Original Article

Machine learning using the extreme gradient boosting (XGBoost) algorithm predicts 5-day delta of SOFA score at ICU admission in COVID-19 patients

Jonathan Montomoli [1], Luca Romeo [2], Sara Moccia [2,3], Michele Bernardini [2], Lucia Migliorelli [2], Daniele Berardini [2], Abele Donati [4,5], Andrea Carsetti [4,5], Maria Grazia Bocci [6], Pedro David Wendel Garcia [7], Thierry Fumeaux [8], Philippe Guerci [9], Reto Andreas Schüpbach [7], Can Ince [10,*], Emanuele Frontoni [2], Matthias Peter Hilty [7], RISC-19-ICU Investigators [**]

[1] Department of Anaesthesia and Intensive Care, Infermi Hospital, AUSL della Romagna, Rimini 47923, Italy
[2] Department of Information Engineering, Università Politecnica delle Marche, Ancona 60131, Italy
[3] The BioRobotics Institute and Department of Excellence in Robotics and AI, Scuola Superiore Sant'Anna, Pisa 56127, Italy
[4] Anesthesia and Intensive Care Unit, Azienda Ospedaliero Universitaria Ospedali Riuniti, Ancona 60126, Italy
[5] Department of Biomedical Sciences and Public Health, Università Politecnica delle Marche, Ancona 60126, Italy
[6] Department of Anaesthesia and Intensive Care, Fondazione Policlinico Universitario A. Gemelli IRCCS, Università Cattolica del Sacro Cuore, Rome 00168, Italy
[7] Institute of Intensive Care Medicine, University Hospital of Zurich, Zurich 8091, Switzerland
[8] Swiss Society of Intensive Care Medicine, Basel 4001, Switzerland
[9] Department of Anesthesiology and Critical Care Medicine, University Hospital of Nancy, Nancy 54511, France
[10] Department of Intensive Care Erasmus MC, University Medical Center Rotterdam, Rotterdam, 3015 GD, Netherlands

A R T I C L E   I N F O

A B S T R A C T

Background: Accurate risk stratification of critically ill patients with coronavirus disease 2019 (COVID-19) is essential for optimizing resource allocation, delivering targeted interventions, and maximizing patient survival probability. Machine learning (ML) techniques are attracting increased interest for the development of prediction models as they excel in the analysis of complex signals in data-rich environments such as critical care.

Methods: We retrieved data on patients with COVID-19 admitted to an intensive care unit (ICU) between March and October 2020 from the RIsk Stratification in COVID-19 patients in the Intensive Care Unit (RISC-19-ICU) registry. We applied the Extreme Gradient Boosting (XGBoost) algorithm to the data to predict as a binary outcome the increase or decrease in patients' Sequential Organ Failure Assessment (SOFA) score on day 5 after ICU admission. The model was iteratively cross-validated in different subsets of the study cohort.

Results: The final study population consisted of 675 patients. The XGBoost model correctly predicted a decrease in SOFA score in 320/385 (83%) critically ill COVID-19 patients, and an increase in the score in 210/290 (72%) patients. The area under the mean receiver operating characteristic curve for XGBoost was significantly higher than that for the logistic regression model (0.86 *vs.* 0.69, $P < 0.01$ [paired *t*-test with 95% confidence interval]).

Conclusions: The XGBoost model predicted the change in SOFA score in critically ill COVID-19 patients admitted to the ICU and can guide clinical decision support systems (CDSSs) aimed at optimizing available resources.

Introduction

The coronavirus disease 2019 (COVID-19) outbreak represents one of the most critical global health emergencies in modern times, with >4.7 million deaths reported worldwide as of the end of September 2021 [1]. The COVID-19 pandemic has posed an unprecedented healthcare challenge, with intensive care unit (ICU) capacity rapidly exceeded around the world in the first weeks of the outbreak and subsequent resurgences [2]. The ability to predict patient outcomes by analyzing ICU medical records is hampered by numerous challenges such as a lack of structured clinical data, missing values, and datasets with a limited number of patients. Under these conditions, predicting the probability that a patient will either develop complications associated with COVID-19 or improve is important as it may help to define a personalized risk profile that will optimize clinical

---

* Corresponding author: Erasmus MC, University Medical Center, Dr. Molewaterplein 40, 3015 GD, Rotterdam, The Netherlands.
E-mail address: c.ince@erasmusmc.nl (C. Ince).
** See Appendix for the list of contributing investigators from the RISC-19-ICU Investigators.

management [3]. The analytical capability of machine learning (ML) methods has proven extremely accurate and in some cases, superior to classical statistical approaches [4]. This was confirmed by our recent work in this area in which we proposed ML-based methodologies for predicting the risk of certain conditions and complications related to chronic diseases [5–7]. The use of ML to design a Clinical Decision Support System (CDSS) also has practical value beyond clinical diagnosis and disease modeling [8].

Real-world datasets from the ICU usually consist of data with high dimensionality in terms of both an absolute number of monitored parameters and sampling frequency. On the other hand, the collected features are usually characterized by noise and/or redundancy. While managing and modeling this amount of data, there are several challenges such as overfitting, low interpretability, data heterogeneity, and missing values.

Data-driven techniques may be useful for analyzing stored multifactorial temporal ICU data to construct advanced ML models that can predict clinical outcomes and reveal complex patterns that may not be obvious to physicians [9]. Predictive ML models can also aid physicians in predicting early-stage disease by identifying the most relevant clinical factors in the risk profile of a given condition. Among existing ML algorithms, the Extreme Gradient Boosting (XGBoost) model has gained popularity for its generalizability, low risk of overfitting, and high interpretability; it outperforms other data mining methods for predictive medicine tasks based on tabular (e.g., electronic health record [EHR]) data [10] and has been applied to critical care situations such as cardiovascular compromise with volume resuscitation [9,10] and other conditions [11–13].

