

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

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Abstract

Background: At present, the diagnosis of COVID-19 depends on real-time reverse transcriptase polymerase chain reaction (RT-PCT). On imaging, computed tomography (CT) manifestations resemble those seen in viral pneumonias, with multifocal ground-glass opacities and consolidation in a peripheral distribution being the most common findings. Although these findings lack specificity for COVID-19 diagnosis on imaging grounds, CT could be used to provide objective assessment about the extension of the lung opacities, which could be used as an imaging surrogate for disease burden. Chest CT scan may be helpful in early diagnosing of COVID-19. **Objective:** The current study investigated the diagnostic accuracy and false-positive rate of chest CT in detecting COVID-19 pneumonia in a population with clinical suspicion using RT-PCR testing as reference standard. **Materials and Methods:** In this prospective single center study performed on 612 cases with clinical suspicion of COVID-19, all adult symptomatic ED patients had both a CT scan and a PCR upon arrival at the hospital. CT results were compared with PCR test (s) and diagnostic accuracy was calculated. **Results:** Between February 15, 2020 to July 15, 2020, 612 symptomatic ED patients were included. In total, 78.5% of patients had a positive PCR and 82.8% a positive CT, resulting in a sensitivity of 94.2%, specificity 76.4%, likelihood ratio (LR) + 2.94 and (LR) - 0.18. The PPV was 76.7% and NPV 94.1%. The sensitivity of the CT tended to be higher (100.0%) in those with severe risk pneumonia than in patients with low/medium risk pneumonia (90.3%, $P = 0.42$). In patients with sepsis, sensitivity was significantly higher than in those without sepsis (99.5 vs. 63.5%, $P < 0.001$). The diagnostic ability of chest CT was found to be rather high with 92.1%, concordance rate between findings of CT and PCR. In 48 (7.8%) patients discordant findings between CT and PCR were observed. The positive predictive values (PPV) and accuracy of chest CT in diagnosing COVID-19 were higher in patients ≥ 60 years than that in patients < 60 years ($P = 0.001$ and 0.004 , respectively). The

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specificity and NPV of chest CT in diagnosing COVID-19 were greater for women than that for men ($P = 0.007$ and 0.03 , respectively); and no difference existed for sensitivity, PPV and accuracy ($P = 0.43$, 0.69 and 0.31 , respectively). In most cases, the CT scan was considered suspicious for COVID-19, while the PCR was negative (37/48, 70.8%). In the majority of these, the diagnosis at discharge was pulmonary infection ($n = 26$; 74.3%). The current study included repeated PCRs and explored discordant test results, which showed that in about 45.9% of patients with false-positive CT scans, other viral pathogens were detected. The false-positive rate of CT findings in the diagnosis of COVID-19 pneumonia was 7.2%. **Conclusion:** High diagnostic accuracy of chest CT findings with typical and relatively atypical CT manifestations of COVID-19 leads to a low rate of missed diagnosis. Normal chest CT can be found in RT-PCR positive COVID-19 cases, and typical CT manifestations can be found in RT-PCR negative cases. Therefore, a combination of both CT and RT-PCR for future follow-up, management and medical surveillance is recommended considering the false-positive results of chest CT in the diagnosis of COVID-19 pneumonia.

Key words: Chest CT findings; COVID-19; false-positive chest CT; RT-PCR

Introduction

In late December 2019, a lower respiratory tract febrile illness was reported in a cluster of patients from Wuhan City, Hubei Province, China and a novel strain of coronavirus was isolated from the bronchoalveolar lavage of infected patients.^[1] World Health Organization on 9 January 2020 named the pulmonary syndrome as Coronavirus Disease 2019 (COVID-19).^[2] At the time of writing this article on 24th July, 2020 the number of confirmed cases stand at 15,688,759 with 637,332 reported deaths, this is according to an online virus tracker created by The Lancet, and hosted by Johns Hopkins University.^[3] As of late June 2020, the number of cases of confirmed COVID-19 globally is over 10 million affecting virtually every territory, other than isolated South Pacific island states and Antarctica. The United States had more than two million cases, Russia more than one million, India and four other countries has >250,000 cases.^[3] A study study calculated the incubation period in the group to be 5.2 days on average.^[4]

Corona virus disease 2019 (COVID-19) is a highly contagious disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2).^[5] Currently, reverse-transcriptase-polymerase-chain-reaction (RT-PCR) is the reference standard in diagnosing COVID-19.^[6] However, PCR may have suboptimal sensitivity, for instance because in early stages of COVID-19, the viral load is below detection limit or because of technical issues, i.e., sampling errors.^[7] In addition, in practice, it may take up to 24 hours to get a test result, although same day results are achieved most of the times.^[8]

