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Original Research Article

Radiological Features on HRCT Associated with Poor Outcomes among COVID-19 Patients

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Abstract

Background: Ever since the beginning of the COVID-19 pandemic, physicians started investigating the clinical features and lab markers that can assist in predicting the outcome among hospitalized COVID-19 patients.

Aim: This study aimed to investigate the association between initial chest CT scan findings and adverse outcomes of COVID-19.

Material and Methods: This was a single centre; hospital (inpatient) based prospective cohort study involving 497 COVID-19 patients admitted to the hospital. The adverse outcome included death and mechanical ventilation. We collected data about 14 identifiable parameters available for the HRCT scan.

Result: Among 14 studied parameters, only 8 features differed significantly among the patients who had favourable and unfavourable outcomes. These features included number of lobes of lungs involved (3 versus 5, p = 0.008), CT Severity score (16 versus 20, p = 0.004), air bronchogram (p=0.003), crazy paving (p=0.029), consolidation (p=0.021), and pleural effusion (p=0.026). We observed that high CT scores coupled with the diffuse distribution of lung lesions were responsible for poor prognosis in most patients.

Conclusion: Several features of HRCT when combined can accurately predict adverse outcomes among participants and help in triaging the patient for admission in ICU.

Keywords: COVID 19, Clinical Features, Mortality, Morbidities.

Introduction

During the global spread of COVID-19, it was quickly realised that most COVID-19 patients recover without any complications or long-term disability[1]. Simultaneously it was also realised that only a small proportion of all COVID-19 positive patients suffer from a severe disease marked by acute respiratory failure requiring assisted ventilation[1]. Therefore, various waves of COVID-19 were marked by saturation of hospitals including Intensive Care Unit (ICU) beds [2-4]. During the sudden surge in the number of COVID-19 cases, especially at the peak of a COVID-19 wave and the limited number of hospital beds especially the ICU beds, physicians were faced with an ethical dilemma in prioritizing patients for admission to hospitals and ICU beds[5-7]. Sometime after the pandemic began, Physicians, Pathologists, and Radiologists started looking for clinical clues that can assist in predicting the outcome among hospitalized COVID-19 patients. Several large-scale hospital-based studies reported clinical characteristics, laboratory markers, radiological features and outcomes among hospitalized patients suffering from COVID-19 [8-11]. These studies suggested that COVID-19 is associated with significant inflammation of various organ systems of the body resulting in neurologic, cardiovascular, coagulation, and other end-organ manifestations [8-11]. Several prognostic models were built based on these parameters to predict the severity and outcome among patients. The prognostic models were developed on three fronts: clinical features, laboratory markers, and radiological features[9,11,12]. The radiological models were built around the changes in lungs seen either on X-ray and/or CT-Scan [13,14].

As mentioned earlier one of the hallmarks of COVID-19 is extensive involvement of the pulmonary system culminating in ARDS leading to respiratory failure and unfortunately death among a significant proportion of all hospitalized patients[15]. The extent of lung involvement may assist the physician in triaging and risk stratification of patients to decide who will benefit from treatment. Thus, radiologic investigation including chest X-rays and CT -scans can assist in assessing the degree of pulmonary involvement in the earlier stage of COVID-19. The empirical studies suggest that chest x-ray is inappropriate for determining the prognosis and risk stratification of COVID-19 patients [16,17]. On the other hand, retrospective studies conducted till now reported that the sensitivity of chest CT for COVID-19 pneumonia is much superior to a chest x-ray [18,19]. Moreover, few studies even suggest that CT-scan’s sensitivity may even be better than Polymerase Chain Reaction (PCR) [18]. This is because there is always a delay in obtaining the results from the PCR test, the results of the CT scan are available almost immediately. Perhaps the most crucial advantage of the CT scan over other diagnostics modalities is that it can assist in the differential diagnosis of the presenting complaint including confirming alternative diagnoses [20-22]. Hence, we designed this study intending to examine the findings of a High-Resolution CT-Scan at the time of admission with the clinical outcome among hospitalized COVID-19 patients. The purpose of this study is to draw specific patterns and also to identify the features and of lung abnormalities on admission for timely therapeutic strategy, better clinical decisions, , and reduce mortality.

Material and Methods

Study Design: This was a hospital-based, single-centre, prospective, observational study.