We speculated that the XGBoost model can be used as a platform to predict disease course in COVID-19 patients. To test this hypothesis, in the present study, we applied the model to predict changes in the Sequential Organ Failure Assessment (SOFA) score in COVID-19 patients within the first 5 days of admission to the ICU. We also compared the performance of the XGBoost model with that of a standard regression method.

Methods

Setting and descriptive statistics

The study population was retrieved from the RIsk Stratification in COVID-19 patients in the Intensive Care Unit (RISC-19-ICU) registry, which includes patients diagnosed with COVID-19 and admitted to the ICU or semi-ICU. The registry was launched on March 17, 2020, and was created for near real-time tracking of patients at up to 96 centers in 15 different countries who developed a critical illness due to COVID-19 [14,15]. The number of critically ill COVID-19 patients has been increasing steadily, with 1613 individual admissions at the end of October 2020. Patient characteristics at ICU admission are reported as counts, percentages (%), means, standard deviations, or medians and interquartile ranges (IQRs) as appropriate. These were compared between patients with an increase *vs.* a decrease in SOFA score of ≥2 points within the first 5 days of ICU admission using the independent samples *t*-test or Wilcoxon rank-sum test for continuous variables and the chi-squared test for categorical variables. Statistical analysis was performed with a fully scripted data management pathway using R v3.6.3 (cran.r-project.org).

A two-sided *P*-value <0.05 was considered statistically significant.

Prediction model

Study variables

The SOFA score assesses the acute morbidity of critically ill patients and has been validated in different settings [16]. Patient characteristics and laboratory and physiologic parameters at the time of ICU admission or within the first 24 h were used as predictors [Fig. 1 and Supplementary Table S1]. Features with >70% missing values were excluded from the model.

Predicted outcome

Predicting the probability of organ failure can help physicians in deciding whether to intensify or de-escalate monitoring and treatment. We used the XGBoost model to predict the change in SOFA score of patients on day 5 after ICU admission (pattern discrimination). An increase in SOFA score ≥2 points or a decrease of ≤2 points according to the Sepsis-3 definition was defined as worsening or improvement, respectively, of the patient's clinical status [17].

Model development

The process used to construct the XGBoost model to predict the increase or decrease in SOFA score is shown in Fig. 2. The gradient tree boosting algorithm extends the concept of adaptive boosting by sequentially adding predictors and correcting previous models using the gradient descent algorithm [18]; the learning process involves iteratively refitting a weak classifier to errors in previous models. Each successive classifier focuses on patients misclassified in the previous round of fitting to minimize the generalization error. A classification tree was used as the weak learner, and the learning objective function was binary logistic.

Once the worsening or improvement of critically ill COVID-19 patients was detected in the features, we analyzed where this information was encoded (feature importance). The model was constructed using the entire RISC-19-ICU dataset after excluding patients with a change in SOFA score ≤1 and those with a missing SOFA score at admission or on day 5 after admission. The model was tested using a 10-fold cross-validation (CV-10) procedure that divided the entire study cohort into 10 non-overlapping folds for each cross-validation cycle by selecting 9 folds for training and 1 for testing. To improve generalizability, ML model complexity was modulated by optimizing the parameters controlling the training process (e.g., hyperparameters) using nested cross-validation within the training set. XGBoost hyperparameters included the number of iterations of the boosting procedure, learning rate, maximum depth of a tree, and subsample ratio of the training features. The optimal hyperparameters were determined by implementing a grid search and optimizing the macro-recall in a nested 5-fold CV. Hence, each split of the outer loop was trained with the optimal hyperparameters tuned in the inner loop. Although this procedure is computationally costly, it allows an unbiased and robust performance evaluation [19]. We compared the predictive performance of the XGBoost model to that of a standard logistic regression-based prediction model based on a confusion matrix and area under the receiving operating characteristic (ROC) curve with a 95% confidence
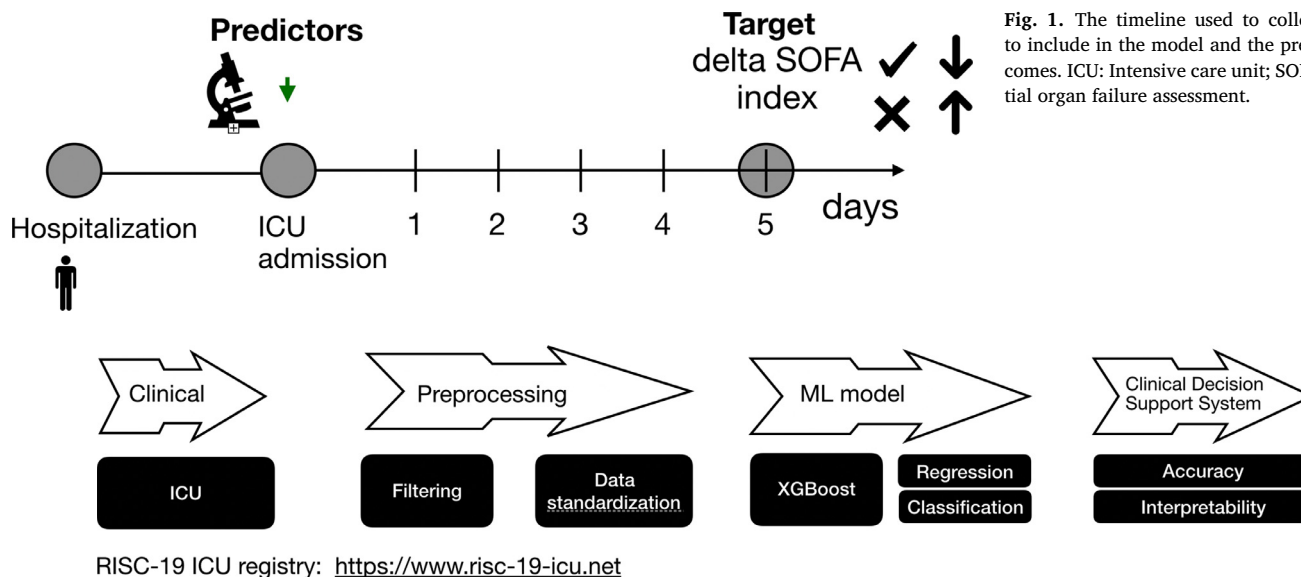
Fig. 1. The timeline used to collect features to include in the model and the predicted outcomes. ICU: Intensive care unit; SOFA: Sequential organ failure assessment.