As most COVID-19 patients present with pneumonia, computed tomography (CT) scanning of the thorax could be helpful in screening and diagnosing. In addition, CT has the advantage that the results can be available almost directly.^[9] Chest CT can show characteristic findings including areas of ground-glass, with or without signs of reticulation (so called “crazy paving pattern”), consolidative pulmonary opacities

in advanced stages and the “reverse halo” sign.^[10] Since peripheral areas of ground glass are a hallmark of early COVID-19, which can easily be missed at chest X-rays, CT scanning has an advantage over chest X-rays in the early stages of COVID-19.^[11]

Objective of the Study

The current prospective study investigated the diagnostic accuracy and false-positive rate of chest CT in detecting COVID-19 pneumonia in a population with clinical suspicion using RT-PCR testing as reference standard.

Materials and Methods

Setting

This study was performed on 612 cases with clinical suspicion of COVID-19 referred to a tertiary care hospital in South India between February 15, 2020 to July 15, 2020. This study is reported in line with the STARD guidelines for diagnostic accuracy studies.^[12]

Patients and design

All adult (18 years or older) patients between February 15, 2020 and July 15, 2020 with respiratory symptoms including dyspnoea, coughing, sore throat, and fever were scanned in a CT scan unit. Of these patients, a nasopharyngeal and/or oropharyngeal swab was taken and tested for presence of SARS-CoV-2. If the first PCR was negative, a second PCR was performed within 48 hours after the first test in patients who were still admitted to the hospital, if deemed indicated by the clinicians. The current study included all symptomatic patients who received a chest CT and at least one PCR test for detection of COVID-19.

RT-PCR

Laboratory confirmation of SARS-CoV-2 was performed with RT-PCR assay. The SARS-CoV-2 laboratory test was based on the detection of unique sequences of virus RNA by nucleic acid amplification test such as real-time

reverse transcription-polymerase chain reaction (RT-PCR) and targeted the SARS-CoV-2 *E* (envelope protein) and *RdRp* (RNA-dependent RNA polymerase) genes⁹. All swabs were also tested for Influenza A, B, respiratory syncytial virus (RSV) and human metapneumovirus.

Chest CT

The chest CT was obtained in a GE (General Electric Medical Systems, Milwaukee, WI, USA) 16 slice MDCT machine upon arrival at the ED. CT scans were performed in caudo-cranial scanning direction without intravenous contrast injection, at 120kVp and 50-210 mAs, depending on their weight, using 16 x 1.25 collimation, 0.5s rotation time reconstructed at 1.25 mm slices with 1.25 mm increment. Patients were instructed to hold their breath if clinically possible. Images were reconstructed using a moderately soft reconstruction filter ("DETAIL") at mediastinal window and a sharp reconstruction filter ("LUNG") at lung window settings. Initial judgement of the CT scan was performed by a senior resident with scans being assessed as a dichotomous outcome: being either suspicious or not suspicious for COVID-19-related pneumonia. In case of pneumonia, in which COVID-19 was unlikely but could not be excluded, the scan was judged positive. The final reading and reporting were performed by an experienced chest radiologist within 12 hours of scanning. Since the PCR results were available after 12-24 hours, both readers were unaware of the PCR test results.

Data collection

From electronic medical records, the following data was retrieved: demographic data (age, sex); comorbidity; duration and severity of current disease; PCR results and other microbiological data; CT scan reports; discharge diagnosis. Severity of disease was classified in two ways: (1) using the severity score for community acquired pneumonia, quantified by the CURB-65 score (Confusion, Urea, Respiration, Blood pressure, Age; low/medium risk: 0-2 vs. high risk: 3-5,^[13] and (2) by establishing the absence or presence of sepsis using the SOFA score (Sepsis-related Organ Failure Assessment; 0-1 vs. ≥ 2).^[14]

Data analysis and statistics

The current study performed a descriptive analysis of baseline characteristics of included patients. Collected data were tabulated using Microsoft Excel 2010 Microsoft Corp., Redmond, WA, USA, and statistical analyses were conducted using SPSS Statistical Package (version 20.0), IBM SPSS Statistics for Windows, V.20.0, IBM Corp., Armonk, New York, USA. Continuous variables were reported as medians with interquartile ranges (IQRs) and categorical variables as proportions. In case of missing values, valid percentages were used. The current study compared the CT scan results with the PCR testing results. Diagnostic accuracy of the CT scan in terms of sensitivity, specificity, positive, and negative predictive value (PPV and NPV, resp.) and likelihood ratios (LRs) was assessed. Next, the

diagnostic accuracy (sensitivity, specificity, PPV, NPV, and LR) with respect to the severity of disease and the absence/presence of sepsis was calculated. The Chi Square test was used to compare the sensitivity and specificity between patients with low and high severity of disease. Discordances between CT results and PCR testing results were further investigated by retrieving data on alternative diagnoses and, if possible, duration of symptoms [using ancillary viral/bacterial test results and discharge diagnoses in medical charts (e.g., pneumonia caused by influenza)]. These data were analyzed in a descriptive way. In all cases, *P* values of less than 0.05 were considered significant.

