



Use of Artificial Intelligence to Triage Patients with Flu-Like Symptoms Using Imaging in Non-COVID-19 Hospitals during COVID-19 Pandemic: An Ongoing 8-Month Experience

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Abstract

Background Evaluation of suspected coronavirus disease-2019 (COVID-19) patient is a diagnostic dilemma as it commonly presents like influenza in early stages. Studies and guidelines have emerged both for and against the use of imaging as a frontline tool to investigate such patients. Reverse transcriptase-polymerase chain reaction (RT-PCR) is suggested as the backbone of diagnosis. We designed and tested a diagnostic algorithm using artificial intelligence (AI) to determine the role of imaging in the evaluation of patients with acute flu-like presentation.

Materials and Methods Overall, 3,235 consecutive patients with flu-like presentation were evaluated over a period of 240 days. All patients underwent plain radiographs of chest with computer-aided detection for COVID-19 (CAD4COVID) AI analysis. Based on the threshold scores, they were divided into two groups: group A (score < 50) and group B (score > 50). Group A patients were discharged and put on routine symptomatic treatment and follow-up with RT-PCR, while group B patients underwent high-resolution computed tomography (HRCT) followed by COVID-19 AI analysis and RT-PCR test. These were then triaged into COVID-19 and non-COVID-19 subgroups based on COVID-19 similarity scores by AI, and lung severity scores were also determined.

Results Group A had 2,209 (68.3%) patients with CAD4COVID score of <50 while 1,026 (31.7%) patients comprised group B. Also, 825 (25.5%) patients were COVID-19 positive with COVID-19 similarity threshold of >0.85 on AI. RT-PCR was positive in 415 and false-negative in 115 patients while 12 patients died before the test could be done. The sensitivity and specificity of CAD4COVID AI analysis on plain radiographs for detection of any lung abnormality combined with HRCT AI analysis was 97.9% and 99% using the above algorithm.

Conclusion Combined use of chest radiographs and plain HRCT with AI-based analysis is useful and an accurate frontline tool to triage patients with acute flu-like symptoms in non-COVID-19 health care facilities.

Keywords

- ▶ artificial intelligence
- ▶ computed tomography
- ▶ COVID-19
- ▶ flu

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Introduction

Coronavirus disease-2019 (COVID-19) was declared a pandemic worldwide in 2020. It is not only contagious and causes acute respiratory distress but also multiple organ failure in severe cases.^{1–4} Apart from its prevalence and being contagious, its diagnosis poses a great challenge. Reverse transcriptase-polymerase chain reaction (RT-PCR), which is considered the gold standard for diagnosis of COVID-19, is mired with issues of low sensitivity of 66% with a high false-negative rate of 33 to 66% along with a false-positive rate of 12 to 16%, apart from the fact that the test is time consuming.⁵ The role of imaging in the diagnosis of COVID-19 is also under debate. Computed tomography (CT) has a high sensitivity of 97%⁶ and is a valuable imaging tool for the clinical diagnosis of early-stage COVID-19, especially when there are insufficient RT-PCR tests as was used in Wuhan in the early pandemic period.^{7,8} CT has been shown to detect lesions in the early stage of the disease even when RT-PCR may be negative;⁹ however, it has a low specificity of 25 to 35%, and it may be difficult to distinguish cases of COVID-19 from other viral cases of pneumonia and similar look-alike lung pathologies.⁵ American College of Radiology (ACR) Guidelines, however, do not relegate it as the frontline test to diagnose COVID-19 primarily due to risk of contamination of radiology departments and risk of exposure to health workers.¹⁰ Hence, there is a need to add more tools to the use of CT to make it more specific for the detection of COVID-19. Artificial intelligence (AI) is an attractive tool to achieve this need. It has been used in many facilities to make the diagnosis of COVID-19 more specific and has been shown to have an accuracy of 90%.¹¹ The use of AI not only speeds up the diagnosis but also has the potential to calculate disease severity by performing accurate lung segmentations. As most of the countries around the world are dealing with this pandemic by setting up COVID-19-dedicated hospitals, at the same time still a majority of health care providers constitute non-COVID-19 health care facilities that continue to face the dilemma as to how to triage patients coming with flu-like symptoms while facing constrained resources including manpower, personal protective equipment kits, lack of free testing, and above all the fear of contracting the contagion while treating such patients. Chest radiographs still form the frontline screening tools in non-COVID-19 hospitals even though they have poor sensitivity in early detection of COVID-19.¹² AI tools have now been developed to make chest radiographs efficient in the detection of early lung changes so that rapid treatment and triage can be done in such patients.^{13,14}

This study was designed to test algorithms using AI along with chest radiograph and CT imaging as frontline tests to triage patients coming to non-COVID-19 hospitals with flu-like symptoms (→ Fig. 1).

Materials and Methods

The study comprised 3,235 consecutive patients with flu-like symptoms of fever, sore throat, and cough with constitutional symptoms or with respiratory discomfort who were referred to our institute from various primary