Fig. 2. Description of the steps applied to build and test the prediction model. ICU: Intensive care unit; ML: Machine learning; RISC-19-ICU: RIsk Stratification in COVID-19 patients in the Intensive Care Unit; XGBoost: Extreme gradient boosting.

interval (CI). All experiments were reproducible and were performed using Python 3.7 with a 2.3 GHz Intel Core i7 quad-core processor and 16 GB RAM.

Results

Of the 1613 patients included in the RISC-19-ICU registry as of October 2020, 1030 had stayed in the ICU for ≥ 5 days and had valid SOFA scores both at ICU admission and on day 5 after admission. The model was applied to the entire RISC-19-ICU cohort comprising 675 patients with an absolute change in SOFA score of ≥ 2 points between the two time points. The median age of patients was 64 years (IQR: 56–63 years) and 74% were males. At ICU admission, the median SOFA score was 11 (IQR: 6–14), the median time from symptom onset was 8 days (IQR: 6–11 days), median arterial oxygen partial pressure to fractional inspired oxygen ratio (pO_2/FiO_2) was 122 (IQR: 81–171), and 86% of patients were mechanically ventilated [Table 1].

The model correctly predicted SOFA worsening in 320/385 patients (83%) with increased SOFA score and improvement in 210/290 patients (72%) with a decreased score, with an area under the mean ROC curve of 0.86 (95% CI: 0.85–0.90; Fig. 3A). As expected, the features most relevant to changes in the SOFA score were its components including Glasgow coma scale score, state of shock, use of vasopressors, and bilirubin concentration [Fig. 3B]. However, other features are known to be related to patient outcomes such as type of respiratory support, Acute Physiology and Chronic Health disease Classification System (APACHE) II score, and Simplified Acute Physiologic Score (SAPS) II score also contributed to the correct prediction. Notably, while the prevalence of diabetes was similar between patients with improved *vs.* worsened SOFA scores, the presence/absence of diabetes mellitus was among the most relevant conditions for predicting the change in SOFA score on day 5 after ICU admission.

Because of differences in the management of missing data, the predictive model developed by standard logistic regression included 669 patients. SOFA worsening was correctly predicted

in 263/380 patients (69%) presenting an increased SOFA score while SOFA improvement was correctly predicted in 210/287 (72%) patients with a decreased SOFA score, corresponding to an area under the mean ROC curve of 0.69 (95% CI: 0.66–0.72; Supplementary Figure S1a). The XGBoost model performed significantly better than the logistic regression model in predicting an increase or decrease in SOFA score on day 5 ($P < 0.01$; paired *t*-test). Interestingly, the most important features with the logistic regression model differed from those identified by the XGBoost model, with SAPS II score, bilirubin concentration, and use of norepinephrine at ICU admission being the only three features common to both models [Supplementary Figure S1b].

Discussion

The results of the present study showed that the XGBoost model based on an ML algorithm was more effective than the classical method of logistic regression in identifying critically ill COVID-19 patients admitted to the ICU whose clinical condition was likely to worsen or improve. After mortality, disease severity was found to be the most important determinant of resource use in the management of critically ill patients, which is especially important during the current COVID-19 pandemic [14].

Health informatics technology is highly valuable for predictive medicine as it provides clinicians with tools for obtaining information regarding individuals at risk, disease onset, and potential interventions. However, EHRs have been unable to reduce the clerical burden or improve clinical care by supporting physicians in clinical decision-making [20]. EHRs should provide reliable and clinically significant information, facilitate the early detection of treatable conditions, and produce a measurable improvement in clinical practices. Driven by increases in computational power, storage, and memory and the generation of staggering volumes of data, ML methodologies can facilitate the accurate analysis and optimal use of EHR data.

Table 1

Characteristics at ICU admission of critically ill COVID-19 patients that have experienced a change in SOFA score of at least two points between ICU admission and day 5, stratified by an increase or decrease in SOFA score during the first 5 days of ICU treatment.