Study Settings: The present study was conducted at the Department of Pulmonary Medicine, LN Medical College, Bhopal. It is a tertiary care institute.

Study Duration: The total duration of the study was 18 months.

Study Outcomes: Primary outcome parameters were the radiological changes/features on High-Resolution CT scans among the COVID-19 patients. The secondary objective of the study was to classify COVID-19 diagnosed patients based on the CO-RADS Score[23,24].

Sample Size Calculation: We enrolled all participants fulfilling the selection criteria in the present study. Following this approach, we recruited 524 participants for the present study.

Case Definition: A patient presenting with signs and symptoms suggestive of COVID-19 and fulfilling the below-mentioned selection criteria.

Inclusion Criteria:

1. Age>= 18years
2. Patients tested COVID-19 positive on RT PCR.
3. Laboratory confirmed RAT positive.
4. The patient admitted to the inpatient department.
5. Patients gave consent to participate in the study.

Exclusion Criteria:

1. Women patients who were pregnant.
2. Patients without the known outcomes i.e., LAMA, referred out etc.
3. Contraindications to CT scan.

Informed Consent: A bi-lingual (Hindi & English) consent form was drafted following the prescribed guidelines for research on human participants. The contents of the consent form were explained to all the prospective participants. All the questions from participants about the study, procedure, follow-up, and data privacy were answered. The participants were informed and explained that they have the right to withdraw from the study at any point in time.

Data Collection: The data were collected through a paper-based proforma. The proforma had three parts: (i) Clinical findings. (ii) Laboratory findings and (iii) Radiological findings.

Source of Data: There were two data sources. First was the interview with the participants containing details about the demographic details, clinical history, symptoms, signs, and previous treatments (if any). The second source of the data was clinical records containing details about the clinical examination, laboratory & radiographic findings.

High-Resolution CT scan: The patients underwent HRCT during deep inspiration breath-hold in the supine position. The CT scans were collectively evaluated by two experienced (>10 years) radiologists, who were blinded to the patient's status. The following imaging characteristics were recorded: ground glass opacity, consolidation, reticular pattern, lesions distribution (peribronchovascular or peripheral), side of lung involvement, crazy paving,pleural effusion, number of lung zones involved, cavity and tree-in-bud pattern[23,24].The CT severity score (CSS) for each patient was calculated based on the percentage of lung zone involvement. In this regard, the right and left lungs were divided into three (upper, middle, and lower)and two (upper and lower) zones, respectively[24]. The scoring system was as follows: score 0 representing no involvement, score 1 representing < 5% involvement, score 2 representing 5–25% involvement, score3 representing 26–50% involvement, score 4 representing51–75% involvement, score 5 representing >75% involvements. Finally, the sum of the scores yielded the total CSS, ranging from 0 to 25[24].

Statistical Analysis Plan

The primary outcome was the radiological features among laboratory-confirmed COVID-19 patients admitted to our institute. We aimed to identify from the collected data the radiological features among patients having adverse/terminal outcomes. The data were analysed using Stata 17.1 version. For the interval and ratio data types, the author calculated the mean, median, mode, and standard deviation[25]. For the nominal and ordinal data, the author calculated the frequency, percentage, and proportion. The interval and the ratio data variables were analysed using a student's t-test test. Categorical variables were analysed using chi-square (χ^2) tests[26]. A P-value < 0.05 was considered statistically significant.

Results

During the period of the study, a total of 934 COVID-19 patients came to the emergency/inpatient department of the institute. After clinical and laboratory examination, about 387 COVID-19 patients were recommended home isolation and 547 patients were admitted to the hospital. Out of 547 admitted patients, 23 were excluded using the selection criteria and 524 COVID-19 patients were enrolled in the present study. Of the 524 enrolled participants, the clinical outcome wasn't available for 27 patients. Thus, data on only 497 patients were included in the present study.

Overall, the mean age of the participants was 57.7 (±8.6) years. Further, of the total participants, 194 (39%) were female and 303 (61%) were male. Among the study participants: 35.2% had diabetes, 21.3% had hypertension, 20.1% were smokers, 26.4% had pre-existing pulmonary disease, and 22.7% had a history of CVD. Collectively, about 12.9% of participants had multiple morbidities. Overall, 26% required admission to the ICU and 4.1% required mechanical ventilation. Lastly, 32 (6.4%) died because of COVID-19-related complications.