Ethical considerations

All examinations performed in studies involving human participants were in accordance with the ethical standards of the Institutional Ethics Committee (IEC) and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Informed consent was obtained from all patients prior to their enrollment in this study.

Results

Patient characteristics

During the study period, 612 symptomatic ED patients had both a chest CT and RT-PCR test for diagnosing COVID-19. The median age of these patients was 60.5 years and 62.5% were male [Table 1]. Most patients (88.3%) had one or more comorbidities. Cardiovascular comorbidity (31.2%) was highly prevalent, as was chronic pulmonary disease (29.0%). In total, 551 (90.0%) patients were admitted to the hospital.

Table 1: Demographics and patient characteristics

<i>n</i> (%), median (IQR)	All patients (<i>n</i> =612)
Demographics	
Age (years)	60.5 (34-82)
Male	383 (62.5)
Female	229 (37.5)
Comorbidity	
No comorbidity	72 (11.7)
Hypertension	164 (26.7)
Diabetes mellitus	125 (20.4)
Myocardial infarction	28 (4.5)
Cerebrovascular disease	12 (1.9)
Heart failure	33 (5.3)
Peripheral vascular disease	11 (1.7)
COPD	178 (29.0)
Malignancy	3 (0.4)
Chronic kidney disease	50 (8.1)
Chronic liver disease	18 (2.9)
Chest CT	
CT suspicious for COVID-19	507 (82.8)
RT-PCR	
PCR SARS-CoV2 positive	481 (78.5)
Admission	551 (90.0)

Of the chest CT scans, 507 (82.8%) were judged as suspicious for COVID-19. In 481 (78.5%) patients, the PCR was positive for SARS-CoV-2 (1st and 2nd PCR positivity) [Table 2]. In 22 of these patients, a PCR was necessary on a second sample to confirm the suspected diagnosis, because the first PCR was negative or inconclusive.

Diagnostic performance of Chest CT in different age and sex groups

The performance of chest CT in diagnosing COVID-19 in different age and sex groups is reported in the current study [Table 3]. The positive predictive values (PPV) and accuracy of chest CT in diagnosing COVID-19 were higher in patients ≥ 60 years than that in patients < 60 years ($P = 0.001$ and 0.004 , respectively). The specificity and NPV of chest CT in diagnosing COVID-19 were greater for women than that for men ($P = 0.007$ and 0.03 , respectively); and no difference existed for sensitivity, PPV and accuracy ($P = 0.43$, 0.69 and 0.31 , respectively).

Diagnostic accuracy of Chest CT for COVID-19 in all patients and subgroups

In total, 78.5% of patients had a positive PCR and 82.8% a positive CT, resulting in a sensitivity of 94.2%, specificity 76.4%, likelihood ratio (LR) + 2.94 and (LR) - 0.18. Sensitivity was higher in patients with high risk pneumonia ($n = 48$, 100%) and with sepsis ($n = 421$, 99.5%) [Table 4]. In 131 patients with a negative PCR, 94 CT scans were judged as not suspicious for COVID-19. This results in a sensitivity of 94.2% and specificity of 76.4% of the CT for diagnosing COVID-19 [Table 4]. The PPV was 76.7% and NPV 94.1% [Figures 1-12].

Diagnostic accuracy of the chest CT in relation to disease severity

Of all patients, 92.2% were classified as severe risk pneumonia according to the CURB-65 score, with 68.8% having sepsis (SOFA score ≥ 2) [Table 4]. The sensitivity of the CT tended to be higher (100.0%) in those with severe risk pneumonia than in patients with low/medium risk pneumonia (90.3%, $P = 0.42$). In patients with sepsis, sensitivity was significantly higher than in those without sepsis (99.5 vs. 63.5%, $P < 0.001$).

Analysis of discordant CT and PCR results

In 48 (7.8%) patients discordant findings between CT and PCR were observed. In most cases, the CT scan was considered suspicious for COVID-19, while the PCR was negative (37/48, 77.0%). In the majority of these, the diagnosis at discharge was pulmonary infection ($n = 26$; 54.1%). In 17 of these 48 patients, other viral pathogens (Influenza A virus: $n = 4$; Human metapneumovirus: $n = 8$; Rhinovirus: $n = 3$, non-COVID corona virus: $n = 2$) and in 9 patients, bacterial pathogens were mycoplasma ($n = 6$) and Chlamydia ($n = 3$). Median duration of symptoms at the moment of CT scanning and PCR was 5 days (in 1 less than 48 hours) in these 7 patients.

