Chapter 13
Predicting the COVID-19 Patients Status Using Chest CT Scan Findings: A Risk Assessment Model Based on Decision Tree Analysis

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Abstract

Background

The role of chest computed tomography (CT) to diagnose coronavirus disease 2019 (COVID-19) is still an open field to be explored. The aim of this study was to apply the decision tree (DT) model to predict critical or non-critical status of patients infected with COVID-19 based on available information on non-contrast CT scans.

Methods

This retrospective study was performed on patients with COVID-19 who underwent chest CT scans. Medical records of 1078 patients with COVID-19 were evaluated. The classification and regression tree (CART) of decision tree model and *k*-fold

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cross-validation were used to predict the status of patients using sensitivity, specificity, and area under the curve (AUC) assessments.

Results
The subjects comprised of 169 critical cases and 909 non-critical cases. The bilateral distribution and multifocal lung involvement were 165 (97.6%) and 766 (84.3%) in critical patients, respectively. According to the DT model, total opacity score, age, lesion types, and gender were statistically significant predictors for critical outcomes. Moreover, the results showed that the accuracy, sensitivity and specificity of the DT model were 93.3%, 72.8%, and 97.1%, respectively.

Conclusions
The presented algorithm demonstrates the factors affecting health conditions in COVID-19 disease patients. This model has the potential characteristics for clinical applications and can identify high-risk subpopulations that need specific prevention. Further developments including integration of blood biomarkers are underway to increase the performance of the model.

Keywords Chest CT scan without contrast · Coronavirus disease · COVID-19 · Disease outcome · Decision tree

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1 Introduction

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which causes coronavirus 2019 (COVID-19) disease appears to have emerged at the Huanan Seafood Market in Wuhan, China [1, 2]. On March 11, 2020, this disease was declared as a pandemic by the World Health Organization (WHO) [3]. As of October 18, 2022, COVID-19 has affected virtually all countries and territories of the world, through successive outbreaks of SARS-CoV-2 variants of differing virulence [4]. To date, more than 630 million confirmed COVID-19 cases and 6.5 million deaths have been reported in the world [5]. The first reported COVID-19 case in Iran was identified in Qom on February 19, 2020 [6]. Since that time the number of Iranian cases has risen to over 7.5 million with more than 144 thousand deaths [5].

COVID-19 can lead to respiratory infection, liver disease, gastrointestinal and neurological disorders [7, 8]. In addition, the virus can cause respiratory conditions such as pneumonia, pulmonary edema, and acute respiratory distress syndrome (ARDS) [9]. For this reason, imaging tools such as non-contrast chest computed tomography (CT) scanning have been applied as an unambiguous tool in diagnosis quantification and follow-up of patients with COVID-19 [10]. The lungs of patients with COVID-19 symptoms show visual hallmarks, such as ground-glass opacities (GGOs) and areas of increased lung density called consolidation [10]. Furthermore, patients with more severe forms of the disease have shown more extensive effects with increasing time from onset of symptoms such as linear opacities, a crazy-paving pattern, reverse halo signs, pleural effusion, intralesional traction bronchiectasis, and lymphadenopathy [11, 12].

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Classification and regression tree (CART) decision tree (DT) analysis is a data mining technique used for establishing classification in systems based on multiple covariates or for developing prediction algorithms for a target variable [13]. The analysis has been widely applied in medicine and public health. Moreover, the DT model is a strong statistical method for classifying, predicting, interpreting, and processing data. The algorithm can be considered as nonparametric and can efficiently manage large, complex datasets without imposing a complex parametric structure. Furthermore, both heavily skewed data and missing values are easily managed without the need for data transformation. Numerous factors have been shown to influence the conditions of COVID-19 patients such as specific signs on high-resolution computed tomography (HRCT), lesion type, presence of diffuse opacity, age, and gender. The computer-based model can be graphically represented as a tree structure that makes the interpretation easy and useful in clinical approaches. In addition, the algorithm has numerous merits including the capability of splitting sequential data into the best predictive groups [14].

The aim of the current retrospective study, with such a large sample size population, was to apply the CART decision tree model to predict critical/non-critical status of patients with COVID-19 based on chest CT findings. We also attempted to identify independent risk factors in the patients. Additionally, receiver operating characteristic (ROC) analysis was applied to assess the ability of DT model for the prediction of critical and non-critical status.