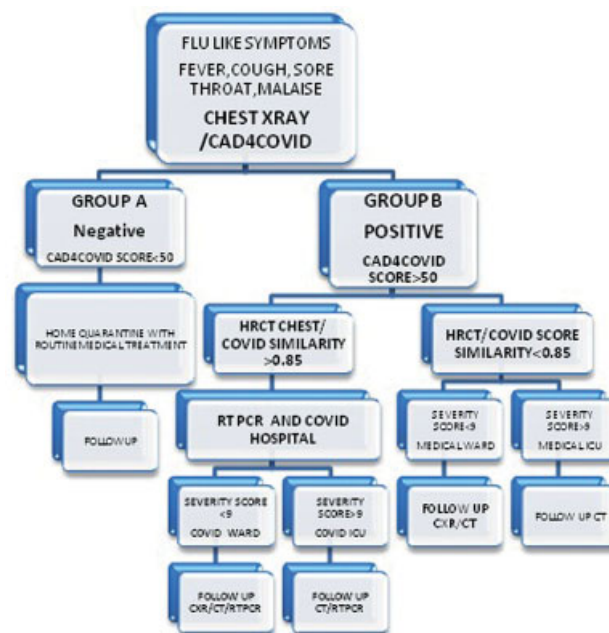


Fig. 1 Proposed imaging algorithm for flu-like presenting patients. CAD4COVID, computer-aided detection for coronavirus disease-2019; CXR, chest X-ray; HRCT, high-resolution computed tomography; ICU, intensive care unit; RT-PCR, reverse transcription polymerase chain reaction.

and secondary health care facilities for imaging and diagnosis in a period of 240 days, that is, from March 2020 to November 2020. All the patients underwent flu diagnostic evaluation as per → Fig. 1. The chest radiographs were done on portable X-ray system, which was a makeshift arrangement near the entrance of the institute. History and informed consent were obtained from all the patients along with a history of any contact or any recent travel outside the district. Body temperature was recorded of all the patients with a thermal scanner. Under all protective gear, the chest radiograph was obtained in posteroanterior or anteroposterior views and images digitally processed. These were then transferred to computer-aided detection for COVID-19 (CAD4COVID) AI software (Delft Imaging Hwetogenbosch, the Netherlands) and CAD4COVID threshold determined on heat texture image map. The patients having a threshold score of <50 were classified as group A and were put on symptomatic treatment and follow-up. Group B patients were those with a threshold score of >50 and were labeled as positive for an underlying lung abnormality and underwent plain high-resolution computed tomography (HRCT) examination on 128 slice scanner (Siemens Go Top, Erlangen Germany AG). The images were transferred to COVID-19 AI software (Quibim, Valencia, Spain; Thirona BV Nijmegen, the Netherlands). A threshold of 50 was based on T score = 50 based on the area under the curve with threshold 50 having a sensitivity of 91% and specificity of 87%. The patients with COVID-19 similarity threshold of >0.85 were labeled as positive for COVID-19 disease. The CT severity scores were determined in these patients based on the percentage of lobes of lung involved with 0 to 25% as score 1, 25 to 50% score 2, 50 to 75% score 3, and 75 to 100% score 4 for each lobe

Table 1 The patient demographics of both groups

S. No.	PARAMETER	GROUP A(n=420)	GROUP B(n=60)
		MEAN	MEAN
1	Age (YEARS)	39.5	51.2
2	Sex		
	Males	336(80%)	51(85%)
	Females	84(20%)	9(15%)
3	Symptoms		
	fever	330(79%)	52(86%)
	cough	180(42.8%)	38(63%)
	Breathing diffic	75(17.8%)	28(46%)
	constit. Sympt	370(88%)	40(66%)
	others		
	diabetes	45(10.7%)	14((23%)
	hypertension	55(13.0%)	18(30%)
	nasal allergies	80(19%)	25(61%)
4	Duration of Symptoms	< 7 days	<7 days
5	Total leucocyte count		
	normal	375(89%)	45((75%)
	Lymphopenia	30(7%)	23(38%)
6	Spo2		
	>95	385(91%)	37(61%)
	90-95	35(8.5%)	18(30%)
	<90	0	5(9%)

of the lung and totally added to form a total severity score with the maximum score being 20. The percentage of lung involved by COVID-19 was also determined. All patients with a score of less than 9 were transferred to COVID-19 isolation wards and those with scores more than 9 to COVID-19

intensive care units for further management. The patients with COVID-19 thresholds of less than 0.85 were labeled as non-COVID-19 cases of pneumonia and transferred to non-COVID-19 medical wards. The follow-ups were done as per **flowchart 1**.

Results

The patient demographics are enlisted in **Table 1**. The mean age of patients was 39.5 and 51.2 years in groups A and B with 80 and 85% being males, respectively. The commonest symptoms seen were fever (79%, 86%) and cough (42.8%, 63%) in group A and group B patients, respectively, followed by constitutional symptoms, respiratory discomfort, and malaise with loss of appetite. Comorbidities were seen in 60% of the patients; 89% of group A and 75% of group B patients had normal total leucocyte counts, while lymphopenia was seen in 38% of group B patients. A total of 91% of group A patients and 61% of group B patients had normal SPO₂ levels. Group A patients formed the majority of patients, that is, 2,209/3,235 (**Fig. 2**) with a mean CAD4-COVID score of 35 (**Fig. 3**). There were 22 false-positives due to artifacts of overlying scapulae and 28 false-negative patients who had focal ground-glass opacities with a threshold less than 50. The pattern of distribution of lesions in group A patients is enlisted in **Table 2**. Group B patients comprised 1,026 patients with a mean CAD4COVID score of 72 and underwent plain HRCT examination with COVID-19 AI analysis of images (**Fig. 4A and B**). The patterns of