Table 2: Overview of Chest CT and PCR results

	PCR SARS-CoV2 positive	PCR SARS-CoV2 negative	Total
CT suspicious for COVID-19	470	37	507
CT not suspicious for COVID-19	11	94	105
Total	481	131	612

Table 3: Diagnostic performance of chest CT for COVID-19 infection with RT-PCR result as reference

	n (%)	Sensitivity	Specificity	PPV	NPV	Accuracy	P
Total	612 (100)	94.2	76.4	76.7	94.1	66.5	-
Age							
<60 years	228 (37.3)	92.4	74.4	73.6	91.7	65.1	0.004
>60 years	384 (62.7)	94.8	77.7	77.3	95.2	67.7	0.001
Sex							
Male	383 (62.5)	95.8	77.3	75.9	93.7	64.2	0.03
Female	229 (37.5)	95.4	76.7	76.1	95.1	67.5	0.007

Table 4: Diagnostic accuracy of Chest CT for diagnosing COVID-19 in relation to disease severity

	n (%)	Sensitivity	Specificity	PPV	NPV	LR+	LR-
Total	612 (100)	94.2	76.4	76.7	94.1	2.94	0.18
Disease severity							
CURB-65 0-2	48 (7.8)	90.3	73.1	71.3	90.7	2.89	0.17
CURB-65 ≥ 3	654 (92.2)	100.0	57.2	56.1	100.0	2.27	0.14
SOFA score 0-1	191 (31.2)	63.5	72.7	48.4	85.1	2.13	0.44
SOFA score ≥ 2	421 (68.8)	99.5	69.4	76.2	96.3	2.91	0.03

In 11 patients (1.7%) with a suspicious CT scan and a negative PCR, another diagnosis than pulmonary infection was made. Seven patients had another pulmonary diagnosis (bronchiectasis ($n = 2$), asthma ($n = 4$), pleural effusion due to ascites ($n = 1$)), while in 4 patients, a cardiac diagnosis (heart failure ($n = 3$), acute coronary syndrome ($n = 1$)) was made.

In 11 patients (1.7%), CT scans were not suspicious for COVID-19, while the PCR was positive. In 2 of these patients, a second PCR was positive after a first negative test. In these cases, the CT scan was not repeated to check for new abnormalities. In one patient, respiratory symptoms were present for less than 48 hours, in 6 patients, symptoms were present for more than 48 hours, and in 2 patients, symptom duration was not clear. Summarized data validation table has been provided for reference [Table 5].

Discussion

In this prospective study in patients presenting to the hospital with a clinical suspicion of COVID-19, results showed that 76.7% of patients had a positive PCR and 82.8% a positive CT, resulting in a sensitivity of 94.2%, specificity

Table 5: Summarized data validation table

Serial Number	Parameter	Result
1	Study period	February 15, 2020-July 15, 2020
2	Total number of patients suspected with clinical suspicion of COVID-19	612
3	Male : Female	383 : 229
4	Age <60 years: ≥60 years	228 : 384
5	Patients with no comorbidity	72
6	Patients with comorbidity	540
7	CURB-65 0-2 clinical criteria	564
8	CURB-65 ≥3 clinical criteria	48
9	SOFA 0-1 clinical criteria	191
10	SOFA ≥2 clinical criteria	421
11	CT suspicious for COVID-19	507
12	Total PCR SARS-CoV2 positive	481
13	1 st PCR SARS-CoV2 positive	459
14	2 nd PCR SARS-CoV2 positive	22
15	Total CT- PCR concordant results	564
16	Total Patients with CT (positive) results	507
17	Total Patients with CT (negative) results	105
18	Total Patients with PCR (positive) results	481
19	Total Patients with PCR (negative) results	131
20	Total CT- PCR discordant results	48
21	CT (positive) PCR (negative) discordant results	37
22	CT (negative) PCR (positive) discordant results	11
23	Total false-positive CT results	37
24	False-positive rate of CT findings in the current study	7.2%
25	False-positive CT results secondary to infection	26
26	False-positive CT results secondary to other viral pneumonia (Non-COVID19) In 17 patients, other viral pathogens (Influenza A virus: <i>n</i> =4; Human metapneumovirus: <i>n</i> =8; Rhinovirus: <i>n</i> =3, non-COVID corona virus: <i>n</i> =2)	17
27	False-positive CT results secondary to bacterial pneumonia In 9 patients, bacterial pathogens were mycoplasma (<i>n</i> =6) and Chlamydia (<i>n</i> =3).	9
28	False positive CT results secondary to alternate diagnosis Seven patients had another pulmonary diagnosis (bronchiectasis (<i>n</i> =2), asthma (<i>n</i> =4), pleural effusion due to ascites (<i>n</i> =1)), while in 4 patients, a cardiac diagnosis (heart failure (<i>n</i> =3), acute coronary syndrome (<i>n</i> =1))	11