Table 1: Descriptive Characteristics of Study Participants (n=497)

Variable	Favourable Outcomes (n=465)	Adverse Outcome (n=32)	P-value
Age			
Mean (±SD)	52.3(±SD)	66.7(±SD)	0.039
Gender			
Male	283 (93.4%)	20 (6.6)	0.078
Female	182 (93.8%)	12(6.2)	
Co-Morbidity			
History of CVD	96 (20.6%)	17 (53.1)	0.032
H/O Pulmonary Disease	120 (25.9%)	11(34.3)	0.081
Diabetes	153 (33.3%)	22 (68.6)	0.064
Hypertension	88 (18.8%)	18 (56.3)	0.037
BMI	25.8	29.3	0.078
Obese	85 (18.2%)	24 (66.7%)	0.008
Chronic Renal Disease	37 (7.9%)	6 (18.7%)	0.042
Smoker	78 (16.8%)	22(68.6%)	0.024

Table 1 illustrates the descriptive characteristics of the participants. The mean age of the participants who had favourable and adverse outcomes were 52.3 and 66.7 years, respectively (p=0.039). Most of the patients with unfavourable outcomes were multimorbid: 24 (66.7%) with an unfavourable outcome and 40 (8%) with favourable outcome (p=0.003). The mean BMI among the participants with favourable and unfavourable outcomes was 25.8 and 29.3 Kg/sqm (p=0.078).

Table 2 illustrates the radiological findings of the HRCT. Among all the features identified on the HRCT, the features that differed significantly were the number of lobes involved (3 versus 5), CT Severity score (16 versus 20), and air bronchogram (58% versus 97%), crazy paving (47.5% versus 68.8%). The HRCT features that didn't differ significantly among the survivors and non-survivors: ground glass opacity (91% versus 87.5%), reticular pattern (34% versus 39%), bilateral lung involvement (81% versus 90.6%), presence of diffuse lesions (45% versus 56%).

Table 2: Radiographical Features identified on HRCT scan (n=497)

CT- Feature	Favourable Outcomes (n=465)	Adverse Outcome (n=32)	P-value
Ground Glass	424 (91%)	28 (87.5%)	0.066
Consolidation	254 (54.6%)	30 (93.8%)	0.021
Reticular Pattern	159 (34.1%)	13 (39.1%)	0.068
B/L Lung involvement	377 (81%)	29 (90.6%)	0.092
Crazy Paving	221 (47.5%)	22 (68.8%)	0.029
Pleural effusion	103 (22.1%)	15(46.9%)	0.026
Peri-bronchovascular Lesions	98 (21.1%)	17 (53.1%)	0.026
Diffuse Lesions	212(45.6%)	18 (56.3%)	0.068
Interlobular septal thickening	282 (60.6%)	29 (90.6%)	0.042
Air bronchogram	273 (58.7%)	31 (96.9%)	0.003
Pleural effusion	103 (22.1%)	17 (53.1%)	0.032
Emphysema	131 (28.2%)	14 (43.8%)	0.073
Number of Lobes involved (median)	3	5	0.008
CT- Severity Score (median)	16	20	0.004
CT-Score >=18	179 (38.5%)	23 (71.9%)	0.011