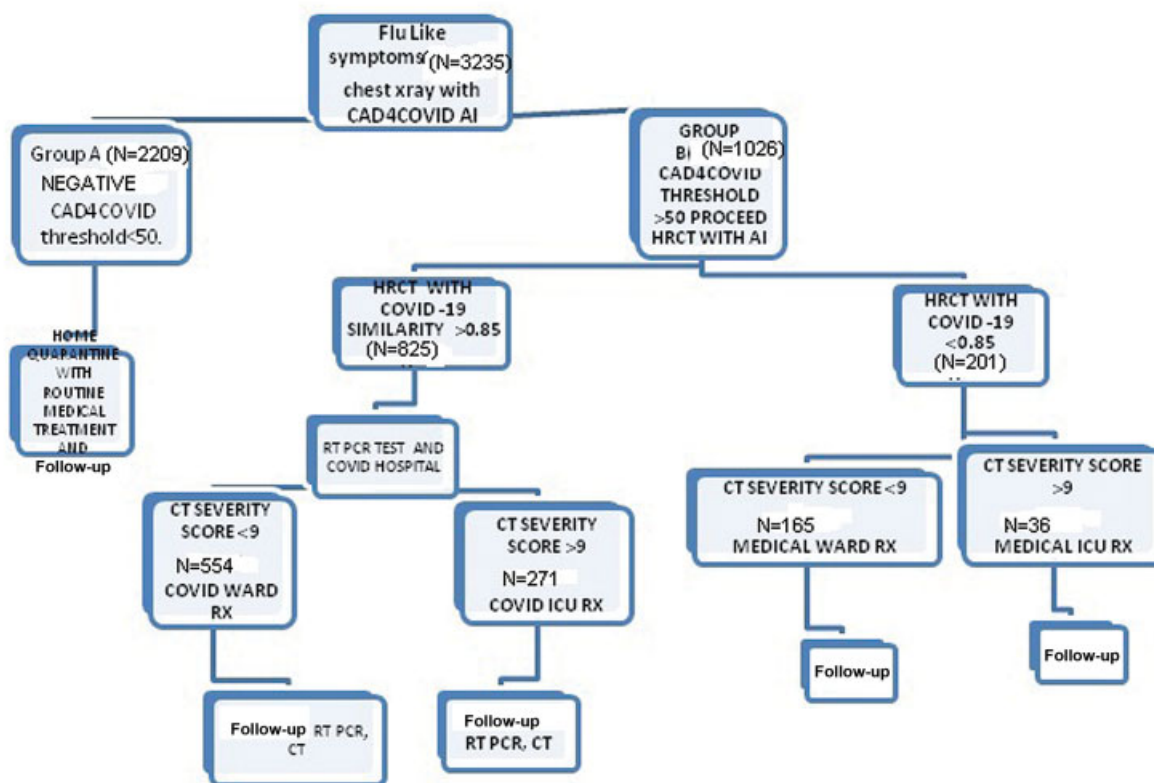


Fig. 2 Algorithm with patient numbers in the study. CAD4COVID, computer-aided detection for coronavirus disease-2019; CXR, chest X-ray; HRCT, high-resolution computed tomography; ICU, intensive care unit; RT-PCR, reverse transcription polymerase chain reaction.

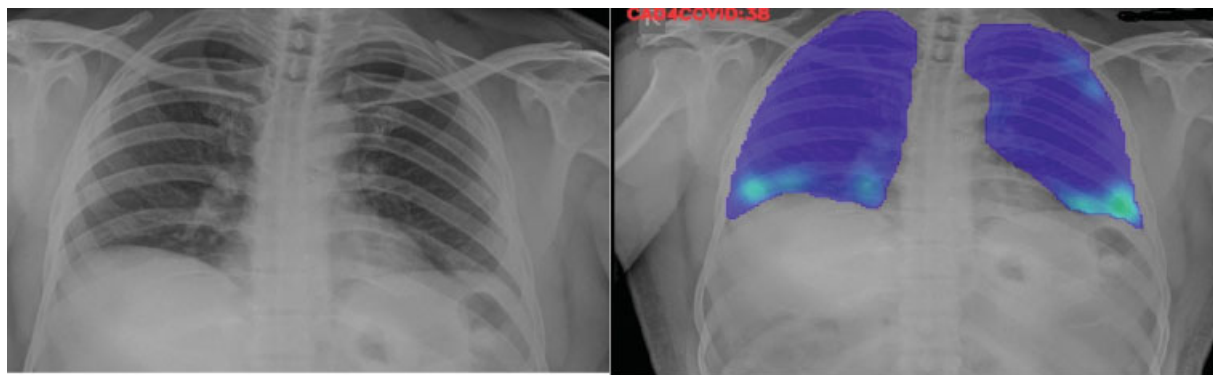


Fig. 3 Plain radiograph chest and CAD4COVID analysis image in group A patient showing threshold score of 38. CAD4COVID, computer-aided detection for coronavirus disease-2019.

Table 2 The pattern of lesions seen in group A on plain radiographs

S.No	Pattern	No. of patients	CAD4COVID threshold
1	Normal	1117	15
2	Increased markings	450	28
3	Linear atelectasis/fibrotic bands	546	35
4	Non specific small nodule	23	38
5	Calcification	21	40
6	Pleural thickening	15	30
7	Extra pulmonary shadows	37	45