Figure 1: Axial CT images in patients with Influenza pneumonia. 58-year-old male, day 6 after symptom onset showing subpleural areas of mixed ground-glass opacities and extensive consolidation in basal segments of bilateral lower lobes

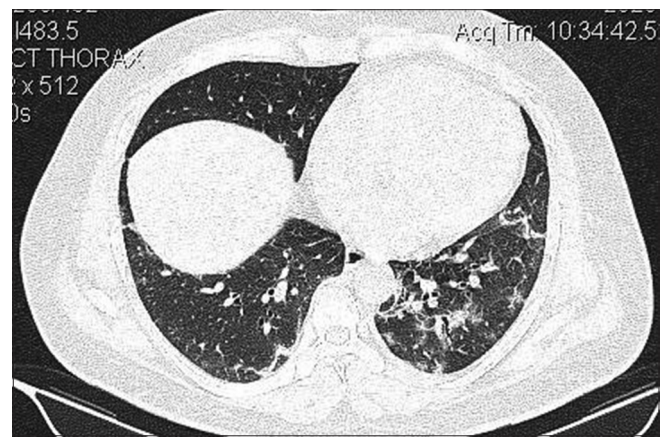


Figure 2: Axial CT images in a patient with Human metapneumovirus pneumonia. A 43-year-old male, day 4 after symptom onset showing mixed ground-glass opacities in posterior segments of right upper lobe and basal segments of left lower lobe

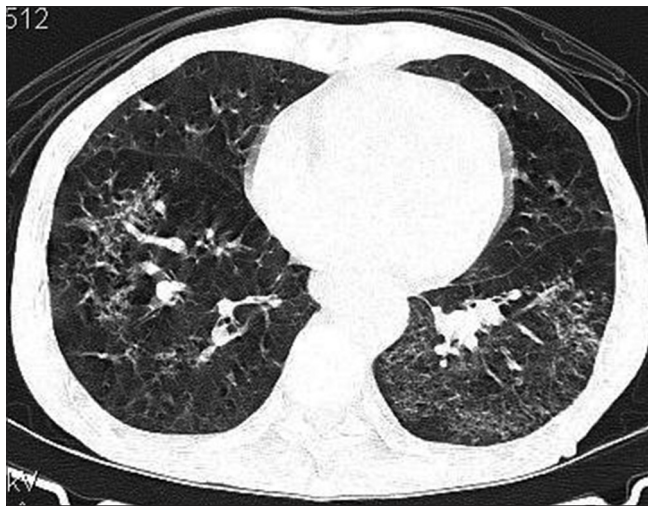


Figure 3: Axial CT images in patients with Mycoplasma pneumoniae. A 71-year-old female, day 10 after symptom onset: bilateral, peripheral ground-glass opacity associated with smooth interlobular and intralobular septal thickening representing a crazy-paving pattern

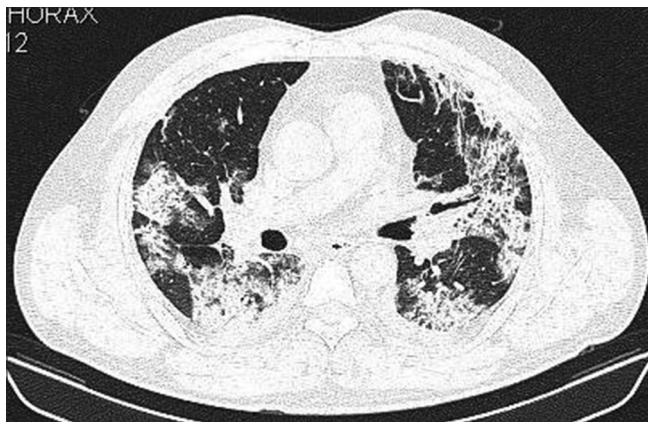


Figure 5: Serial axial CT images in a 48-year-old male with Chlamydia pneumoniae, day 7 after symptom onset showing round areas of mixed ground-glass reticular opacities and consolidation in bilateral lower lobe posterior zones, and posterior segments of bilateral upper lobes

76.4%, likelihood ratio (LR) + 2.94 and (LR) - 0.18. The PPV was 76.7% and NPV 94.1%. Sensitivity of the CT was higher in patients with more severe disease - high CURB-65 score (≥ 3) or sepsis (SOFA ≥ 2) - than in those who were less severely ill. In 92.1% of all patients, the results of the chest CT and the PCR test were concordant; however, in 11 (1.7%) of patients with a positive PCR, CT scans were not considered suspicious for COVID-19. In addition, in about 28.2% patients tested negative by PCR, the CT was positive. Most of these patients had a discharge diagnosis of pneumonia (70.2%), which was caused by another viral pathogen in one-half of patients.

