

Original Article

Additive Value of Computed Tomography Severity Scores to Predict Lengths of Stay in Hospital and ICU for COVID-19 Patients: A Machine Learning Study

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ABSTRACT

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Chest CT severity score;
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Introduction: During the outbreak of COVID-19, most hospitals faced resource shortages due to the great surges in the influx of infected COVID-19 patients and demand exceeding capacities. Predicting the lengths of stay (LOS) of the patients can help to make proper resource-planning decisions. CT-SS accurately determines the disease severity and could be considered an appropriate prognostic factor to predict patients' LOS.

In this study, we evaluate the additive value of CT-SS in the prediction of hospital and ICU LOSs of COVID-19 patients.

Methods: This single-center study retrospectively reviewed a hospital-based COVID-19 registry database from 6854 cases of suspected COVID-19. Four well-known ML classification models including kNN, MLP, SVM, and C4.5 decision tree algorithms were used to predict hospital and ICU LOSs of COVID-19 patients. The confusion matrix-based performance measures were used to evaluate the classification performances of the ML algorithms.

Results: For predicting hospital LOS, the kNN model with an accuracy of 77.1%, sensitivity of 100.0%, precision of 68.6%, specificity of 54.2%, and AUC of around 99.4% had the best performance among the other three ML techniques. This algorithm with 94.4% sensitivity, 74.6% specificity, 84.5% accuracy, 78.8% precision, 85.9% F-Measure, and an AUC of 95.3% had also the best performance for predicting ICU LOS of the patients.

Conclusion: The performances of the ML predictive models for predicting hospital and ICU LOSs of COVID-19 patients were improved when CT-SS data was integrated into the input dataset.

Introduction

During the outbreak of COVID-19, the hospital systems were tremendously overloaded and

there appeared a huge demand for hospital beds.¹ Due to the great surges in the influx of infected COVID-19 patients and demand exceeding capacities, most hospitals faced

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the formation of queues and crowding which usually led to the extended average length of stay (LOS) for infected patients and the increased workload and strain on medical staff.²⁻⁸

The hospital LOS is an efficient indicator to evaluate the treatment management process of patients, as higher morbidity and mortality rates were reported for COVID-19 patients with prolonged LOSs.^{1,2,9} Prediction of the hospital LOS could lead to the optimal allocation of limited hospital resources, providing better healthcare services for patients, and reducing the pressure on health systems.^{1,10,11} Therefore, identifying the most important and relevant factors to predict the hospital LOS and developing an efficient predictive model would have a critical role in battling the COVID-19 pandemic.

Artificial Intelligence (AI) is a well-known analytical technique for making clinical decision support systems (CDSS).^{10,12} These AI-based CDSSs improve patient management and healthcare delivery by providing timely information. Machine learning (ML) as a sub-branch of AI is an efficient method to achieve proper decision-making in healthcare interventions. ML approach extracts useful and practical patterns from a big raw dataset.⁹⁻¹¹

For predicting the LOS of COVID-19 patients in the hospital and intensive care unit (ICU), ML-based models were evaluated in the prior studies.^{1,9-21} In these studies, the ML predictive models were mainly developed using demographics, risk factors, clinical manifestations, and laboratory results. The COVID-19 disease is a very contagious viral infection disease which causes serious lung infection. Its clinical manifestations ranged from asymptomatic or mild flu-like symptoms

to severe complications including potentially respiratory failure, ICU hospitalization, and ultimately death in some cases.^{1,10,11} Chest computed tomography (Chest CT) is an efficient imaging modality with high sensitivity for demonstrating pulmonary pneumonia. Chest CT manifestations of pulmonary pneumonia, especially chest CT severity score (CT-SS), could accurately characterize the extent of the disease and severity of pulmonary involvements.^{22,23} CT-SS accurately determines the disease severity and could be considered an appropriate prognostic factor to predict the amount of patients' need for healthcare services. Therefore, CT-SS might improve the performances of the prognostic ML algorithms to predict hospital and ICU LOSs of patients with COVID-19 pneumonia.

In this study, we evaluate the additive value of CT-SS in the prediction of hospital and ICU LOSs of COVID-19 patients using four ML algorithms including K-nearest neighborhood (kNN), multilayer perceptron (MLP), support vector machine (SVM), and C4.5 decision tree algorithms. The prognostic performances of these well-known ML algorithms are evaluated in the presence and absence of CT-SS data.

Methods

Data set description and participants

This is a single-center study that retrospectively reviewed a hospital-based COVID-19 registry database from Shahid Mostafa Khomeini Hospital, Ilam City, Iran. A total of 6854 cases of suspected COVID-19 were referred to the ambulatory and emergency departments of Shahid Mostafa Khomeini Hospital from January 9, 2020, until January 20, 2021. Of

those, the COVID-19 disease of 1853 cases was confirmed by real-time reverse transcriptase PCR (RT-PCR) test. Only positive COVID-19 patients were included in the study. Patient informed consent was not required due to the retrospective and non-interventional nature of the study.

The exclusion criteria were as follows: Non-COVID-19 cases, non-hospitalized patients, cases with admission time before January 9, 2020, or after January 20, 2021, patients younger than 18 years, and subjects without chest CT data and clear disposition. After applying the inclusion/exclusion criteria, records of 815 COVID-19 patients were entered into the study (Figure 1).

For each patient, 73 features in five main classes were registered. The main classes

of the registered data were demographics (eight variables), clinical manifestations (21 variables), comorbidities (13 variables), laboratory results (28 variables), imaging data (CT-SS), and output variables (two variables as lengths of stay in hospital (Hospital LOS) and ICU (ICU LOS)).