distribution of lesions on plain radiographs and HRCT are enlisted in ►Table 3 and 4. A total of 825 (25.5%) patients of COVID-19 were detected by COVID-19 AI analysis using a threshold cut-off of 0.85 (►Fig. 5A and B). The distribution of various cut-off scores is shown in ►Fig. 6. A total of 201 patients had non-COVID-19 diseases, as tabulated in ►Table 5 and ►Fig. 7A and B). RT-PCR was done in 530 patients of whom 380 were positive and 150 false-negatives. A total of 35 patients were detected positive on repeat RT-PCR after 2 days. In 12 patients, RT-PCR could not be done as they died. A total of 554 patients had CT severity scores of less than 9 (►Fig. 8) while 271 patients had scored more than 9 (►Fig. 9A and B). Correlation of these scores was done with a clinical respiratory status of patients (►Table 6). The patients in both groups were triaged as per the depicted ►Fig. 2. The follow-up data were collected in 2,187 patients of group A, all of whom showed complete recovery while the remaining 22 patients were lost to follow-up. In group B, 11 patients of COVID-19 died on the first day of admission while hospital mortality was seen in 32 more patients of COVID-19 and 13 in non-COVID-19 category. CAD4COVID analysis on plain radiographs at a threshold of 50 achieved sensitivity and specificity of 97.9% and 99%, respectively, in the present study to detect any significant chest pathology (►Table 7). The overall prevalence of chest infection detected by the use of CAD4COVID analysis in patients with flu-like presentation in the present study during the pandemic was 30.5%, with an incidence of COVID-19 being 25.5% in the present time period of 8 months. This prevalence, however, varied in each month depending upon the progression of the pandemic (►Fig. 10).

Discussion

During an outbreak of a highly infectious disease like COVID-19 with a person-to-person transmission, health care personnel have increased workload and work stress due to limited experience and available tools to triage these patients. Although Pan et al⁷ have shown that CT scan can show findings in the early and asymptomatic phase, another study by Chung et al¹⁵ has shown that CT may be normal in the early stages of the disease and can limit radiologists' ability to screen asymptomatic patients. However, in the symptomatic phase, that is, from day 5 to day 10 following infection, radiology is fast and very accurate in forming the diagnosis of COVID-19 with 97% sensitivity of CT. Majority of these patients with mild to severe flu-like symptoms present first to non-COVID-19 hospitals for which diagnosis and triaging these patients is a big challenge. This study comprised a cohort of 3,235 patients evaluated with the use of AI along with plain chest radiographs and HRCT as frontline tools to diagnose and triage these patients into no chest infection and those with infections of COVID-19 and non-COVID-19 types. The algorithm used in the study was designed to combine the benefits of lower cost, quicker results, high sensitivity, and improved accuracy of both CT and plain chest radiograph using AI. RT-PCR, which has problems of limited availability, longer test times, reduced sensitivity, high false-negatives of 33 to 66% resulting in high nosocomial infections and social distress, and lastly issues of repeated testing, was kept as second-line test for confirmation of COVID-19 diagnosis. The present study was started in the early phase of the pandemic when 87% of patients presenting with flu-like symptoms to general health care non-COVID-19 facilities still had non-COVID-19 type of etiology. These months being the onset of spring season had a predominance of seasonal flu due to changes in weather; however, the study showed that as the pandemic progressed not only there was an increased number of patients, but also 25% of these were those of COVID-19 disease as is shown in ►Fig. 10. The study showed that combined use of plain radiographs of the chest with AI-based analysis like CAD4COVID (at a cut-off threshold score of 50) with HRCT and AI analysis could detect COVID-19 disease with high sensitivity and specificity of 97.9% and 99%, respectively, in these symptomatic patients. The use of plain radiographs as