2 Methods

2.1 Study Design and Patients

This was a retrospective study in which we collected both demographic characteristics and radiologic information of 1078 patients with COVID-19, who were referred to Baqiyatallah Hospital, Tehran, Iran, during the first wave of the pandemic, from March to April 2020. The inclusion criteria were (1) positive results on a reverse-transcriptase–polymerase-chain-reaction (RT-PCR) assay of a specimen obtained on a nasopharyngeal swab; (2) having related symptoms (like fever, dry cough, shortness of breath, and aches); and (3) willingness of the patients to participate in the study. The exclusion criteria were (1) logistical impediments to data collection; (2) incomplete data; and (3) revoking of consent [15]. According to patient clinical outcomes, the individuals were divided into two groups as critical and non-critical. Patients admitted to the routine ward of the hospital and then discharged ($n = 909$) were considered as non-critical patients. The critical group included those who died ($n = 104$) or who were admitted to the intensive care unit (ICU) ($n = 65$). This study was approved by the Ethics Committee of Baqiyatallah University of Medical Sciences, Tehran, Iran, with code IR.BMSU.REC.1399.024 and the patients were enrolled after giving written informed consent.

2.2 CT Protocol and Evaluation of Chest CT

The images of non-contrast chest CT scans were acquired using a 16-row detector CT scanner (General Electric GE, Optima, USA), with patients in a supine position and at full inspiration. The detailed parameters for CT acquisition based on a low-dose thoracic CT scan protocol were as follows: tube voltage 100 kVp, 120 mA, slice thickness of 2.5 mm, reconstruction interval of 1.25 mm, pitch 1.75, speed 35 mm/rot, detector configuration 16 × 1.25, computed tomography dose index 3.5 mGy. The findings of CT scans were evaluated by two blinded radiologists who were in agreement with the results of images. The inter-rater coefficient agreement between the two radiologists was $r = 0.98$; $p < 0.0001$. If the radiologists disagreed about the COVID-19 diagnosis, a third party joined the discussion and this was continued until agreement was achieved. According to Fleischner Society Nomenclature recommendations [16, 17], the images of initial chest CT scan were assessed for some features of patients, including GGO (Fig. 13.1) pericardial effusion, crazy-paving pattern (Fig. 13.2), consolidation (Fig. 13.3), pleural effusion,

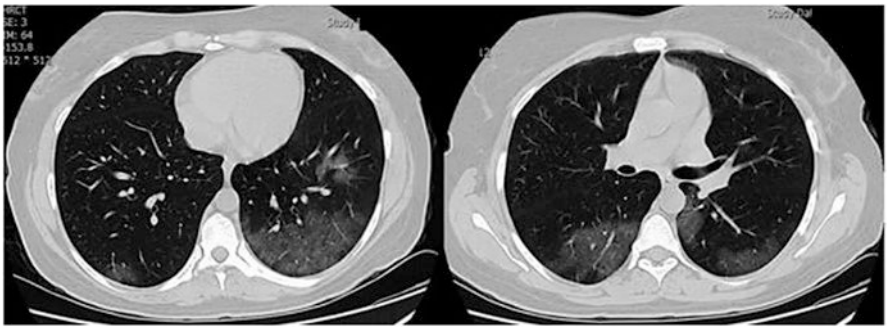

Fig. 13.1 Two axial chest CT scans without contrast show bilateral and multifocal patchy subpleural ground-glass opacities (GGOs) in a patient with COVID-19 pneumonitis

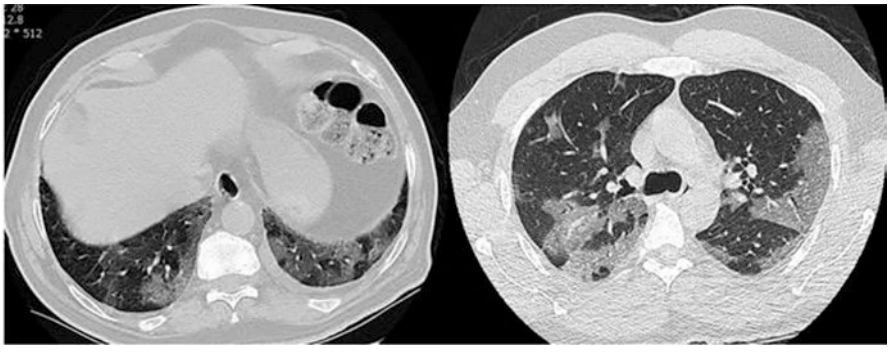

Fig. 13.2 Two axial chest CT scans without contrast show multifocal subpleural patchy ground-glass opacities (GGOs) with interlobular septal thickening (crazy-paving) in lower lobes of both lungs in a patient with COVID-19 pneumonitis