Variables	Decreased SOFA score at day 5 in the ICU	Increased SOFA at day 5 in the ICU	P-value
Patients (*n*)	293	383	
Characteristics			
Age (years)	61.4 (12.7)	63.9 (11.7)	0.010
Male sex (%)	80 (4)	70 (5)	<0.010
Body mass index (kg/m^2)	29.4 (5.3)	28.8 (5.6)	0.170
Time from symptom onset to hospitalization (days)	7.6 (5.6)	7.4 (5.3)	0.710
Time from hospitalization to ICU admission (days)	2.9 (6.3)	2.8 (4.9)	0.960
Preexisting conditions			
Number of preexisting conditions	0.7 (1.0)	0.7 (1.1)	0.930
Ischemic heart disease	147 (50.2)	182 (47.5)	0.540
Chronic heart failure	33 (11.3)	42 (11.0)	1.000
Atherosclerotic arteriopathy	23 (7.8)	43 (11.2)	0.180
Arterial hypertension	73 (24.9)	104 (27.2)	0.570
Diabetes mellitus	36 (12.3)	39 (10.2)	0.460
Insulin-dependent diabetes mellitus	37 (12.6)	53 (13.8)	0.730
Physiologic status at ICU admission			
APACHE II score	16.8 (6.6)	16.5 (7.4)	0.530
SAPS II score	55.8 (17.0)	53.9 (17.9)	0.150
SOFA score	13.8 (3.9)	11.7 (4.0)	<0.010
-Respiratory system sub-score	3.0 (0.9)	2.8 (0.9)	<0.010
-Coagulation system sub-score	0.2 (0.5)	0.3 (0.6)	0.660
-Liver sub-score	2.4 (1.6)	1.7 (1.7)	<0.010
-Cardiovascular system sub-score	2.2 (1.6)	1.7 (1.7)	<0.010
-Central nervous system sub-score	2.6 (1.9)	2.2 (1.9)	0.010
-Renal sub-score	3.8 (0.7)	3.7 (1.0)	0.020
Mean arterial pressure (mmHg)	80.0 (15.1)	84.3 (15.6)	<0.010
Norepinephrine dose (μg/kg)	7.3 (9.7)	4.4 (14.2)	0.020
PaO$_2$/FiO$_2$ ratio (mmHg)	151.4 (149.5)	162.0 (194.0)	0.470
Ventilatory ratio	2.0 (1.0)	2.1 (1.5)	0.510
Laboratory measurements at ICU admission			
White blood cell count (g/L)	10.1 (7.1)	9.4 (5.2)	0.180
Neutrophil granulocyte count (g/L)	8.3 (6.6)	7.8 (3.9)	0.300
Lymphocyte count (g/L)	1.3 (2.1)	1.7 (2.2)	0.060
IL-6 (ng/L)	125.0 (75.9, 289.0)	129.7 (66.5, 253.3)	0.600
C-reactive protein (mg/L)	147.1 (79.2, 241.1)	135.6 (62.5, 219.0)	0.160
Procalcitonin (μg/L)	0.3 (0.2, 1.1)	0.4 (0.2, 1.0)	0.710
D-dimers (μg/L)	1.4 (0.8, 3.3)	1.2 (0.7, 2.8)	0.030
Lactate dehydrogenase (U/L)	522.0 (376.0, 701.0)	494.0 (387.0, 691.5)	0.980
Ferritin (μg/L)	1527.0 (1002.0, 2801.0)	1141.0 (657.8, 2205.0)	0.010
Bilirubin (μmol/L)	9.3 (6.1, 14.0)	6.0 (1.0, 9.8)	<0.010
Creatinine (μmol/L)	83.8 (66.8, 114.0)	84.0 (62.0, 109.6)	0.460
Creatine kinase (U/L)	139.0 (64.0, 365.0)	177.5 (88.0, 350.5)	0.100
Myoglobin (μg/L)	77.0 (50.2, 294.0)	78.5 (36.0, 203.5)	0.670
Troponin (ng/L)	18.0 (10.0, 45.9)	15.3 (9.0, 34.0)	0.300
Albumin (g/L)	29.0 (25.0, 33.0)	30.0 (26.0, 33.0)	0.600
ICU outcome			
ICU survival	223 (80.5)	249 (66.9)	<0.001
ICU length of stay (days)	17.8 (16.7)	20.3 (13.9)	0.068

Estimates are reported as mean (standard deviation) or median (IQR) according to data distribution.

APACHE: Acute Physiology and Chronic Health disease Classification System; COVID-19: Coronavirus disease 2019; ICU: Intensive Care Unit; IQR: Interquartile range; SAPS: Simplified Acute Physiologic Score; SOFA: Sequential Organ Failure Assessment.

From a pathophysiologic standpoint, the deterioration of organ function as represented by an increasing SOFA score is particularly important for critically ill patients diagnosed with COVID-19. A recent study demonstrated a relationship between SOFA score and changes in microcirculation in COVID-19 patients: only patients with a score <10 could enhance their oxygen extraction capacity by increasing capillary density and capillary hematocrit, while those with a score ≥10 lacked this capacity and had higher levels of microcirculatory leukocytes and microaggregates [21]. Interestingly, microvascular dysfunction was recently shown to contribute to the association between COVID-19 outcome and diabetes [22]. This was supported by a study conducted in France that reported an adjusted 2-fold increased risk of mortality within 7 days of hospital admission in diabetes patients with COVID-19 and microvascular complications compared with patients without such complications [23].

Thus, systemic impairment of the microcirculation may lead to worse outcomes in COVID-19 patients.