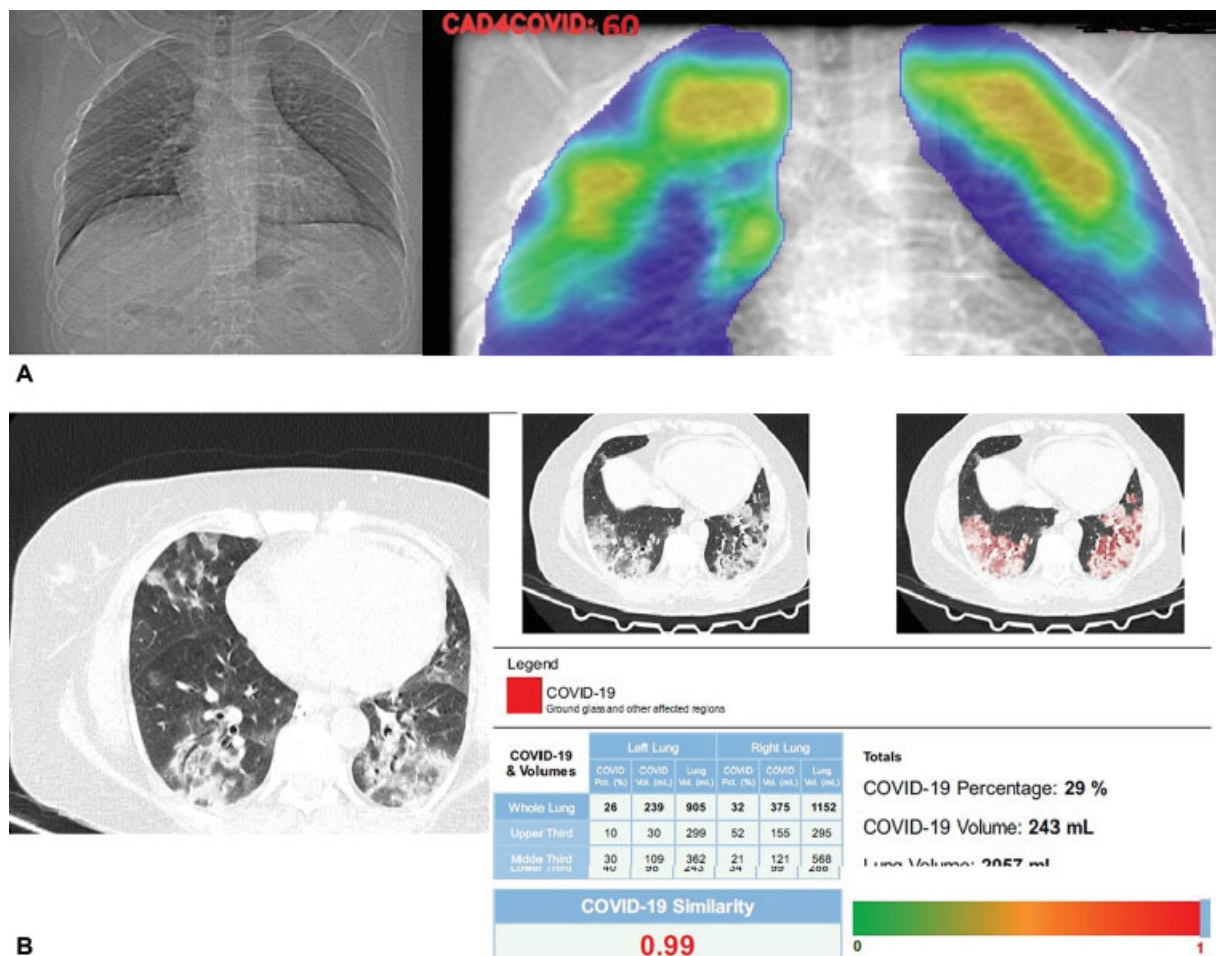


Fig. 4 (A) Plain radiograph chest and CAD4COVID analysis image in group B patient with a score of 60. (B) HRCT axial image and COVID-19 analysis showing COVID-19 similarity of 0.99 in COVID-19 patient. CAD4COVID, computer-aided detection for coronavirus disease-2019.

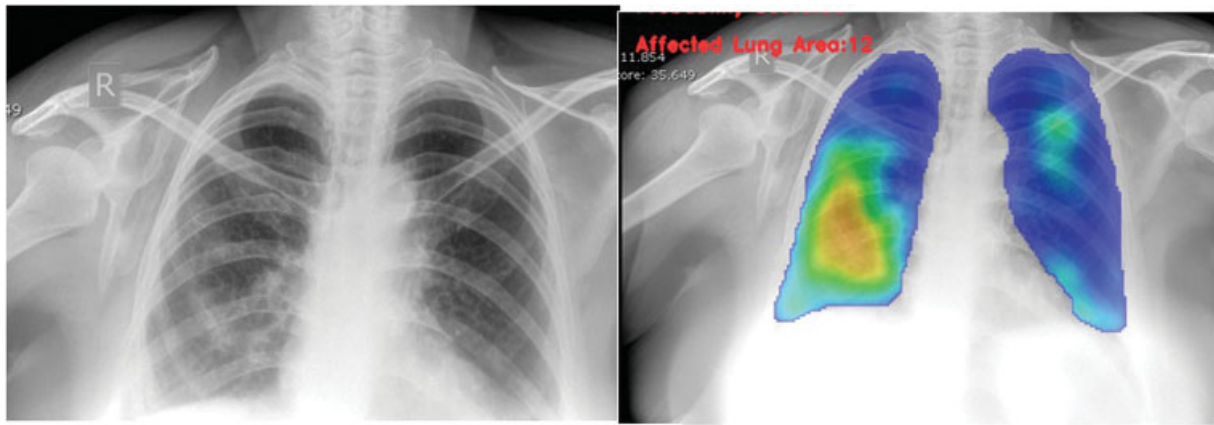
Table 3 The pattern of lesions seen in group B on plain radiographs with CAD4COVID score. CAD4COVID, computer-aided detection for coronavirus disease 2019

S.No.	Pattern	No. of patients	CAD4Covid Threshold
1	Consolidations	42	65
	unilateral	13	55
	bilateral	38	90
2	Central opacities	16	75
3	Peripheral opacities	35	90
4	Pleural effusions	5	65
5	Mediastinal/hilar pathology	2	70

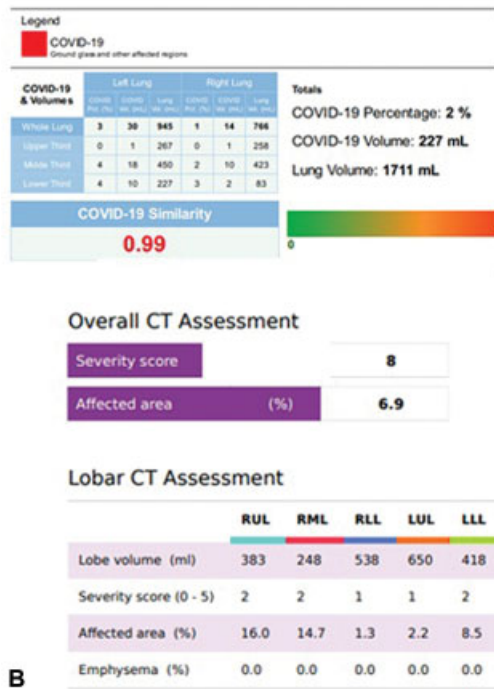
Table 4 The pattern of lesions seen in group B on high-resolution computed tomography with severity scores