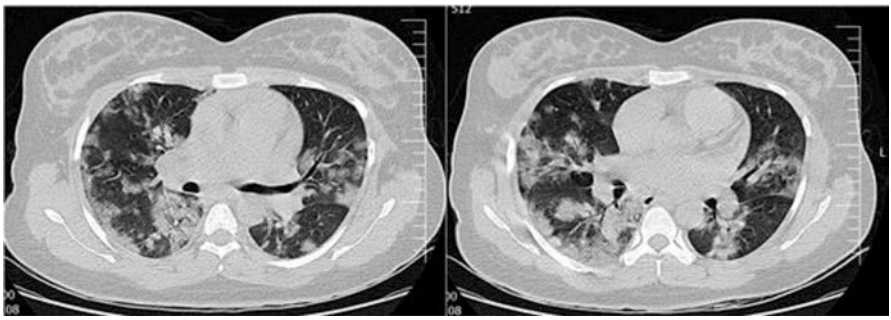

Fig. 13.3 Two axial chest CT scans without contrast showing bilateral and multifocal patchy consolidation in a patient with COVID-19 pneumonitis

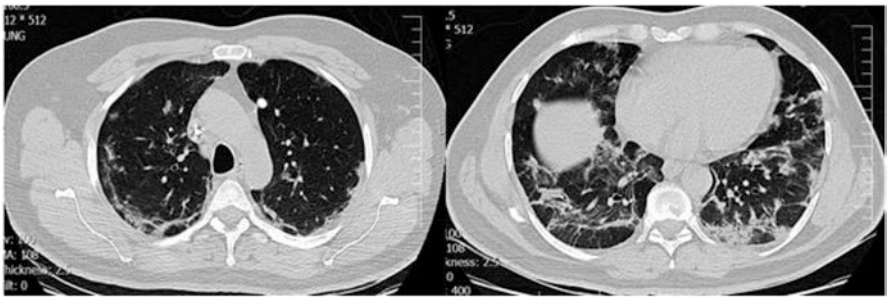

Fig. 13.4 Two axial chest CT scans without contrast show bilateral and multifocal linear opacities with architectural distortion in a patient with COVID-19 pneumonitis

reversed halo sign, linear opacities (Fig. 13.4), intralesional traction bronchiectasis, and lymph node enlargement [16]. Afterward, scores of thin-section CT involvement were assigned based on the abnormal areas involved as a way of measuring the extent of lesions [18]. A score, ranging from 0 to 5, was given to each lobe as follows: 0 (no involvement); 1 (<5% involvement); 2 (25% involvement); 3 (26–49% involvement); 4 (50–75% involvement); and 5 (>75% involvement). A score from 0 to 5 was assigned to each lobe, with a total possible score from 0 to 25.

2.3 Statistical Analysis

The results were described as mean ± SD in continuous variables. In addition, frequency and percentage of categorical variables were reported. The chi-square test was used to evaluate the association between categorical variables and the Mann–Whitney *U* and independent *t* tests were performed to compare means between number of involved lobes and age in the two groups. In addition, the CART method

was used to build a risk assessment model to predict critical/non-critical patient conditions using both demographical and clinical factors, including age, gender, lesion type, specific signs, presence of diffuse opacity, underlying disease, number of involved lobes, and total opacity score. Afterward, the *k*-fold cross-validation method was used to validate the model. The value of *K* was considered equal to 10 and the set of *N* (1078) patients was split into *k* mutually exclusive subsets of size *N*/*k*. Afterward, *k*–1 subsets were used as a training set to fit a model, which was used to predict the left-out validation subset. Next, this process was repeated *k* times, each time excluding a different validation subset and then an estimate of the model performance was calculated from the predicted values. Therefore, each patient was included in a validation set once and *k*–1 times in the training sets. Lower *k* values typically led to estimates of prediction error biased upward and higher *k* values minimized bias but increased variance [19, 20]. In the DT analysis, each fork was split into a predictor variable and each end node contained a prediction for the outcome variable. Additionally, ROC analysis was performed to assess the ability of DT model for prediction of critical and non-critical condition. The level of significance for statistical tests was 0.05. The R-4.0.0 software (dtree package) was used for statistical analysis.