A recent report exploring host-specific genetic factors associated with COVID-19 severity found a genetic correlation between type II diabetes and COVID-19 outcome, although there was no evidence of a causal association in the Mendelian regression analysis; the observed correlation may have been attributable to pleiotropic effects between type II diabetes and body mass index, which were shown to be causally linked to COVID-19 severity [24]. In the present study, we found that while diabetes was among the most important features for the prediction of changes in SOFA score, there was no difference in the prevalence of diabetes between patients with improved *vs.* worsened SOFA scores. Thus, a prediction model that can accurately estimate changes in SOFA score may aid in the early identification of patients with impaired physiologic adaptation and
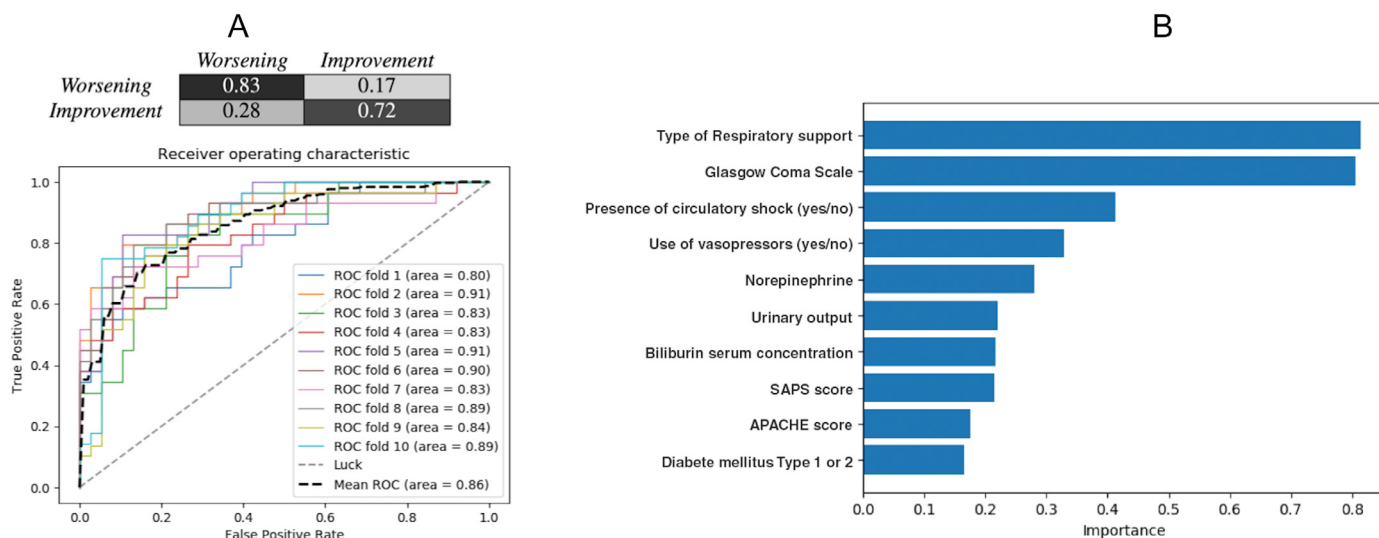
A

	Worsening	Improvement
Worsening	0.83	0.17
Improvement	0.28	0.72

B

Fig. 3. The description of the model performance (A) and the most important features identified by the model (B). APACHE: Acute Physiology and Chronic Health disease Classification System; COVID-19: Coronavirus disease 2019; ICU: Intensive Care Unit; ML: Machine Learning; RISC-19-ICU: RIsk Stratification in COVID-19 patients in the Intensive Care Unit; ROC: Receiving Operating Characteristics; SAPS: Simplified Acute Physiologic Score; SOFA: Sequential Organ Failure Assessment.

yield insight into the pathophysiologic mechanisms underlying the development of severe COVID-19. Based on this rationale, ML algorithms provide a means of developing a CDSS that can predict the risk of short-term complications in ICU patients.

We demonstrated the superiority of the XGBoost model over a logistic regression model for predicting changes in SOFA score in critically ill COVID-19 patients. Compared with traditional methods that use univariate and multivariate statistics for pattern discrimination, an ML approach based on the XGBoost algorithm has superior detection sensitivity and generalizability because it combines multiple types of information across several variables (e.g., a high-dimensional problem) based on a relatively small dataset. XGBoost also has advantages over other ML methods: it makes no assumptions regarding data distribution and uses individual decision trees, and may thus be unaffected by multicollinearity. Another benefit of ensemble methods such as XGBoost is that they automatically estimate feature importance from a trained predictive model, yielding a score for the utility or value of each feature in the construction of boosted decision trees within the model. The more an attribute is used to make key decisions in decision trees, the higher its relative importance. Consequently, the most important features identified by the model are potential targets for therapeutics aimed at preventing deterioration of the patient's condition. In our study, the most important features contributing to changes in SOFA score identified by the XGBoost model differed from those identified by standard logistic regression; the increased/decreased risk of organ failure in COVID-19 patients likely resulted from interaction among several processes, and may therefore be difficult to detect with conventional approaches. Thus, the application of the XGBoost model to critically ill COVID-19 patients provided clinically useful prognostic information that may help to optimize resource allocation and aid physicians in making personalized treatment decisions.

This study had some limitations that must be addressed to establish accurate and validated models for the creation of a CDSS that has clinical utility. First, although the XGBoost algorithm has a low risk of overfitting, the lack of an external validation cohort of ICU patients undermines the generalizability of our

predictive model. Additionally, while XGBoost identified important global features contributing to changes in SOFA score, our model was not fully tailored to support clinical decisions. Further investigation using XGBoost and *post hoc* interpretability methods is needed to evaluate local feature importance and relationships.