CT-SS determines the severity of pulmonary involvements in CT images. Lung lobes were visually scored as 0, 1, 2, 3, 4, and 5 for no involvement, less than 5% involvement, 5%–25% involvement, 25%–50% involvement, 50%–75% involvement, and more than 75% involvement, respectively. CT-SS was the sum of these scores and ranged from 0 to 25. Two radiologists separately reviewed CT images and any disagreements were resolved through consulting with an attending radiologist with 23 years of experience. Figures 2 - 5 show the

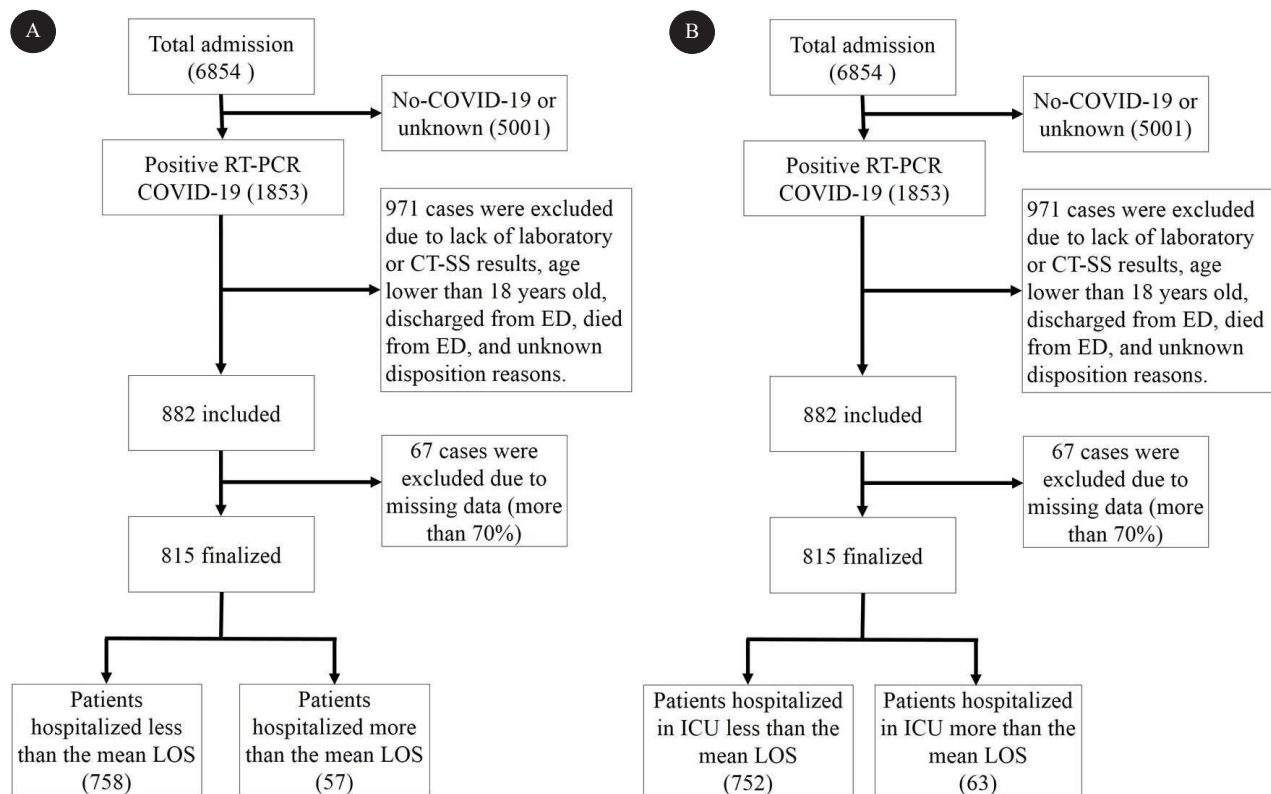


Figure 1. Flowchart describing patient selection in the prediction of a) hospital LOS and b) ICU LOS.