3 Results

The study population consisted of 1078 confirmed patients with COVID-19 who underwent CT scans including 169 critical and 909 non-critical subjects. The baseline characteristics and chest CT features according to critical and non-critical status are given in Table 13.1. The age of participants in the critical group was significantly higher than those in the non-critical group (61.24 ± 13.48 vs. 51.47 ± 14.02, $p < 0.001$). The frequency of the involved lobe number in the non-critical group was higher than that in the critical group, except for the number of lymph nodes less than 1, which was significantly different between the groups ($p < 0.001$). The results showed that there was a significant relationship between gender, lesion distribution, lesion type, specific HRCT signs, presence of diffuse opacity, and underlying disease ($p < 0.001$).

The DT derived from CART analysis is shown in Fig. 13.5. This had a depth of three levels from the root node and three intermediate nodes, including six terminal nodes. Each node represented the probability of being critical/non-critical for the corresponding branches. This shows that in order to predict patient status, the total opacity score should be bifurcated at a score of 7.5. If the value was more than 7.5, the lesion type was checked in the next step. If this value was less than 7.5, age was bifurcated at 62.5 (years). Then, comparisons with the presented variables continued at each node split to reach a branch, to predict either the critical or non-critical status of the patient. The number and percentage of cases that we obtained using this model are presented at the end of each branch.

Table 13.1 Baseline characteristics and chest CT features in patients with COVID-19 based on critical and non-critical status

Parameter	Critical patients (n = 169)	Non-critical patients (n = 909)	Total patients (n = 1078)	p-Value
Age (years), mean±SD	61.24 ± 13.48	51.47 ± 14.02	53 ± 14.37	<0.001[a]
Total opacity score, mean±SD	13.71 ± 6.26	4.86 ± 3.52	6.24 ± 5.19	<0.001[a]
Male gender, n (%)	123 (72.8)	614 (67.5)	737 (68.4)	0.179[b]
Lesions distribution, n (%)				<0.001[b]
Bilateral + multifocal	165 (97.6)	766 (84.3)	931 (86.4)	
Others	4 (2.4)	143 (15.7)	147 (13.6)	
Lesions type, n (%)				
GGO*	13 (7.7)	401 (44.1)	414 (38.4)	<0.001[b]
GGO + crazy paving	19 (11.2)	114 (12.5)	133 (12.3)	0.637
Consolidation	12 (7.1)	30 (3.3)	42 (3.9)	0.019
GGO + Consolidation	125 (74)	364 (40)	489 (45.4)	<0.001
Specific signs of HRCT#, n (%)				
None	78 (46.2)	617 (67.9)	695 (64.5)	
Liner opacity	24 (14.2)	150 (16.5)	174 (16.1)	0.455[b]
Reversed halo sign	6 (3.6)	43 (4.7)	49 (4.5)	0.499
Pleural effusion	34 (20.1)	21 (2.3)	55 (5.1)	<0.001
Intralesional traction bronchiectasis	17 (10.1)	44 (4.8)	61 (5.7)	0.007
Lymphadenopathy	10 (5.9)	34 (3.7)	44 (4.1)	0.189
Presence of diffuse opacity, n (%)				
Yes	118 (69.8)	63 (6.9)	181 (16.8)	<0.001[b]
No	51 (30.2)	846 (93.1)	897 (83.2)	
Number of involved lobes, n (%)				<0.001[c]
0	51 (30.2)	846 (93.1)	897 (83.2)	
1	1 (0.6)	5 (0.6)	6 (0.6)	
2	33 (19.5)	10 (1.8)	49 (4.5)	
3	35 (20.7)	15 (1.7)	50 (4.6)	
4	30 (17.8)	13 (1.4)	43 (4)	
5	19 (11.2)	14 (1.5)	33 (3.1)	
Underlying disease, n (%)				
None	159 (94.1)	882 (97)	1041 (96.6)	
Pulmonary	1 (0.6)	6 (0.7)	7 (0.6)	0.919[b]
Cardiac	8 (4.7)	20 (2.2)	28 (2.6)	0.057
Kidney	1 (0.6)	1 (0.1)	2 (0.2)	0.289

*GGO ground-glass opacities, #$HRCT$ high-resolution computed tomography
[a]Independent t test
[b]Chi-square test
[c]Mann–Whitney U test