S.No.	Pattern	No. of patients	Covid 19 Similarity threshold	CT Severity score
1	Focal GGO	320	0.9	8
2	Confluent GGO	125	0.99	>14
3	Diffuse GGO	146	0.7	12
3	Crazy paving pattern	115	0.92	9
4	Consolidations	100	0.85	6
5	Pleural effusions	17	0.2	0
6	Mediastinal	2	0.02	0

a first-line tool in non-COVID-19 facilities in such patients not only saves cost but also reduces unwanted use of CT as a blind screening tool for all flu patients. The present study shows that this algorithm is faster and more accurate than the conventional path of using RT-PCR as a frontline tool to screen all flu patients. Only a few studies have been done so far using AI with COVID-19 detection by imaging.^{11,16} The study also shows that estimation of CT severity scores had a good correlation with respiratory status of patients, especially with correlation with PAO₂/FiO₂ values, and can help to decide the intensive care strategy in these cases. We used a cut-off severity score of more than 9 to categorize as a severe infection. Yang et al¹⁷ also showed in their study that CT severity scores had sensitivity and specificity of 83% and 94%, respectively, to detect severe COVID-19 disease. Follow-up CT if required in these patients having a baseline pretreatment severity score can also be of help to monitor the progress of the disease. Based on the initial experience of the use of this new tool of AI combined with plain radiograph and CT, this study shows that imaging can play an important role in the diagnostic workup of patients presenting with flu-like symptoms. It can also predict the severity of the disease, which can influence the prognosis and follow-up of these patients. Despite the pandemic, there are a large number of patients who are non-COVID-19 and need



A



B

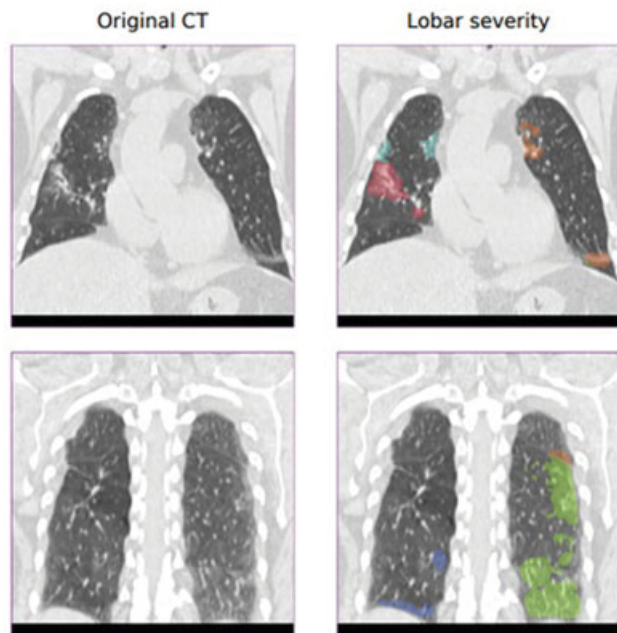


Fig. 5 (A) Group B patient with a plain chest radiograph and AI map with CAD4COVID score of 78. (B) Same patient showing HRCT coronal image with color-coding of COVID-19 lesions with COVID-19 similarity of 0.99 and a severity score of 8. AI, artificial intelligence; CAD4COVID, computer-aided detection for coronavirus disease-2019; COVID, coronavirus disease; HRCT, high-resolution computed tomography.

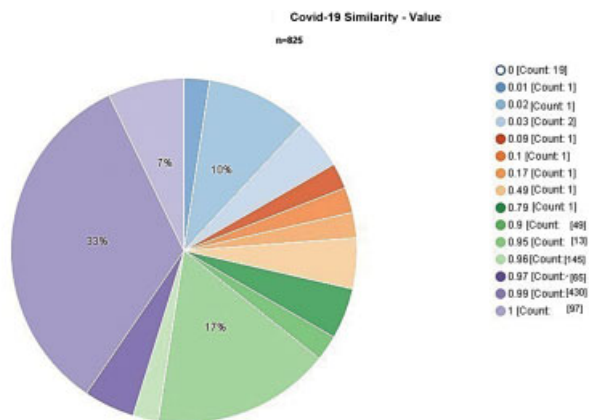


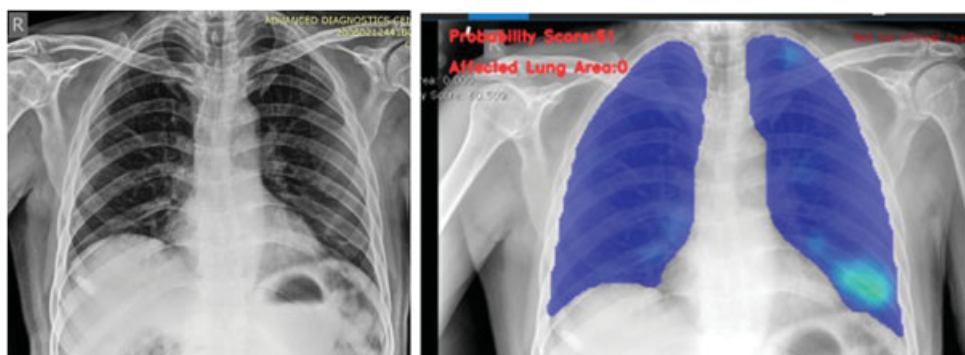
Fig. 6 Pie chart showing the distribution of coronavirus disease-2019 (COVID) similarity values in group B patients.

diagnostic services in non-COVID-19 hospitals. Chadha et al¹⁸ have shown that the burden of seasonal influenza is not recognized in India, and there is no reliable national data registry. The absence of data does not mean an absence of seasonal influenza even during times of COVID-19 pandemic. It is known that influenza disease exists in India, the types and subtypes of strains circulating in the country, and the seasonality of annual outbreaks are also known. Hence, there is a likelihood of concurrent outbreaks of COVID-19 and non-COVID-19 disease in the country depending upon season and geographic location. Ongoing pandemic has currently raised fear and anxiety in patients with flu-like symptoms, and we have seen an increasing trend by patients to report to non-COVID-19 hospitals that were not seen in prepandemic times, thus posing a diagnostic challenge. Blind use of RT-PCR screening to evaluate all patients with flu-like presentation