To conclude, we developed a prediction model using ML methodology for evaluating the risk of organ failure in COVID-19 patients in the ICU. The predictive performance of our model was superior to that of a standard regression approach, and we anticipate that it will be further developed and adapted to the changing needs of a rapidly growing prospective RISC-19-ICU cohort and will provide clinically relevant information regarding outcomes such as the need for endotracheal intubation and renal replacement therapy as well as mortality. Moreover, our model has high interpretability as it identifies features that are directly related to the development of complications associated with COVID-19; and extending the model to non-ICU departments can help to identify patients with a high probability of noninvasive ventilation failure and ICU admission for non-respiratory complications. Finally, the integration of the model into the RISC-19-ICU registry can enable profiling of morbidity risk and resource consumption by patients according to their clinical features. This can ensure the appropriate allocation of resources to patients who need them the most through the delivery of appropriate care and personalized interventions.

Conflicts of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Availability of Data and Materials

Any intensive care unit or other center treating critically ill COVID-19 patients is invited to join the RISC-19-ICU registry at https://www.risc-19-icu.net. While the registry protocol prevents the deposition of the full registry dataset in a third-party

repository, analyses on the full dataset may be requested by any collaborating center after approval of the study protocol by the registry board. Reproducibility of the results in the present study was ensured by providing code for registry-specific data transformation and statistical analysis for collaborative development on the GitHub and Zenodo repositories. The registry protocol and data dictionary are publicly accessible at https://www.risc-19-icu.net.

Appendix: RISC-19-ICU investigators

Andorra: Unidad de Cuidados Intensivos, Hospital Nostra Senyora de Meritxell, Escaldes-Engordany (Mario Alfaro-Farias, MD; Gerardo Vizmanos-Lamotte, MD, PhD). **Austria:** Department of Anesthesiology and Critical Care Medicine, Kepler University Hospital GmbH and Johannes Kepler University, Linz (Thomas Tschoellitsch, MD; Jens Meier, MD). **Ecuador:** Unidad de Cuidados Intensivos, Hospital Vicente Corral Moscoso, Cuenca (Hernán Aguirre-Bermeo, MD, PhD; Janina Apolo, BSc; Alberto Martínez, MD). **France:** SCPARE-Intensive Care Unit, Clinique Louis Pasteur, Essey-lès-Nancy (Geoffrey Jurkolow, MD; Gauthier Delahaye, MD); Department of Anesthesiology and Critical Care Medicine, University Hospital of Nancy, Nancy (Philippe Guerci, MD, PhD; Emmanuel Novy MD; Marie-Reine Losser, MD, PhD). **Germany:** Department of Medicine III — Interdisciplinary Medical Intensive Care, Medical Center University of Freiburg, Freiburg (Tobias Wengenmayer, MD; Jonathan Rilinger, MD; Dawid L. Staudacher, MD); Medical Intensive Care, Medical School Hannover, Hannover (Sascha David, MD; Tobias Welte, MD; Klaus Stahl, MD). **Greece:** Greece: Intensive Care Unit, St. Paul ("Agios Pavlos") General Hospital of Thessaloniki, Thessaloniki (Theodoros Aslanidis, MD, PhD). **Hungary:** Department of Anaethesiology and Intensive Care, University of Szeged (Anita Korsos, MD; Barna Babik, MD, PhD). **Iran**: Intensive Care Department, Shiraz University of Medical Sciences, Shiraz (Reza Nikandish, MD). **Italy:** Department of Anesthesia and Intensive Care Medicine, Policlinico San Marco, Gruppo Ospedaliero San Donato, Bergamo (Emanuele Rezoagli,