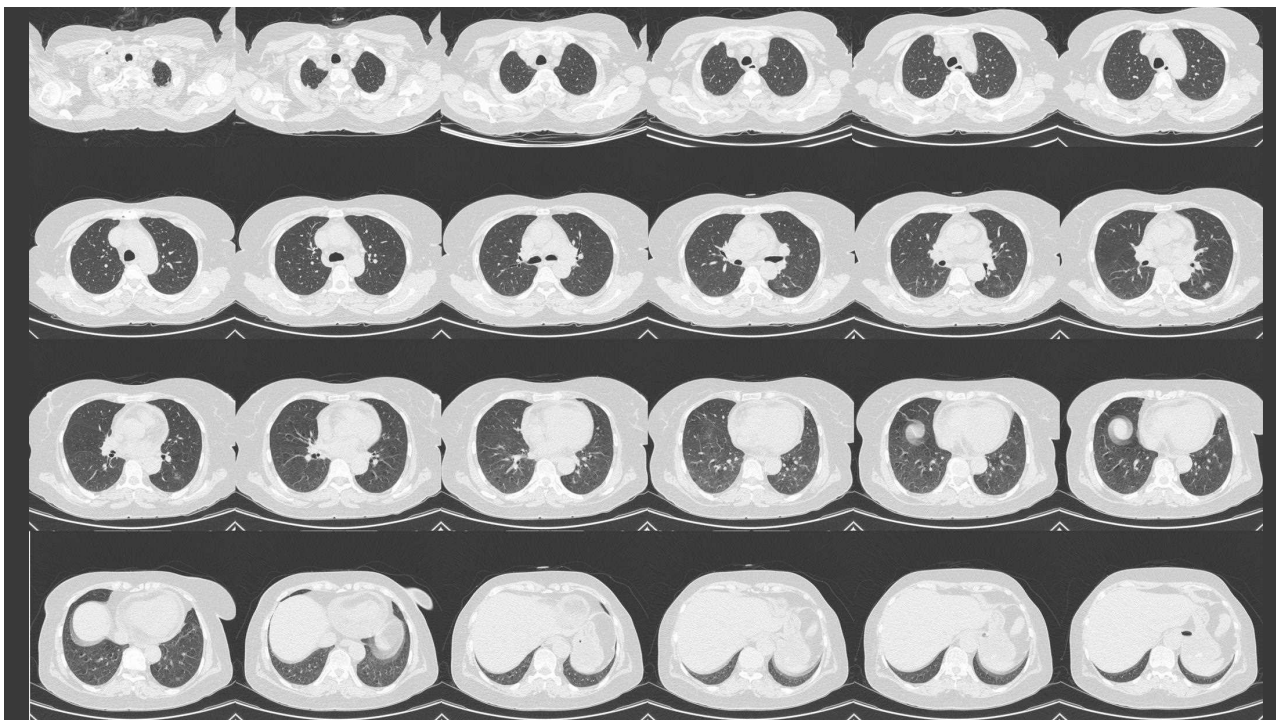


Figure 2. The non-contrast chest CT in a 61-year-old woman infected with COVID-19. Axial CT image shows less than 5% involvement in the left lower lobe (CT-SS=1).



Figure 3. The non-contrast chest CT in a 64-year-old woman infected with COVID-19. Axial CT image shows less than 5% involvement in bilateral upper and lower lobes. Left upper lobe with less than 5% involvement, score 1; Left lower lobe with less than 5% involvement, score 1; Right upper lobe with less than 5% involvement, score 1; Right middle lobe with less than 5% involvement, score 1; and Right lower lobe with less than 5% involvement, score 1 (CT-SS=5).

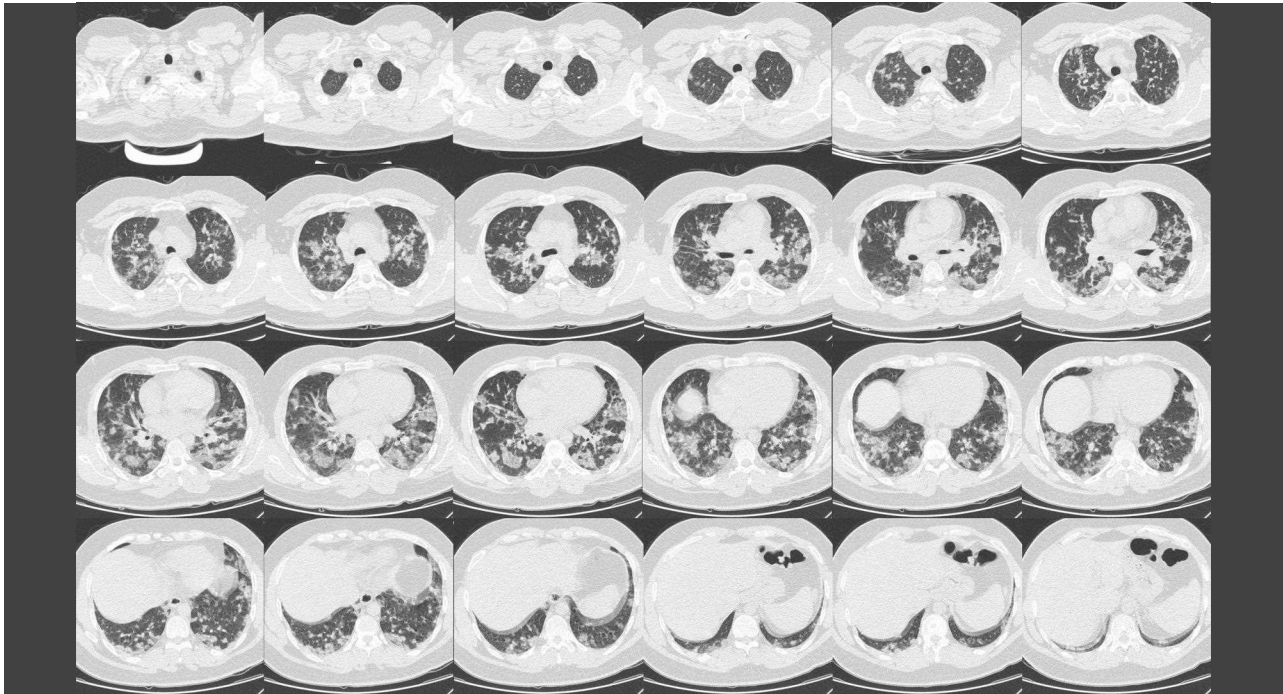


Figure 4. The non-contrast chest CT in a 27-year-old man infected with COVID-19. Axial CT image shows 25%-50% involvement in bilateral upper and lower lobes. Left upper lobe with 25%-50% involvement, score 3; Left lower lobe with 25%-50% involvement, score 3; Right upper lobe with 25%-50% involvement, score 3; Right middle lobe with 5%-25% involvement, score 2; and Right lower lobe with 25%-50% involvement, score 3(CT-SS=14).