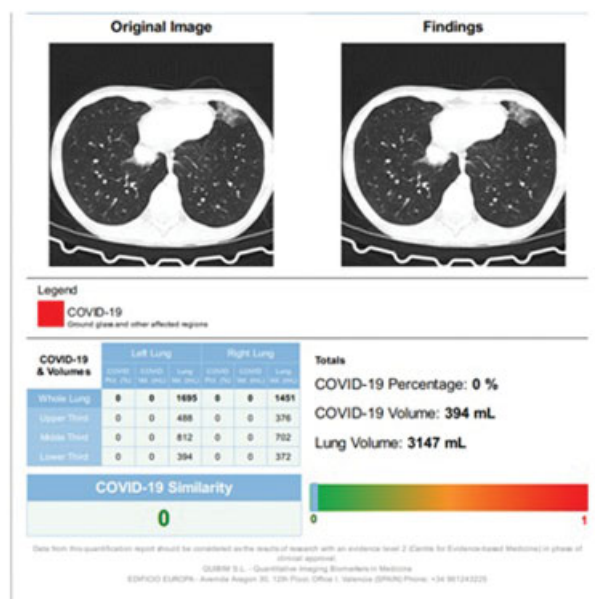
Table 5 The disease distribution in group B patients

S.no.	Disease	No. of patients
1	Covid-19	825
2	Pulmonary edema	
	Cardiac	104
	Renal	7
	Septicemia	9
3	Community pneumonia	
	Bacterial	32
	H1N1	33
	Cocksackie	1
	Adenovirus	1
	CMV	1
4	Tuberculosis	13

would be a waste of resources, more time consuming, and add more confusion in patient management as is being observed in many patients due to high false-negative and positives of RT-PCR. Using this approach alone would also fail to triage other chest infections. At a 25.5% prevalence of COVID-19 disease, this study has shown that with sensitivity and specificity of 97% and 99%, respectively, and using AI, majority of the cases would be correctly flagged as abnormal, and 0.9% (7/825) positive cases would be missed by this algorithm, these results being better than RT-PCR done alone. Similarly, with a specificity of 99%, the likelihood of false-positive is also negligible. Radiology has been the backbone of diagnostic services, and it would not be prudent if these diagnostic examinations are not utilized as frontline modalities provided they are used with proper protective measures. If correctly interpreted, the guidelines issued by ACR¹⁰ should be applied to only COVID-19 hospitals that treat established RT-PCR positive patients where imaging can be supplanted with portable chest radiographs whenever required.



A



B

Fig. 7 (A) Plain radiograph chest and CAD4COVID score of 61 in a Group B non-COVID-19 patient of H1N1 pneumonia. (B) HRCT chest with COVID-19 analysis showing focal GGO in the left lung with COVID-19 similarity of 0, ruling out COVID-19 as a cause. CAD4COVID, computer-aided detection for coronavirus disease-2019; COVID-19, coronavirus disease-2019; GGO, ground-glass opacities; HRCT, high-resolution computed tomography.

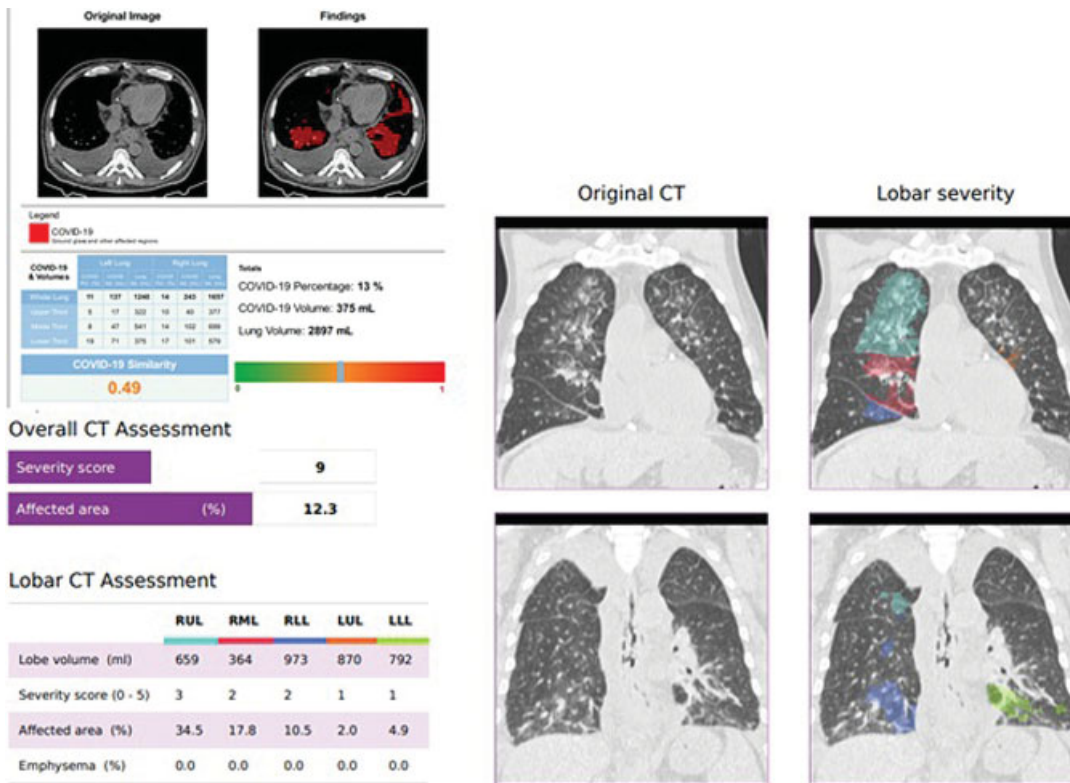


Fig. 8 Group B non-COVID-19 patient with pulmonary edema and pleural effusions with ground-glass opacities with COVID-19 similarity of 0.49 on AI with a severity score of 9 triaged to non-COVID-19 ICU. AI, artificial intelligence; COVID-19, coronavirus disease-2019; ICU, intensive care unit.