MD, PhD; Matteo Giacomini, MD; Alice Nova, MD); Anesthesia and Intensive care, Azienda Ospedaliero-Universitaria di Ferrara, Cona (Alberto Fogagnolo, MD; Savino Spadaro, MD, PhD); UO Anestesia e Terapia Intensiva, IRCCS Centro Cardiologico Monzino, Milan (Roberto Ceriani, MD; Martina Murrone, MD); Department of Internal Medicine, ASST Fatebenefratelli Sacco — "Luigi Sacco" Hospital, Milan (Maddalena A. Wu, MD; Chiara Cogliati, MD); Division of Anesthesia and Intensive Care, ASST Fatebenefratelli Sacco — "Luigi Sacco" Hospital, Milan (Riccardo Colombo, MD; Emanuele Catena, MD); Internal Medicine, Azienda Ospedaliera Universitaria di Modena, Modena (Fabrizio Turrini, MD, MSc; Maria Sole Simonini, MD; Silvia Fabbri, MD); UOC Anestesia e Rianimazione, Ospedale Infermi, Rimini (Jonathan Montomoli, MD, PhD; Antonella Potalivo, MD; Francesca Facondini, MD); U.O Pronto Soccorso — Medicina d'Urgenza, Ospedale Infermi, Rimini (Gianfilippo Gangitano, MD; Tiziana Perin, MD); Department of Anaesthesia and Intensive Care, Fondazione Policlinico Universitario A. Gemelli IRCCS, Università Cattolica del Sacro Cuore, Rome, Italy (Maria Grazia Bocci, MD; Massimo Antonelli, MD). **Netherlands:** Department of Intensive Care Medicine, Erasmus Medical Center, Rotterdam (Diederik Gommers, MD, PhD; Can Ince, PhD). **Spain:** Servicio de Medicina intensiva, Complejo Hospitalario Universitario A Coruña, A Coruña (Raquel Rodríguez-García, MD; Jorge Gámez-Zapata, MD; Xiana Taboada-Fraga, MD); Medical Intensive Care Unit, Hospital Clínic de Barcelona, Barcelona (Pedro Castro, MD; Adrian Tellez, MD); Servicio de Medicina Intensiva, Hospital General San Jorge, Huesca (Arantxa Lander-Azcona, MD; Jesús Escós-Orta, MD); Servicio de Medicina Intensiva, Hospital Universitario de Torrejon, Madrid (Maria C. Martín-Delgado, MD; Angela Algaba-Calderon MD); Servicio de Medicina intensiva, Hospital Verge de la Cinta, Tortosa, Tarragona (Diego Franch-Llasat, MD; Ferran Roche-Campo, MD, PhD); Unidad de Cuidados Intensivos, Hospital Clínico Universitario Lozano Blesa, Zaragoza (Herminia Lozano-Gómez, MD; Begoña Zalba-Etayo, MD, PhD). **Switzerland:** Medizinische Intensivstation, Kantonsspital Aarau, Aarau (Marc P. Michot, MD, Alexander Klarer); Klinik für Operative Intensivmedizin, Kantonsspital Aarau, Aarau, Switzerland (Rolf Ensner, MD); Institut fuer Anesthaesie und Intensivmedizin, Zuger Kantonsspital AG, Baar (Peter Schott, MD; Severin Urech, MD); Department Intensivmedizin, Universitaetsspital Basel, Basel (Nuria Zellweger); Intensivmedizin, St. Claraspital, Basel (Lukas Merki, MD; Adriana Lambert, MD); Department Intensive Care Medicine, Spitalzentrum Biel, Biel, Switzerland (Marcus Laube, MD); Department of Intensive Care Medicine, University Hospital Bern, Inselspital, Bern (Marie M. Jeitziner, RN, PhD; Beatrice Jenni-Moser, RN, MSc); Interdisziplinaere Intensivmedizin, Lindenhofspital, Bern, Switzerland (Jan Wiegand, MD); Interdisziplinaere Intensivstation, Spital Buelach, Buelach (Bernd Yuen, MD; Barbara Lienhardt-Nobbe; AndreaWestphalen, MD); Intensivstation, Regionalspital Emmental AG, Burgdorf (Petra Salomon, MD; Iris Drvaric, MD); Intensivmedizin, Kantonsspital Graubuenden, Chur (Frank Hillgaertner, MD; Marianne Sieber); Institut fuer Anaesthesie und Intensivmedizin, Spital Thurgau, Frauenfeld (Alexander Dullenkopf, MD; Lina Petersen, MD; Ivan Chau, MD); Soins Intensifs, Hopital cantonal de Fribourg, Fribourg (Hatem Ksouri, MD, PhD; Govind Oliver Sridharan, MD); Division of Intensive Care, University Hospitals of Geneva, Geneva (Sara Cereghetti, MD; Filippo Boroli, MD;

Jerome Pugin, MD, PhD); Division of Neonatal and Pediatric Intensive Care, University Hospitals of Geneva, Geneva (Serge Grazioli, MD; Peter C. Rimensberger, MD); Intensivstation, Spital Grabs, Grabs, Switzerland (Christian Bürkle, MD); Institut für Anaesthesiologie Intensivmedizin & Rettungsmedizin, See-Spital Horgen & Kilchberg, Horgen (Julien Marrel, MD; Mirko Brenni, MD); Soins Intensifs, Hirslanden Clinique Cecil, Lausanne (Isabelle Fleisch, MD; Jerome Lavanchy, MD); Pediatric Intensive Care Unit, University Hospital Lausanne, Lausanne (Marie-Helene Perez, MD; Anne-Sylvie Ramelet, MD); Anaesthesie und Intensivmedizin, Kantonsspital Baselland, Liestal (Anja Baltussen Weber, MD; Peter Gerecke, MD; Andreas Christ, MD); Dipartimento Area Critica, Clinica Luganese Moncucco, Lugano (Samuele Ceruti, MD; Andrea Glotta, MD); Interdiszi-plinaere Intensivstation, Spital Maennedorf AG, Maennedorf (Katharina Marquardt, MD; Karim Shaikh, MD); Institut fuer Anaesthesie und Intensivmedizin, Spital Thurgau, Muensterlin-gen (Tobias Hübner, MD; Thomas Neff, MD); Intensivmedizin, Schweizer Paraplegikerzentrum Nottwil, Nottwil, Switzerland (Hermann Redecker, MD); Soins intensifs, Groupement Hospi-talier de l'Ouest Lémanique, Hôpital de Nyon, Nyon (Thierry Fumeaux, MD; Mallory Moret-Bochatay, MD); Klinik für Anaes-thesie und Intensivmedizin, Spitalzentrum Oberwallis, Visp, Switzerland (Friederike Meyer zu Bentrup, MD, MBA) Inten-sivmedizin & Intermediate Care, Kantonsspital Olten, Olten, Switzerland (Michael Studhalter, MD); Intensivmedizin, Spi-tal Oberengadin, Samedan (Michael Stephan, MD; Jan Brem, MD); Intensivstation, Kantonsspital Schaffhausen, Schaffhausen, Switzerland (Nadine Gehring, MD); Anaesthesie Intensivmedi-zin Schmerzmedizin, Spital Schwyz, Schwyz (Daniela Selz, MD; Didier Naon, MD); Medizinische Intensivstation, Kantonsspital St. Gallen, St. Gallen, Switzerland (Gian-Reto Kleger, MD); De-partment of Anesthesiology and Intensive Care Medicine, Kan-tonsspital St. Gallen, St. Gallen (Urs Pietsch, MD; Miodrag Fil-ipovic, MD); Department for Intensive Care Medicine, Kanton-sspital Nidwalden, Stans (Anette Ristic, MD; Michael Sepulcri, MD); Intensivstation, Spital Simmental-Thun-Saanenland AG, Thun, Switzerland (Antje Heise, MD); Service d'Anesthesiologie, EHNV, Yverdon- les-Bains (Marilene Franchitti Laurent, MD; Jean-Christophe Laurent, MD); Institute of Intensive Care Medicine, University Hospital Zurich, Zurich (Pedro D. Wen-del Garcia, MSc; Matthias Hilty, MD; Reto Schuepbach, MD; Dorothea Heuberger, PhD; Philipp Bühler, MD; Silvio Brug-ger, MD, PhD); Interdisziplinaere Intensivstation, Stadtspital Triemli, Zurich (Patricia Fodor, MD; Pascal Locher, MD; Gio-vanni Camen, MD); Abteilung für Anaesthesiologie und In-tensivmedizin, Hirslanden Klinik Im Park, Zürich (Tomislav Gaspert, MD; Marija Jovic, MD); Institut für Anaesthesiolo-gie und Intensivmedizin, Klinik Hirslanden, Zurich (Christoph Haberthuer, MD; Roger F. Lussman, MD). **Turkey:** General Surgery, Samsun Training and Research Hospital, Samsun (Elif Colak, MD).