The diagnostic ability of chest CT was found to be rather high, and in 92.1%, concordant findings of CT and PCR were found. Nevertheless, it should be noted that 4% of COVID-19 were missed and 3.9% were incorrectly assigned



Figure 4: Serial axial CT images in a 67-year-old female with Chlamydia pneumoniae, day 5 after symptom onset showing diffuse bilateral ground-glass opacities with focal consolidations (mixed pattern) and reticulations in the lower lobes



Figure 6: Axial CT image in a 81-year-old female with mycoplasma pneumoniae, day 7 after symptom onset showing ground glass opacification with few areas demonstrating progression to airspace consolidation

a suspected COVID-19. In a situation where isolating each patient separately is not possible, these patients are placed at a COVID-19 cohort, where they can be exposed to COVID-19 positive patients with possible devastating consequences. The results of diagnostic accuracy should be interpreted with care because it is known that both CT and PCR can be false negative in early stages of COVID-19.^[15] This is why the current study included repeated PCRs and explored discordant test results, which showed that in about 45.9% of patients with false positive CT scans, other viral pathogens were detected. This study was performed at the end of the respiratory virus season, and the added value of the CT scan might be lower during typical respiratory virus season.

Not surprisingly, the sensitivity of the CT scan was higher in the more severely ill patients. This finding was reported in other studies as well. These findings are not surprising, because in more severe disease, more abnormalities can be expected to be found on the chest CT.^[16] Interestingly, most patients (90.3%) presented with severe risk pneumonia and many (68.8%) were septic. A chest CT scan can help to

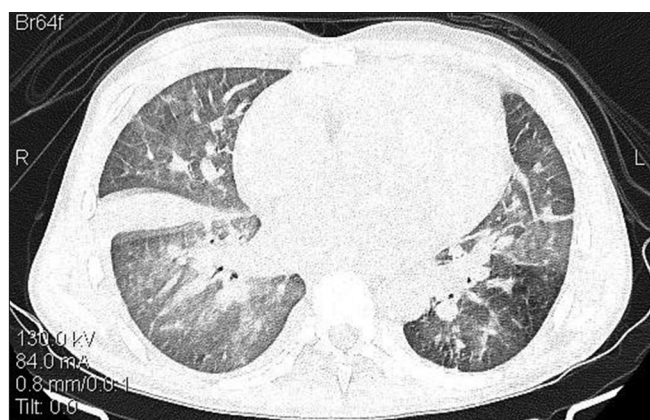


Figure 7: Serial axial CT images in a 44-year-old male with Influenza pneumonia, day 3 after symptom onset showing multifocal mixed ground-glass opacities with peripheral distribution and air-bronchogram sign

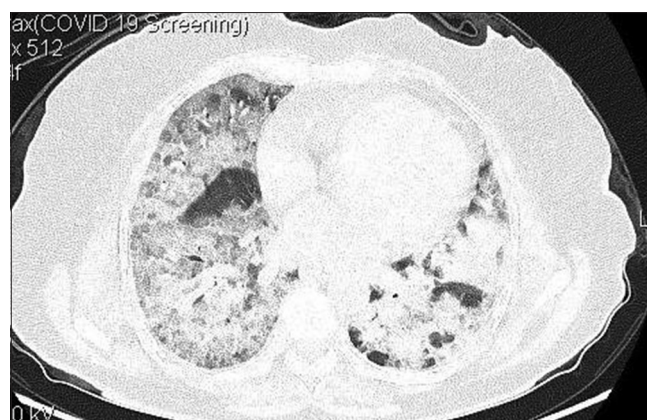


Figure 8: Axial CT images in a 63-year-old female with heart failure, day 4 after symptom onset of breathlessness showing patchy consolidation and fibrosis subsequently progressing to organizing pneumonia on day 11

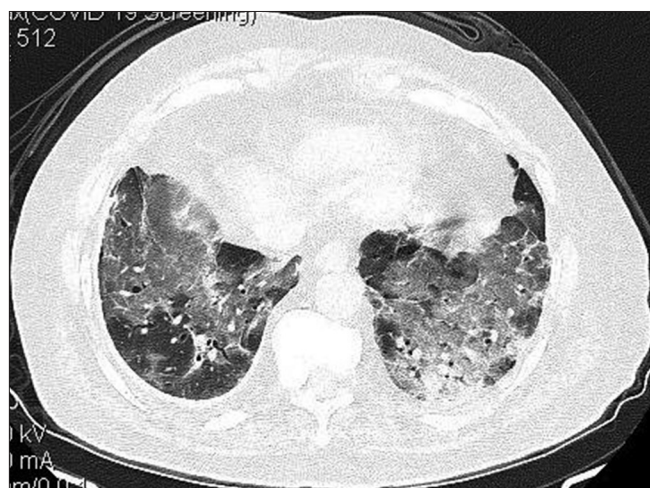


Figure 9: Axial CT image in a 68-year-old male with acute coronary syndrome, day 2 after onset of chest pain showing peripheral distribution of patchy ground-glass opacities plus reticular pattern