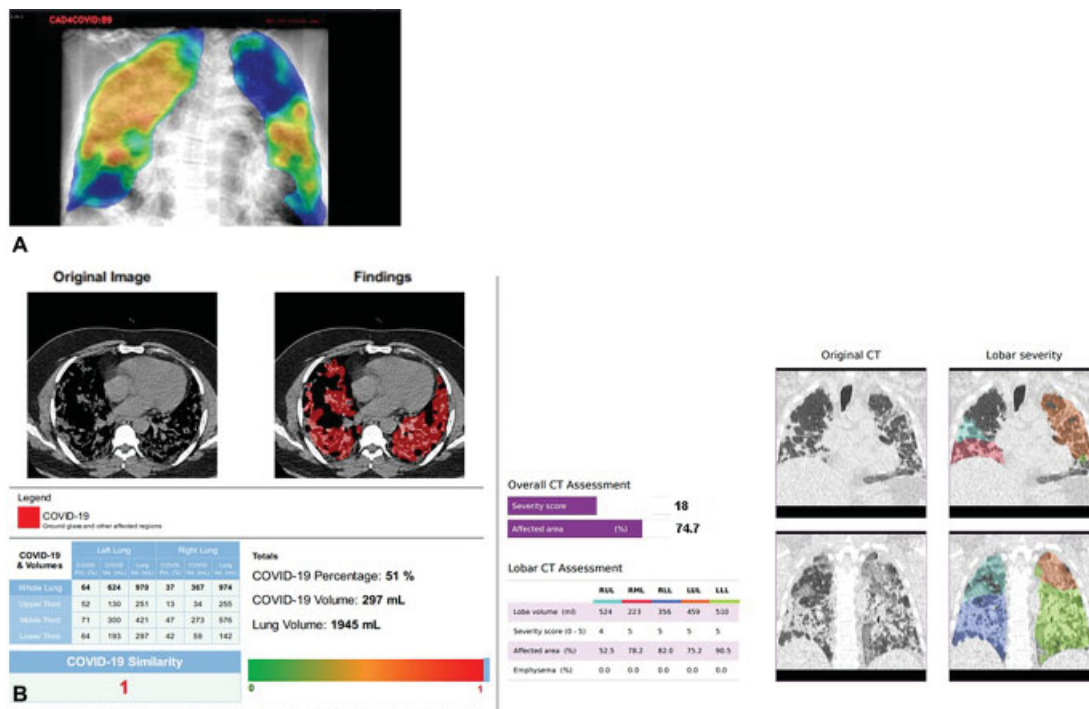


Fig. 9 (A) Group B COVID-19 patient showing CAD4COVID score of 89. (B) Same patient showing HRCT AI analysis with COVID-19 similarity of 1.0 with a CT severity score of 18 categorized as severe disease and triaged to COVID-19 ICU. AI, artificial intelligence; CAD4COVID, computer-aided detection for coronavirus disease-2019; COVID-19, coronavirus disease-2019; CT, computed tomography; HRCT, high-resolution computed tomography; ICU, intensive care unit.

Table 6 The correlation of computed tomography severity scores with severity scores

S.no.	CT Severity Score	No. of patients	Spo2	Pao2/Fio2
1	Less than 9	554	95-100%	>400
2	10 to 14	231	88-94%	360-400
3	Above 14	40	<88%	100-350

Table 7 The sensitivity and specificity analyses of CAD4COVID analysis on plain radiographs. CAD4COVID, computer-aided detection for coronavirus disease 2019

n	3235		
	CAD4COVID		
	Abnormal +	Normal -	Total
Abnormal +	1004	7	1011
Normal -	22	2202	2224
Total	1026	2209	3235
Sample prevalence	0.317		
		95% CI	
Sensitivity - TP proportion	0.979	0.968 to 0.987	
Specificity - TN proportion	0.997	0.993 to 0.999	
FP proportion	0.003	0.001 to 0.007	
FN proportion	0.021	0.013 to 0.032	

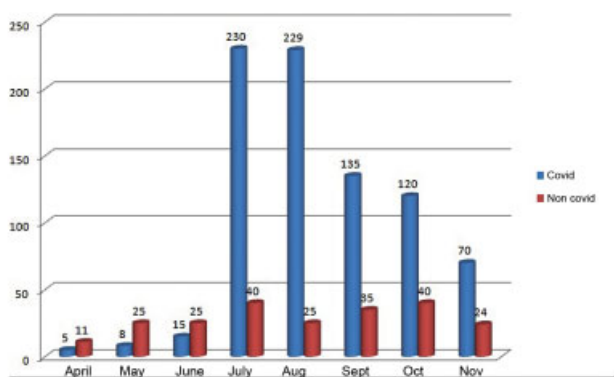


Fig. 10 Bar chart showing the monthly distribution pattern of coronavirus disease-2019 (COVID-19) and non-COVID-19 infections.

To conclude, this study demonstrates that the use of AI-based analysis using chest radiographs followed by HRTC with AI analysis is an accurate, cost-effective, and quicker way to evaluate patients with flu-like presentation and helps to triage them for early and proper management. This algorithm of evaluation for asymptomatic population may be even more valuable and economical in countries with limited RT-PCR testing resources.

Conflicts of Interest

There are no conflicts of interest.

Acknowledgments

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