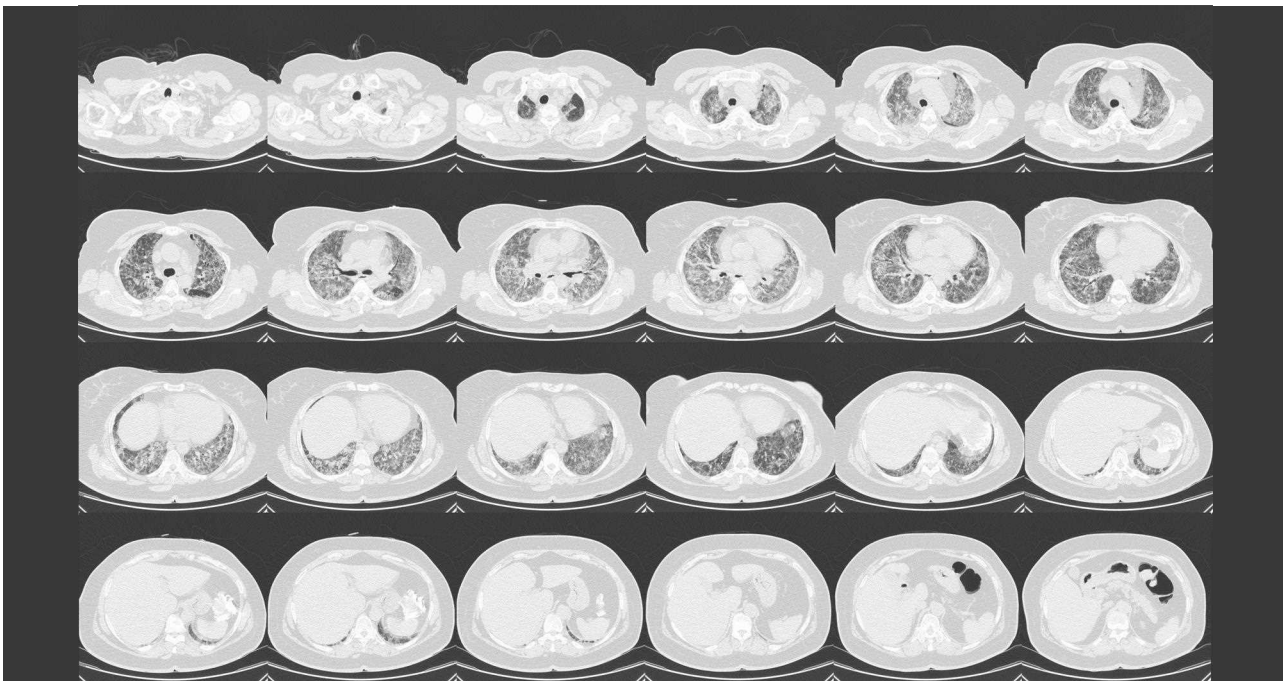


Figure 5. The non-contrast chest CT in a 56-year-old woman infected with COVID-19. Axial CT image shows more than 75% involvement in bilateral upper and lower lobes. Left upper lobe with more than 75% involvement, score 5; Left lower lobe with more than 75% involvement, score 5; Right upper lobe with more than 75% involvement, score 5; Right middle lobe with more than 75% involvement, score 5; and Right lower lobe with more than 75% involvement, score 5(CT-SS=25).

CT images of COVID-19 patients with CT-SSs of 1, 5, 14, and 25, respectively.

Ethical considerations

This study was approved by the local ethical committee (approved number: IR.MEDILAM.REC.1402.294). The identifying information of the patients was concealed during the data collection and presentation to protect the privacy and confidentiality of the patients.

Data preparation

The incomplete records with missing data more than 70% were excluded from the analysis. The missing data imputation was performed using R multivariate imputation by chained equation (MICE) package. MICE is a multiple imputation technique that uses the chained equations approach. This approach is very flexible and can be used to impute missing values of the variables with varying types (e.g. continuous, binary, etc.). Noisy and abnormal values, errors, and meaningless data were checked and the corresponding physicians were contacted if necessary.

The final data set contained 815 COVID-19 patients. In a systematic review and meta-analysis study by Alimohamadi Y, et al., 24 the pooled hospital LOS for COVID-19 patients were reported as 10.15 days, 14.67days,15.12 days, and 16.60 days for age groups of <40 years old, 40-50 years old, 50-60 years old, and >60 years old, respectively. The mean ICU LOS was reported as 7 days in several studies. 9, 13, 14 In our study, these threshold values were also considered for average hospital and ICU LOS magnitudes. The outcome variables were defined as whether the hospital and ICU

LOS of the patients were less than the threshold values or not.

In this refined data set, there were 57 hospitalized patients whose LOS was more than the mean LOS and 63 ICU-admitted patients with ICU LOS values of more than 7 days. The number of records in outcome classes has a significant imbalance. The number imbalance of instances yields results biased toward the dominant class. This problem was resolved using the synthetic minority over-sampling technique (SMOTE) method (<https://imbalanced-learn.org/stable/>).

Feature selection

In data mining studies, the most important and related predictors are determined using feature selection procedures. Feature selection is a critical step in data mining that reduces the dimensions of the dataset and improves the classification performance of ML algorithms. In this study, feature selection was performed using the Boruta feature selection package implemented in the R programming environment (version 4.0.3; <https://www.r-project.org/>). Feature selection was performed for both studies predicting hospital and ICU LOSs of COVID-19 patients, separately. In both Boruta algorithms, the maximal number of importance source runs and the verbosity level (doTrace) were set to 500 and 2, respectively.

Model development

In this study, four well-known ML classification models including kNN, MLP, SVM, and C4.5 decision tree algorithms were used to predict hospital and ICU LOSs of COVID-19 patients. ML models were separately developed for both studies predicting hospital and ICU LOSs

of COVID-19 patients. These ML algorithms were implemented using Waikato Environment for Knowledge Analysis (Weka) software (version 3.9.2, University of Waikato, New Zealand). A ten-fold cross-validation method was used to evaluate the performances of the developed classifiers.

For determining the prognostic significance of CT-SS in the prediction of hospital and ICU LOSs of COVID-19 patients, ML algorithms were separately developed using datasets with and without CT-SS data. The parameters obtained from the confusion matrix including the accuracy, precision, sensitivity, specificity, F-measure, and area under the ROC curve (AUC) indices were used to evaluate the classification performances of the ML algorithms.