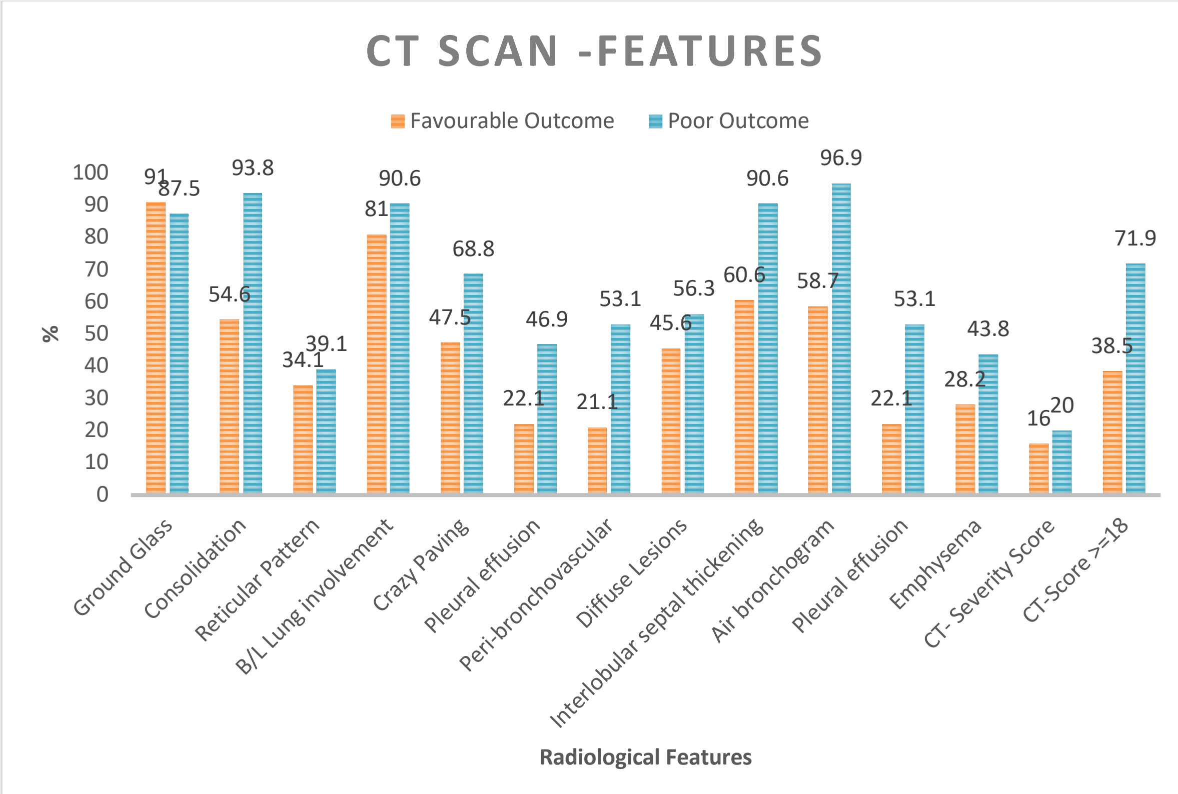

Figure 1: Radiological features on CT scan

Discussion

The ability of the novel SARS-Corona-2 virus to infect a significant proportion of the population at the same time and saturate hospital, especially intensive care unit beds forced physicians to devise a triage mechanism. This was needed to prioritize patients who required urgent care and those who would benefit most from admission to hospitals including ICU. This was necessary because COVID-19 disease is relatively a new disease [27], and the constellation of clinical features [28] including laboratory markers and radiological findings is constantly evolving with the ever-increasing availability of information[29-31]. For triaging patients for hospital admission, physicians started using every information and tool available to them including the severity of presenting complaints, levels of various laboratory markers, and radiological findings [29-31]. Preliminary findings suggested that severe cases of COVID-19 are marked by a myriad of pulmonary complications including features similar to the advanced stages of viral pneumonia superimposed with secondary bacterial infections [10]. Traditionally physicians and pulmonologists have relied on chest HRCT to identify the extent of damage to the lungs from pneumonia. Therefore, it has been postulated that COVID-19-related lung damage/changes can also be best visualized on chest HRCT [32-34].

In the present study, we investigated the potential predictive ability of initial chest HRCT scan findings on the adverse clinical outcomes among COVID-19 positive patients admitted to the hospital. Concerning the adverse outcomes of COVID-19, we assessed whether the initial CT scan findings inform ICU admission, mortality, and disease severity. Our study is one of the many research in a series of studies that investigated the ability of HRCT on admission to predict the development of adverse complications. In the present study, we systematically recorded, reported, and studied a total of 14 radiological parameters identified on chest HRCT among 497 COVID-19 patients admitted to the hospital.