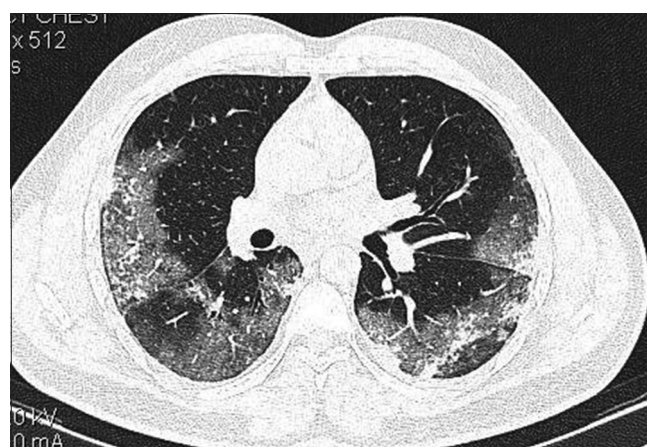


Figure 10: Serial axial CT images in a 66-year-old male with Human metapneumovirus pneumonia, day 7 after symptom onset showing multiple ground-glass opacities and crazy-paving appearance in subpleural distribution

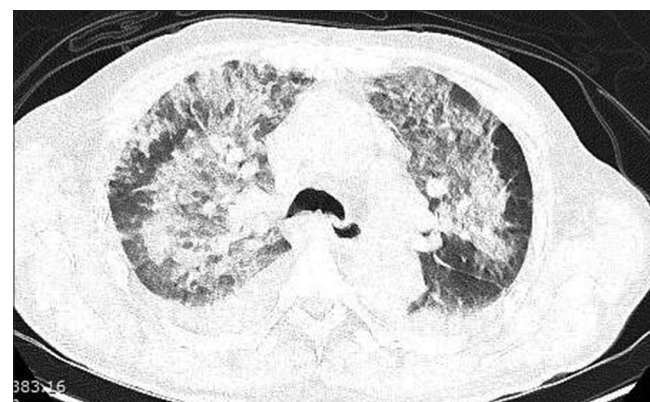


Figure 11: Axial CT image in a 33-year-old male with mycoplasma pneumonia, day 4 after symptom onset showing pure ground glass opacity in bilateral lower lobes showing progression to consolidation in the subpleural regions of bilateral lower lobes

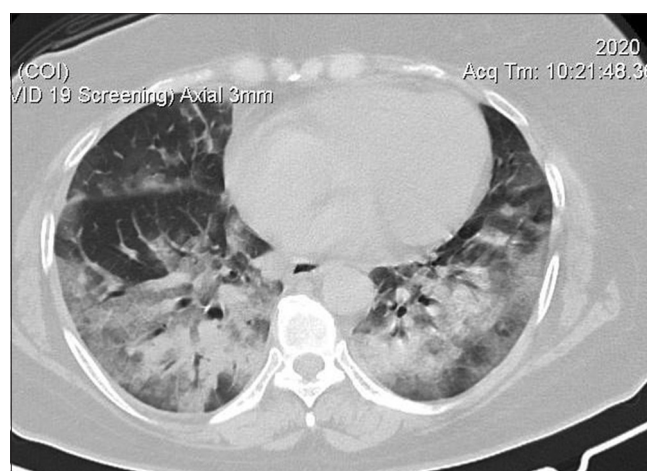


Figure 12: Axial CT image in a 55-year-old female with heart failure, day 3 after symptom onset showing reticular pattern superimposed on the background of GGO – crazy paving appearance with ARDS in bilateral lower lobes

differentiate those with high risk (suspicious CT) and those with low risk of COVID-19 (non-suspicious CT). It would

be interesting to investigate whether combining the results of chest CT with clinical characteristics would increase

the discriminatory value, which is extremely important especially if patients have to be placed in cohorts. It is valuable for radiologists to recognize that the CT findings of COVID-19 overlap with the CT findings of diseases caused by viruses from a different family, such as adenovirus, and have differences as well as similarities with viruses within the same family, such as SARS-CoV and MERS-CoV.