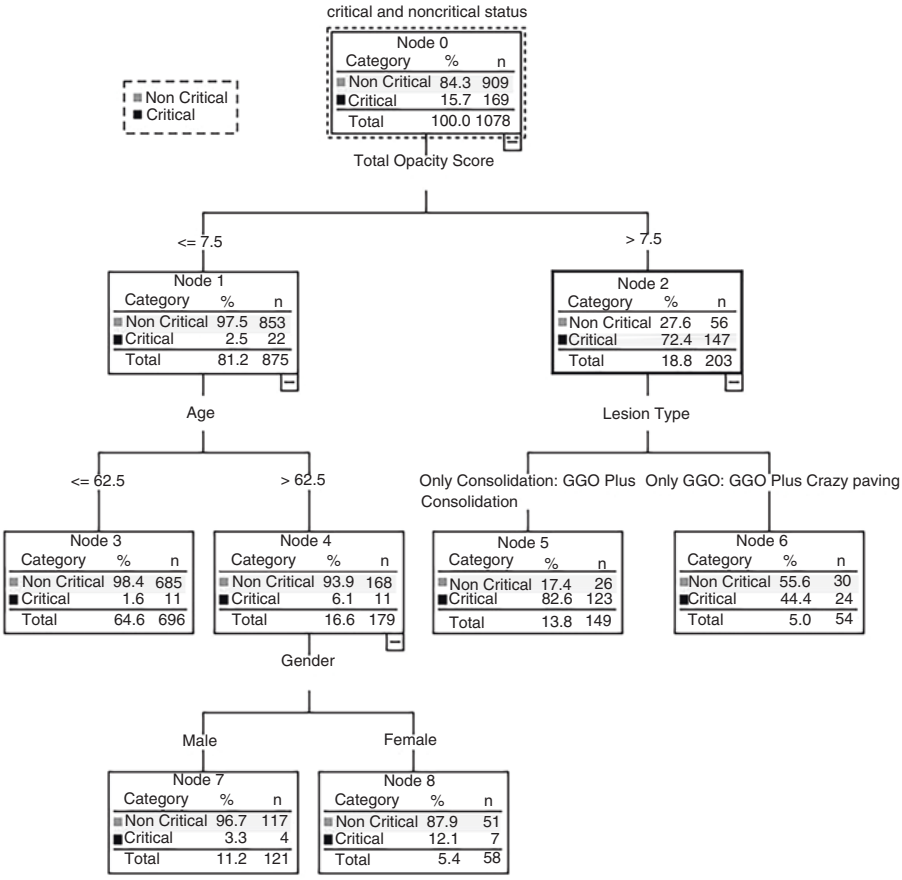

Fig. 13.5 Decision tree predicting the risk for critical or non-critical situation of patients with COVID-19

The use of DT model showed that 72.8% with a critical condition (sensitivity) and 98% of patients with a non-critical status (specificity) were correctly predicted. Also the accuracy index which showed the percentage of true prediction of the patient conditions was 93.3 (accuracy). The risk estimate showed that the proportion of cases that were incorrectly classified was 0.068 (standard error = 0.008).

Based on Fig. 13.6, the ROC analysis of the DT showed excellent performance in predicting the status of patients with COVID-19. The area under the ROC curve (AUC) of the CT-derived opacity score was 0.93 (95% confidence interval 0.91–0.96; $p < 0.001$).

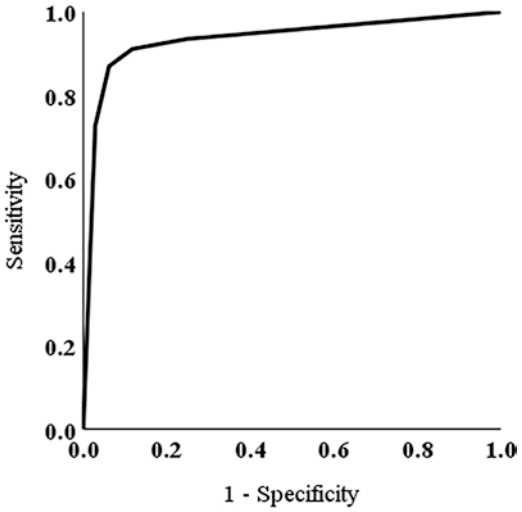

Fig. 13.6 ROC curve for DT, AUC = 93%

4 Discussion

This report describes a means of predicting COVID-19 disease status, which fits with the concept that early diagnosis can aid in patient assessment for enabling the appropriate therapeutic intervention, if needed [21]. Here, we have provided a quantitative means of assessing chest CT imaging as an indicator of signs related to disease advancement, including increase in GGOs, interstitial septal thickening, and consolidative opacities [22].