Among 14 studied parameters, only 8 features differed significantly among the patients who had favourable and unfavourable outcomes. Among these features were number of lobes of lungs involved (3 versus 5, p = 0.008), CT Severity score (16 versus 20, p = 0.004), air bronchogram (58% versus 97%, p=0.003), crazy paving (47.5% versus 68.8%, =0.029), consolidation (54% versus 93%, p=0.021), and pleural effusion (22% versus 46%, p=0.026). Our results suggest that high CT scores coupled with the diffuse distribution of lesions in lung on admission were responsible for ARDS and a poor prognosis in many patients. In the study by Liu *et al*., which also used this criteria as the this study used for the disease severity (WHO), the number of lung lobes involved, and total CT score were directly correlated to disease severity[33]. In contrast to our findings, Auger *et al*. reported that consolidation and crazy paving, did not have a significant association either with mortality or invasive endotracheal [35]. However, Auger *et al*. also observed that the number of lung zones involved was associated with invasive endotracheal ventilation, but not with death[35]. Abdollahi *et al*. conducted a retrospective study in Egypt and reported that number of lung zones involved ,peri-bronchovesicular distribution of lesions, and total CSS were all associated with an increased risk of death and Mechanical ventilation [36]. Moreover, Abdollahi *et al*. also reported that the consolidation was demonstrated to predict severe COVID-19 disease [36]. In contrast to our findings, Abdollahi *et al* observed that the number of lung zones involved did not predict the adverse outcome[36]. Similar to our study, Liu S *et al*., reported that the odds of adverse outcome (need for mechanical ventilation or mortality) is four times higher in patients with more than four lung zones involved than in those without [33].

The HRCT features that didn't differed significantly among the survivors and non-survivors: ground glass opacity (91% versus 87.5%, p=0.066), reticular pattern (34% versus 39%, p= 0.068), bilateral lung involvement (81% versus 90.6%, p=0.092), presence of diffuse lesions (45% versus 56%). In contrast to our findings, Xu *et al*. reported a COVID-19 patient death with diffuse lung involvement on X-ray images and pathological findings of pulmonary oedema and clear film formation on lung biopsy samples [37]. Similar to our findings, Auger *et al*. reported that ground glass opacity did not have a significant association either with invasive endotracheal ventilation or mortality[35].

Comparatively, we noticed several conflicts and contrasts between our findings and several other studies. These differences in radiological findings can be attributed to several factors. First, the pathological changes in the lung are time-dependent [22,38]. In our study, we observed that those who were brought/came to the hospital within one week of the onset of symptoms had less severe changes on HRCT and consequently had a favourable outcome. In comparison, those who were brought to our hospital one week after the onset of symptoms had extensive findings on HRCT and had an unfavourable outcome. Like our study, Bernheim *et al* found that CT results can be negative in the early stages of COVID-19[22]. Thus, future studies should also investigate the influence of the duration of symptoms on the HRCT findings and clinical outcomes.

Secondly, the findings of HRCT are also influenced by the presence of pre-existing morbidity and smoking status[30]. In our study, we observed extensive HRCT findings among patients who smoked tobacco for more than 10 years. Lastly, the findings of HRCT were also influenced by the age of the patient [30,39,40]. It is widely known that there are several age-related changes (e.g., fibrosis or calcification) in the lungs reflecting the accumulation of previous disease, dust, smoke, and surgical interventions[30,39,40]. This is especially true for India because of the high prevalence of tuberculosis and high air pollution, especially in urban areas. All these factors could explain the difference in our findings and other studies.

However, despite these differences, a high CT chest severity score consistently predicted poor outcomes among patients in most of the studies including the present study. Thus, we recommend that a cut-off score or a threshold for CSS should be defined to differentiate high-risk from low-risk patients. In the present study, we considered a threshold for the unfavourable outcomes (CSS > 17) and observed a relatively strong association with poor outcome(s). Cao Y *et al*. also reported that a high CT lung severity score was a sign of poor prognosis and was associated with short-term mortality [41]. Like our study, Zhao *et al*. reported that the CT involvement score can help evaluate the severity and extent of COVID-19 [34]. Lei *et al*. showed that a higher CT score was associated with an increased odd of mortality, which agreed with our results [42].

The strength of the present study includes its large sample size, the inclusion of RT-PCR-positive patients, and the involvement of two independent radiologists in assessing the pulmonary changes. A limitation of this study was that we only used the initial CT scan without repetition. Also, we did not incorporate the influence of supportive therapy on the outcome among patients. Thus, it is suggested to perform longitudinal studies to prospectively re-evaluate the patients with more details for testing generalizability.

Conclusion

HRCT is an excellent tool for triaging patients especially for admission to the ICU. Although, no single parameter or feature on HRCT can predict adverse outcome with absolute certainty. However, constellation of radiological feature when combined and CT severity score can predict the adverse outcome with reasonable accuracy.

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