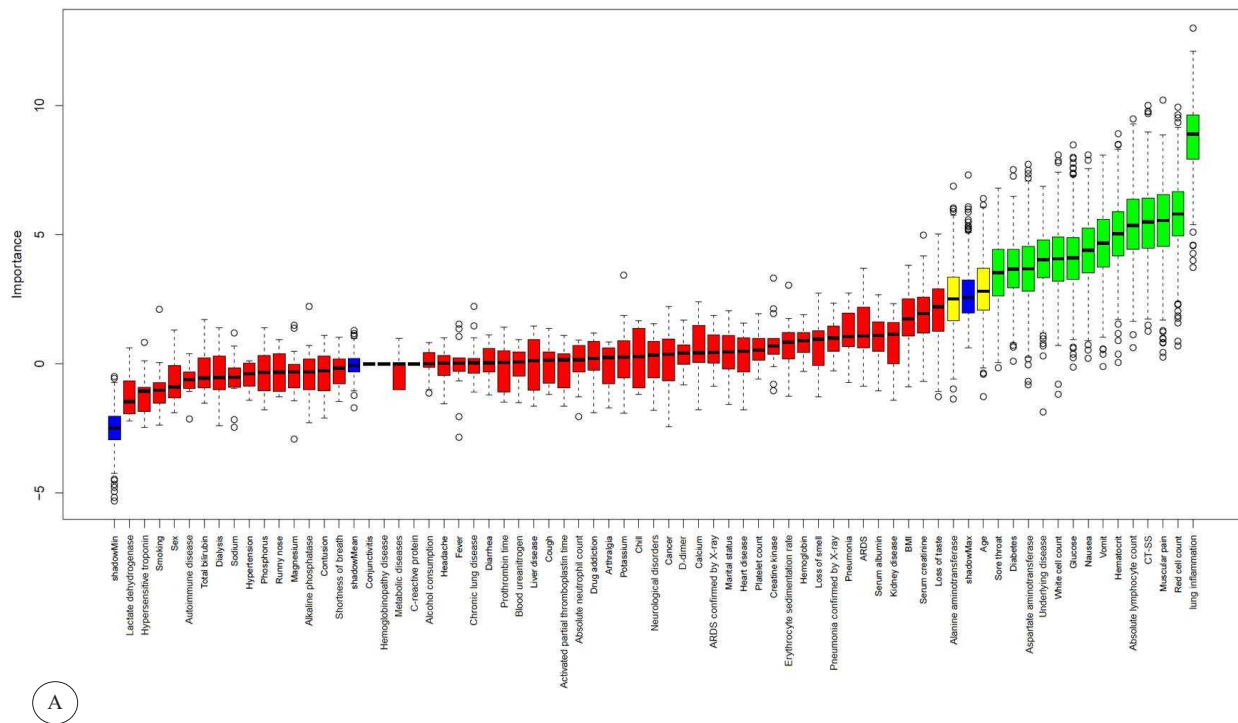
Results

In this study, the hospital and ICU LOS

magnitudes of 815 COVID-19 patients were retrospectively reviewed. This dataset consisted of 57 hospitalized patients with hospital LOS more than the mean LOS (approximately 7%) and 63 ICU-admitted patients with ICU LOS more than 7 days (7.73%). After balancing the dataset, the number of records in the classes of hospitalized patients with hospital LOS more than the mean LOS and ICU-admitted patients with ICU LOS more than 7 days were raised to 758 and 752, respectively.

Feature selection

For the prediction of hospital and ICU LOS magnitudes of COVID-19 patients, 16 and 12 predictors were respectively chosen as the most important and relevant features using the Boruta algorithm. The graphs of variables' importance values for predicting hospital and ICU LOSs of COVID-19 patients are shown in Figure 6. In this figure, the X and the Y



A

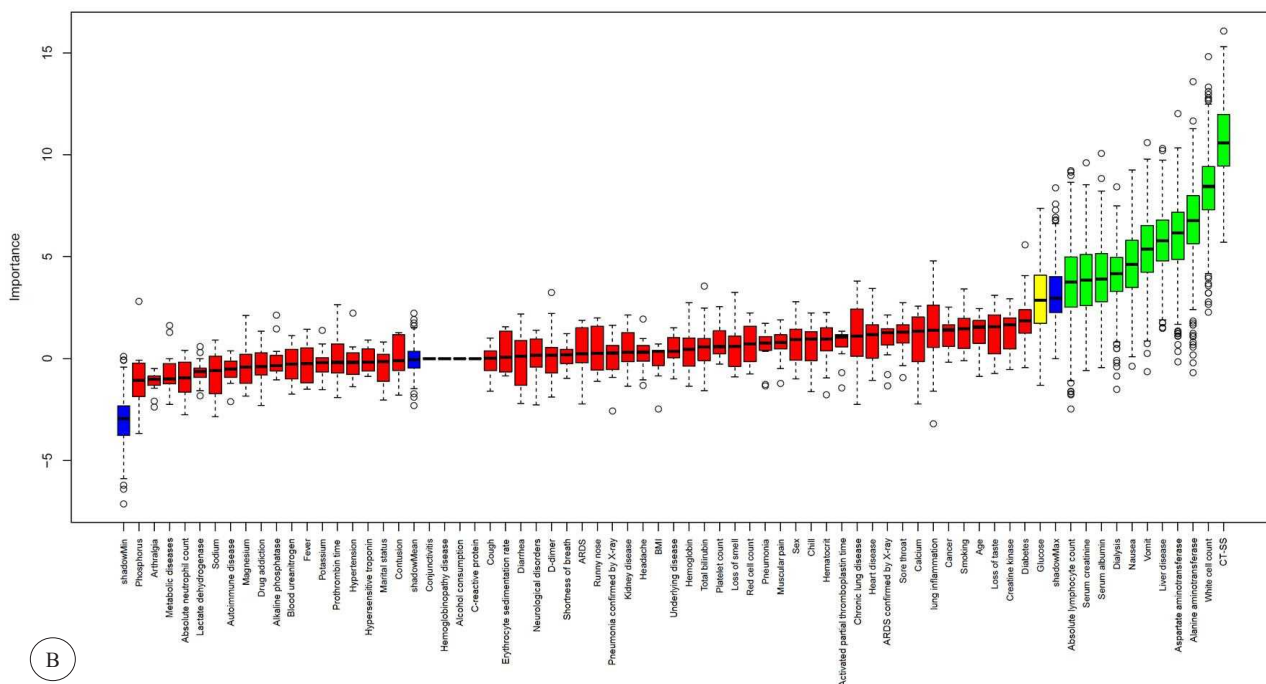


Figure 6. Charts of the Boruta algorithm for feature selection in the prediction of a) hospital LOS and b) ICU LOS. Green, red, and yellow boxes show the confirmed, tentative, and irrelevant features. Blue boxes represent the minimum, average, and maximum of shadow variables.

axes represent the features and the importance of these attributes in predicting the output variable, respectively. These parameters were used to develop ML algorithms.