We found that linear opacities, pure GGOs, mixed GGOs with consolidation, and mixed GGOs with crazy-paving pattern were the most frequent types of lesions with bilateral and multifocal distributions. The total opacity score, number of lung lobes involved, and presence of diffuse opacity were regarded as noticeable variables by data mining. In the DT model, we considered that if the variable scored lower than 7.5, the next essential variable will be age. Using the total opacity score with a score greater than 7.5, along with lesion type as GGOs plus consolidation, we found that the occurrence of the critical condition would give a score of 82.6. It is worth mentioning that when the total opacity score is less than 7.5 and the age of the patient is less than 62.5, the predicted percentage of patients with a non-critical status would be 98.4.

In our study, the difference in age between the two groups was statistically significant consistent with reports that age is one of the most significant risk factors for severe COVID-19 disease outcomes [23–25]. Similar to other chest CT studies, we observed bilateral lung involvement in most of the patients and a reversed halo sign in a small number of patients in both groups [26, 27].

In both groups of this study, the common types of lesions were mixed GGOs with consolidation, mixed GGOs with crazy-paving pattern, liner opacities, and pure GGOs. The frequency of pure consolidation and mixed GGOs with

consolidation lesions showed a significant difference between the groups, being more common in critical patients than in non-critical patients. This implies that the virus has diffused into the respiratory epithelium where it can cause necrotizing bronchitis and diffuse alveolar damage in the critical patients [28]. Also, critical patients showed more intralesional traction bronchiectasis and pleural effusion lesions than the non-critical patients. These extra pulmonary lesions indicate the occurrence of severe inflammation in critical group and are consistent with the findings of other chest CT studies of COVID-19 disease patients [29, 30].

According to our DT model, the total opacity score was the main feature for distinguishing the critical from the non-critical group, with an accuracy of 93.3%. Our findings are consistent with previous studies regarding sensitivity and specificity scores derived from CT imaging of lung lesions of COVID-19 patients [31–33]. However, it is clear that there is considerable scope for further progress in this area in forthcoming studies. One possibility is to incorporate machine learning techniques to extract the most important features for CT image-based classifications, as described in two recent studies [34–36]. As more data become accessible, the procedure described here could be easily repeated to acquire more exact models. We also suggest that further improvements in the predictive performance could be achieved through incorporation of laboratory data into the model. For example, molecular biomarkers could be used to allow determination of the pneumonia-related markers associated with CT features [37–40].

4.1 Strengths and Limitations

The strength of this retrospective study was the large sample size, which enabled a sufficiently powered statistical comparison. Potentially, one of the most important strengths was the use of data derived from chest CT imaging. This is the gold standard method for unambiguous determination of interstitial pneumonia, a distinctive feature of respiratory virus infection [41]. In addition, this method can serve as an additional screening tool to add confidence to a diagnosis, particularly with regard to disease staging [42]. It is also easily implemented and can be particularly valuable in the early stages of a viral outbreak, when molecular diagnostic tools have not been optimized (as seen in the early stages of the current pandemic).

One limitation of this study was that the time of chest CT examination and the onset symptoms were not simultaneous. This made it difficult to summarize the features of a CT scan that could be associated with specific symptoms during the course of the disease. Another limitation was the dependence of this study on the CT and demographic data. The incorporation of data from laboratory biomarker measurements could add further value to the model. For example, point-of-care array devices which provide readouts of circulating molecules associated with the cytokine storm effect could be incorporated into the DT model to increase robustness and performance values [43].

4.2 Conclusion

In summary the results showed that chest CT imaging features were helpful in identifying pulmonary parenchymal abnormalities in patients suspected of having COVID-19 disease. We used the total opacity score as the main feature of the CT results in predicting which patients will develop a critical or non-critical status. The main results of the study showed that 98% of patients with non-critical condition and 72.8% of patients with critical situation were correctly diagnosed. We conclude that the established DT model had high sensitivity and specificity and aided in the identification of risk factors in COVID-19 patients associated with different severity outcomes. We suggest that the use of machine learning approaches with incorporation of molecular and laboratory-based biomarkers will help to improve the performance of the model. Such approaches will help us to manage the current and future pandemics caused by respiratory viruses more effectively.

Availability of Data and Materials

Data are available by contacting the corresponding authors with a reasonable request.

Acknowledgments An early version of this manuscript was submitted as a preprint and is available at https://www.researchsquare.com/article/rs-56387/v3. The present version contains updated information.

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