In other studies, the sensitivity of chest CT for COVID-19 was found to be higher, up to 97% in a study with 1014 Chinese patients, but at the cost of low specificity (25%).^[12] In another study in 81 Chinese patients with PCR proven COVID-19, sensitivity was 93%.^[13] A lower sensitivity of 80% was reported in 30 symptomatic cruise ship passengers.^[14] In contrast, PCR was found to be negative in 71% of 51 Chinese patients, of whom 98% had CT abnormalities.^[17] The current study included all chest CTs with abnormalities that could be related to COVID-19 as suspicious, even though the changes were judged to be more likely non-COVID-19 related pneumonia.

Ai *et al.*^[12] included 1,014 patients in the study who underwent both chest CT and RT-PCR tests between January 6 and February 6, 2020. With RT-PCR as reference standard, the performance of chest CT in diagnosing COVID-19 was assessed. The results showed that 601 patients (59%) had positive RT-PCR results, and 888 (88%) had positive chest CT scans. The sensitivity of chest CT in suggesting COVID-19 was 97%, based on positive RT-PCR results. Of these, 48% were considered as highly likely cases, with 33% as probable cases. Some studies showed better sensitivity for CT as compared to RT-PCR assay performed within 3 days of onset of symptoms.^[18] The arguments in favor of such extensive use of CT were that RT-PCR tests of the sputum or nasopharyngeal swabs require several days whereas CT imaging can show typical features of COVID-19 helping to rapidly screen and stratify patients.^[19] But as the sensitivity of RT-PCR tests improved, the focus of studies shifted from using CT as a diagnostic tool to a prognostication test. A recent study from Italy reported perilesional pulmonary vessel enlargement in areas of lung infiltrates could be an early predictor of lung impairment.^[20]

The probability, that CT findings represent COVID-19, however, depends largely on the pre-test probability of infection, which is in turn defined by community prevalence of infection. If the disease prevalence is high, even atypical presentations are likely to represent COVID-19. When the community prevalence of COVID-19 is low, a large gap exists between positive predictive values of chest CT vs. RT-PCR. This implies that with usage of Chest CT there are a large number of false positive results.^[21] Viral pneumonias can present with significant ground glass opacity and include Cytomegalovirus (CMV), Adenovirus, Herpes Simplex Virus (HSV), Varicella zoster, Measles, Human meta-pneumovirus (HMPV) and Influenza.^[22] GGOs can be

seen in 50-75% with Adenovirus, over 75% with CMV and HSV.^[23] The typical chest CT imaging features of COVID-19 pneumonia can have false-positive results due to their overlap with a number of other conditions. In the current study, the false-positive rate of CT findings in the diagnosis of COVID-19 pneumonia was 7.2%.

It will be of interest to see whether the flu season had ended and how many people having a fever now are actually infected with influenza virus. Precision control measures for COVID-19 should be tailor-designed for high-risk groups based on analytical results. Differentiating people having a flu and preventing them from being infected with COVID-19 in a hospital setting might also be critical. The findings in the current study emphasize the fact that CT has high sensitivity and provides valuable information in suspected cases of COVID-19. Despite limitations like false-positive results, CT still plays a significant auxiliary role in the detection, diagnosis, assessment of disease severity, follow-up assessment and in predicting prognosis.

Limitations of the Study

External validity may be limited in the current study due to its single center set-up. In addition, especially in patients with mild symptoms who were not admitted to the hospital, no second PCR-testing was done after an initial negative result. A third limitation is that many patients who were seriously ill were included in the study.

Conclusion

In conclusion, high diagnostic accuracy of chest CT findings with typical and relatively atypical CT manifestations of COVID-19 leads to a low rate of missed diagnosis. Normal chest CT can be found in RT-PCR positive COVID-19 cases, and typical CT manifestations can be found in RT-PCR negative cases. Therefore, a combination of both CT and RT-PCR for future follow-up, management and medical surveillance is recommended considering the false-positive results of chest CT in the diagnosis of COVID-19 pneumonia. Radiologists should be familiar with the radiological appearances of COVID-19 related pulmonary syndrome as imaging has a critical role in diagnosing, monitoring disease progression and prognostic follow up. For the first time in the era of modern medicine, all of humankind is facing the same threat considering the contagiousness of the coronavirus and the need to reduce nosocomial outbreaks. This also give us ample opportunity to change our research approach that involves better understanding of disease manifestations and to further explore and promote the applications of chest CT for the safe management of patients and health personnel in the setting of pandemics like the present COVID-19 outbreak and threats we might encounter in the near future. It has been over 6 months since we first

heard of COVID-19 and while promising developments are being made on the clinical trials front, there is no real surety that a vaccine might be our only ray of hope in these critical times. Research findings need to be shared amongst countries to provide best health care to humankind during these uncertain times of a pandemic.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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