Evaluation of the developed models

In this study, hospital and ICU LOSs of COVID-19 patients were predicted using kNN, MLP, SVM, and C4.5 decision tree algorithms. These ML models were separately fed using the most important and relevant features with and without CT-SS data and their performances were compared to evaluate the prognostic significance of CT-SS for predicting hospital and ICU LOSs of COVID-19 patients. For both studies predicting hospital and ICU LOSs of COVID-19 patients, the sensitivity, specificity, accuracy, precision, F-measure, and AUC indices of the models developed using

the datasets with and without CT-SS data are listed in Tables 1 and 2. For studies predicting hospital and ICU LOSs of COVID-19 patients, the best results were obtained by the kNN algorithm.

For the dataset without CT-SS data, sensitivity, specificity, accuracy, precision, F-Measure, and AUC of the kNN algorithm in the prediction of hospital LOS of COVID-19 patients were 100%, 55.8%, 77.9%, 69.4%, 81.9%, and 98.5%, respectively. By integrating CT-SS data with the existing dataset, the kNN algorithm reached 100% sensitivity, 54.2% specificity, 77.1% accuracy, 68.6% precision, 81.4% F-Measure, and an AUC of 99.4%.

Sensitivity, specificity, accuracy, precision, F-Measure, and AUC of the kNN algorithm developed using the dataset without CT-SS data for predicting ICU LOS of COVID-19 patients were 93.0%%, 76.3%, 84.6%, 79.7%,

85.8%, and 93.4%, respectively. While the kNN algorithm reached 94.4% sensitivity, 74.6% specificity, 84.5% accuracy, 78.8% precision, 85.9% F-Measure, and an AUC of 95.3% by

integrating CT-SS data with this dataset. For both studies predicting hospital and ICU LOSs of COVID-19 patients, the ROC curves of the selected ML algorithms fed by

Table 1. Performances of ML algorithms to predict the length of stay in hospital for COVID-19 patients.

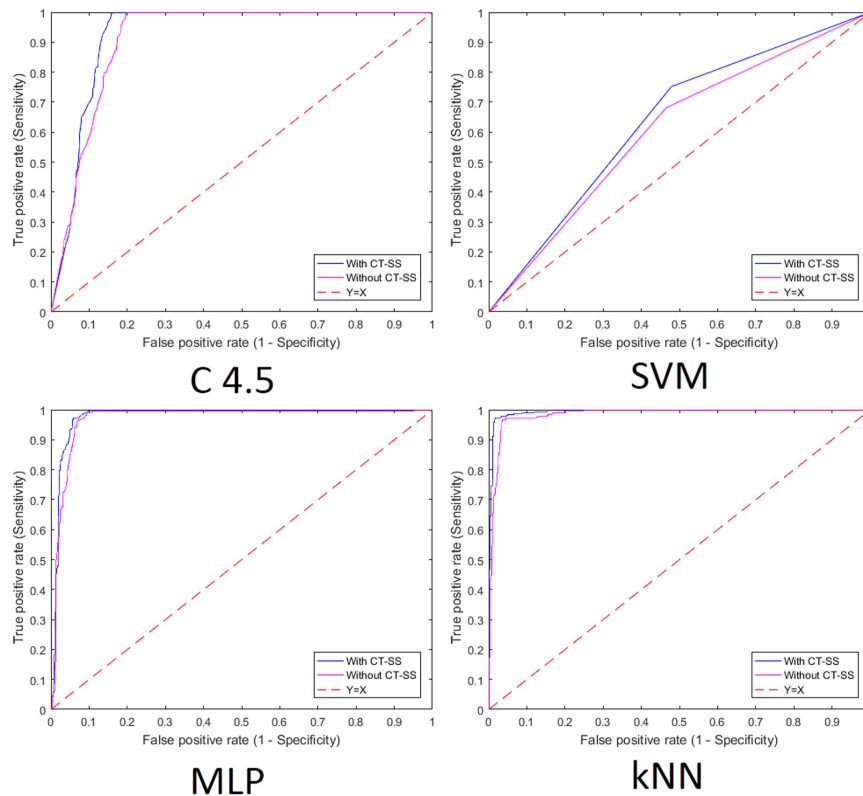
ML algorithm	Sensitivity		Specificity		Accuracy		Precision		F-Measure		AUC	
	With CT-SS	Without CT-SS	With CT-SS	Without CT-SS	With CT-SS	Without CT-SS	With CT-SS	Without CT-SS	With CT-SS	Without CT-SS	With CT-SS	Without CT-SS
C4.5	99.7	100.0	83.6	80.3	91.7	90.2	85.9	83.6	92.3	91.1	92.6	91.2
SVM	75.2	68.2	52.1	53.4	63.7	60.8	61.1	59.4	67.4	63.5	63.7	60.8
MLP	100.0	99.6	89.4	88.3	94.7	93.9	90.5	89.5	95.0	94.3	97.9	97.1
k-NN	100.0	100.0	54.2	55.8	77.1	77.9	68.6	69.4	81.4	81.9	99.4	98.5

C4.5, C4.5 Decision tree; MLP, Multi-layer perceptron; SVM, Support vector machine; k-NN, k-nearest neighbourhood.

