанимационном отделении COVID-19. У мужчин в 4.13 раза чаще диагностировали CO-RADS ≥3 баллов, чем у женщин. Увеличение возраста было связано с повышенной вероятностью классификации с более высокими баллами CO-RADS. Анализ ROC-кривых показал, что CO-RADS ≥3 был оптимальным порогом для различения положительного и отрицательного PCR (индекс Youden J=0.67), с AUC 0.825 (95% CI 0.72-0.93), чувствительностью 91.9% (95% CI 87.7–95.1%), специфичность 75.0% (95% CI 53.3–90.2%) и точность 76.4% (95% CI 70.7–81.4%).

Заключение: Результаты этого исследования показывают, что КТ-обследование может обеспечить быструю и точную диагностику пациентов с подозрением на инфекцию COVID-19, в то время как PCR -тест занимает много времени, а задержка в получении результатов может быть существенной, когда кривая заболеваемости начинает быстро расти.

Ключевые слова

CO-RADS, RT-PCR, SARS-CoV-2, чувствительность, специфичность