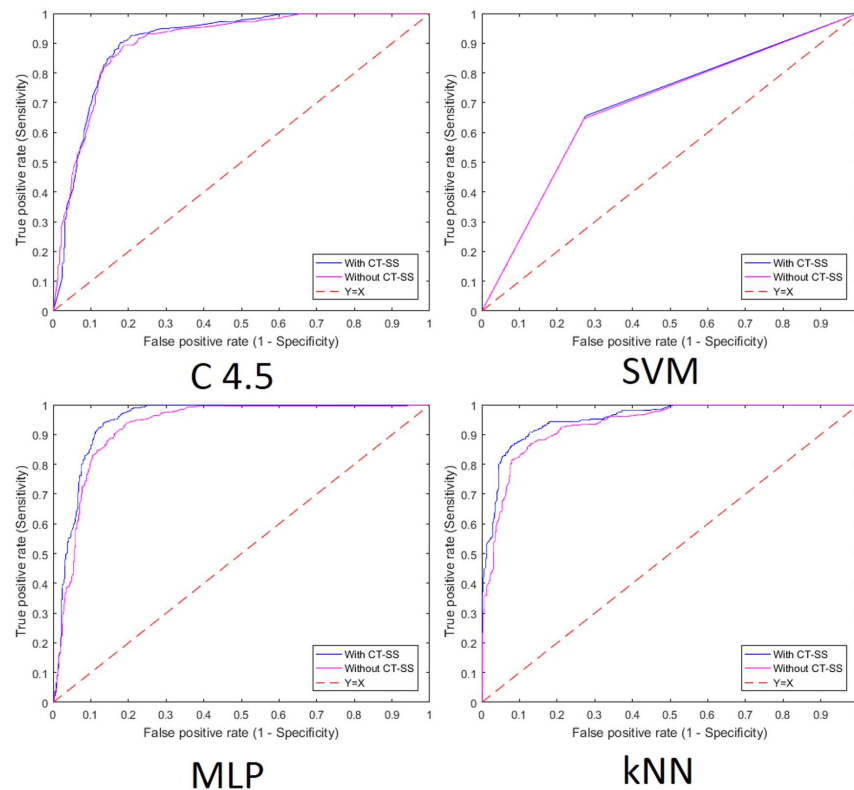
Table 2. Performances of ML algorithms to predict the length of stay in ICU for COVID-19 patients.

ML algorithm	Sensitivity		Specificity		Accuracy		Precision		F-Measure		AUC	
	With CT-SS	Without CT-SS	With CT-SS	Without CT-SS	With CT-SS	Without CT-SS	With CT-SS	Without CT-SS	With CT-SS	Without CT-SS	With CT-SS	Without CT-SS
C4.5	90.4	89.2	81.4	81.0	85.9	85.1	82.9	82.4	86.5	85.7	90.6	90.2
SVM	65.6	64.6	72.5	72.9	69.0	68.8	70.4	70.4	67.9	67.4	69.0	68.8
MLP	95.1	90.3	83.1	83.8	89.1	87.0	84.9	84.8	89.7	87.4	94.6	92.5
k-NN	94.4	93.0	74.6	76.3	84.5	84.6	78.8	79.7	85.9	85.8	95.3	93.4

C4.5, C4.5 Decision tree; MLP, Multi-layer perceptron; SVM, Support vector machine; k-NN, k-nearest neighbourhood.



A



B

Figure 7. ROC curves for ML algorithms fed by the datasets with and without CT-SS data in the prediction of a) hospital LOS and b) ICU LOS.

the datasets with and without CT-SS data are depicted in Figure 7.

The performances of the ML predictive models for predicting hospital and ICU LOSs of COVID-19 patients were improved when CT-SS data was integrated into the input dataset.

Discussion

During the COVID-19 pandemic, most healthcare systems have faced high referral volumes and resource shortages.^{2, 10, 21} Predicting hospital and ICU LOSs for hospitalized patients offers key evidence to improve patient outcomes and proper allocation of restricted hospital resources. ML predictive models are efficient and promising approaches to estimating patients' LOSs in

hospitals and ICUs. A set of ML algorithms were worldwide developed to predict the LOS of COVID-19 patients.^{1, 9-21} Almost all these models are developed using demographics, risk factors, clinical manifestations, and laboratory parameters. In their input datasets, there was a lack of radiological information and the prognostic significance of imaging manifestations in combination with demographics, risk factors, clinical manifestations, and laboratory parameters was not evaluated for predicting hospital and ICU LOS.

CT-SS is a promising radiological index to evaluate the severity of the COVID-19 disease which quantifies the severity and extent of pulmonary involvements. The positive association between CT-SS and the severity of

the COVID-19 disease was reported in pioneer studies.^{22,23,25} Therefore, it would be an efficient predictor to predict the prolonged LOS of the patients in hospitals and ICUs. In this study, four well-known ML models including kNN, MLP, SVM, and C4.5 decision tree algorithms were developed using a hospital-based COVID-19 registry database to determine the prognostic significance of CT-SS to predict hospital and ICU LOSs of COVID-19 patients. In the first step, the prognostic importance of demographic information, risk factors, clinical manifestations, laboratory results, and CT-SS for predicting hospital and ICU LOSs of COVID-19 patients was determined using the Boruta feature selection package. Some features such as age, absolute lymphocyte count, WBC, alanine aminotransferase, aspartate aminotransferase, underlying non-communicable disease, and GI complications were of the highest importance.

Aging is associated with worse clinical outcomes and the severity of COVID-19 disease is higher for elderly patients. Since longer disease courses were observed for these patients. Therefore, hospital and ICU LOSs of elderly patients would be significantly longer than those of younger ones. The existence of underlying diseases, such as diabetes, liver disease, renal dysfunction, etc., in COVID-19 patients is associated with poor clinical outcomes. The health condition of these vulnerable patients gets worse and need more care due to having underlying diseases and COVID-19 simultaneously. Many studies have been conducted to determine laboratory indices that predict the deterioration of the patient's health and, as a result, the patient's greater need for care services that prolong their hospital stay. These studies showed that there were

higher levels of serum renal function index (e.g. creatinine), biochemical indicators of liver function (alanine aminotransferase (ALT) and aspartate aminotransferase (AST)), hematocrit, and WBC for the severe patients. The patients with lower levels of serum albumin and absolute lymphocyte counts had a more severe clinical course. These parameters related to the hospital and ICU LOSs of COVID-19 patients were also reported by several studies and there was a high compliance between our findings and those of these reports.^{9-12, 20, 21} For predicting both hospital and ICU LOSs of the patients, CT-SS is one of the most relevant and important predictors with high importance magnitudes which highlights the necessity of using this parameter in ML modelings for predicting hospital and ICU LOSs.

In the next step, the prognostic performances of the ML models were evaluated using the selected predictors with and without CT-SS data. The integration of CT-SS data with demographics, risk factors, clinical manifestations, and laboratory parameters improved the prognostic performances of the ML models for predicting hospital and ICU LOSs of the patients. For predicting hospital LOS, the kNN model with an accuracy of 77.1%, sensitivity of 100.0%, precision of 68.6%, specificity of 54.2%, and AUC of around 99.4% had the best performance among the other three ML techniques. MLP and C4.5 decision tree models respectively in the next positions had good prognostic performances (AUCs > 92%), and their prognostic performances were better than the SVM model. For predicting ICU LOS, the kNN model with an accuracy of 84.5%, sensitivity of 94.4%, precision of 78.8%, specificity of 74.6%, and AUC of around 95.3% had also the

best performance among the other three ML techniques. After the kNN model, MLP and C4.5 decision tree algorithms had respectively the best prognostic performances (AUCs > 90%), and their prognostic performances were better than the SVM model. The KNN algorithm is one of the popular and simplest classifiers that uses proximity to classify an event. In this supervised learning method, the majority vote of the k-nearest neighbors of a data point in the feature space determines the class of that data point.

In several studies, ML techniques were evaluated to predict hospital and ICU LOSs of COVID-19 patients. Three machine learning algorithms for predicting the likelihood of prolonged hospital LOS of COVID-19 patients were developed by Ebinger J et al. 20 These ML models were developed based on different algorithms including Elastic-net, gradient boosted trees, random forest, SVMs, logistic regression, Eureka classifier, generalized additive models, Vowpal Wabbit classifier, kNNs, residual neural network, Rulefit classifier, and ensemble models. The prognostic performances of the models were evaluated using the data obtained from 966 COVID-19 patients on hospitalization days 1, 2, and 3. The performances of the developed models improved sequentially when the interval between data acquisition and patient admission increased and the best performance was achieved using the obtained data on hospitalization day 3. Based on the data recorded at the first time of admission, the sensitivity, specificity, accuracy, precision, F1, and AUC of the model were 82%, 68%, 74.5%, 68%, 74%, and 80.3, respectively. In Alabbad DA et al. study, 21 ML predictive models were evaluated to predict the ICU LOS

of COVID-19 patients in the eastern province of Saudi Arabia. The four ML models including random forest (RF), gradient boosting (GB), extreme gradient boosting (XGBoost), and an ensemble classifier were developed using a dataset from 895 COVID-19 patients. The RF, GB, XGBoost, and adaptive boosting decision algorithms were combined to form the ensemble classifier. In 10-fold cross-validation and by applying the feature selection procedure, the ensemble classifier with 88.81% sensitivity, 88.81% accuracy, 88.85% precision, and 88.72% F-score reached the best performance. After the ensemble classifier model, RF and XGBoost algorithms had respectively the best prognostic performances and the GB model yielded the weakest results.

These results showed that the ML approach can help healthcare providers and health policymakers to predict patients' LOS and make proper resource-planning decisions. The proper medical resource allocation would improve patient quality of care, result in better patient management, and reduce the severe complications and the resulting mortalities. An optimal clinical decision-making model for predicting the patient's hospital LOS can help in rapid and accurate triage of the patients for new peaks of the pandemic or outbreaks of new diseases (such as the new HMPV outbreaks). The performances of the ML models for predicting hospital and ICU LOSs of COVID-19 patients improved by the integration of CT-SS data with demographics, risk factors, clinical manifestations, and laboratory parameters. Therefore, an ML model with a comprehensive dataset including CT-SS data could lead to early identification of COVID-19 patients with prolonged hospital and ICU LOSs and allow taking the necessary interventions for

the optimal use of hospital resources.

Limitations

This study had some limitations which must be addressed. First, the registered dataset stems from a single referral center with a limited number of patients meeting inclusion criteria which may limit the generalizability of the results. There is a need for larger sample size, prognostic evaluation of more ML algorithms, and multi-site verification to make a valid and generalizable model for multi-national populations. Because the framework and procedures followed are non-case dependent, we believe that the overall results do not change and the integration of CT-SS data with demographics, risk factors, clinical manifestations, and laboratory parameters improves the prognostic performances of the ML models to predict hospital and ICU LOSs.

Conclusion

In this study, the prognostic significance of CT-SS for predicting hospital and ICU LOSs of COVID-19 patients was evaluated using four well-known ML algorithms in the presence and absence of CT-SS data. The results showed that the performances of the ML models for predicting hospital and ICU LOSs of COVID-19 patients improved by the integration of CT-SS data with demographics, risk factors, clinical manifestations, and laboratory parameters. Therefore, an ML model with a comprehensive dataset including CT-SS data could lead to early identification of COVID-19 patients with prolonged LOS in hospital and ICU, optimal allocation of limited hospital resources, and providing better

healthcare services for patients.

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