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jointm.2021.09.002.

References

[1] WHO Coronavirus (COVID-19) Dashboard. https://covid19.who.int. [Last accessed on 2021 September 25].

[2] Rezoagli E, Magliocca A, Bellani G, Pesenti A, Grasselli G. Development of a critical care response - Experiences from Italy during the coronavirus disease 2019 pan-demic. Anesthesiol Clin 2021;39(2):265–84. doi:10.1016/j.anclin.2021.02.003.

[3] Hong Y, Wu X, Qu J, Gao Y, Chen H, Zhang Z. Clinical characteristics of coronavirus disease 2019 and development of a prediction model for prolonged hospital length of stay. Ann Transl Med 2020;8(7):443. doi:10.21037/atm.2020.03.147.

[4] Shillan D, Sterne JAC, Champneys A, Gibbison B. Use of machine learning to anal-yse routinely collected intensive care unit data: a systematic review. Crit Care 2019;23(1):284. doi:10.1186/s13054-019-2564-9.

[5] Bernardini M, Romeo L, Misericordia P, Frontoni E. Discovering the type 2 diabetes in electronic health records using the sparse balanced support vector machine. IEEE J Biomed Health Inform 2020;24(1):235–46. doi:10.1109/JBHI.2019.2899218.

[6] Bernardini M, Morettini M, Romeo L, Frontoni E, Burattini L. Early temporal predic-tion of type 2 diabetes risk condition from a general practitioner electronic health record: a multiple instance boosting approach. Artif Intell Med 2020;105:101847. doi:10.1016/j.artmed.2020.101847.

[7] Romeo L, Armentano G, Nicolucci A, Vespasiani M, Vespasiani G, Frontoni E. A novel spatio-temporal multi-task approach for the prediction of diabetes-related complica-tion: a cardiopathy case of study. In: Proceedings of the twenty-ninth international joint conference on artificial intelligence. Yokohama, Japan: international joint con-ferences on artificial intelligence organization; 2020. p. 4299–305. doi:10.24963/ij-cai.2020/593.

[8] DECIDE-AI Steering GroupDECIDE-AI: new reporting guidelines to bridge the development-to-implementation gap in clinical artificial intelligence. Nat Med 2021;27(2):186–7. doi:10.1038/s41591-021-01229-5.

[9] Zhang Z, Liu J, Xi J, Gong Y, Zeng L, Ma P. Derivation and validation of an ensemble model for the prediction of agitation in mechanically ventilated patients maintained under light sedation. Crit Care Med 2021;49(3):e279–90. doi:10.1097/CCM.0000000000004821.

[10] Liu P, Fu B, Yang SX, Deng L, Zhong X, Zheng H. Optimizing survival analysis of XGBoost for ties to predict disease progression of breast cancer. IEEE Trans Biomed Eng 2021;68(1):148–60. doi:10.1109/TBME.2020.2993278.

[11] Zhang Z, Ho KM, Hong Y. Machine learning for the prediction of volume respon-siveness in patients with oliguric acute kidney injury in critical care. Crit Care 2019;23(1):112. doi:10.1186/s13054-019-2411-z.

[12] Hyland SL, Faltys M, Hüser M, Lyu X, Gumbsch T, Esteban C, et al. Early prediction of circulatory failure in the intensive care unit using machine learning. Nat Med 2020;26(3):364–73. doi:10.1038/s41591-020-0789-4.

[13] Zabihi M, Kiranyaz S, Gabbouj M. Sepsis prediction in intensive care unit using ensemble of XGBoost models. 2019 Comput Cardiol (CinC) 2019:1–4. doi:10.23919/CinC49843.2019.9005564.

[14] Garcia PDW, Fumeaux T, Guerci P, Heuberger DM, Montomoli J, Roche-Campo F, et al. Prognostic factors associated with mortality risk and disease progression in 639 critically ill patients with COVID-19 in Europe: initial report of the international RISC-19-ICU prospective observational cohort. EClinicalMedicine 2020;25:100449. doi:10.1016/j.eclinm.2020.100449.

[15] Garcia PDW, Aguirre-Bermeo H, Buehler PK, Alfaro-Farias M, Yuen B, David S, et al. Implications of early respiratory support strategies on disease progression in critical COVID-19: a matched subanalysis of the prospective RISC-19-ICU cohort. Crit Care 2021;25(1):175. doi:10.1186/s13054-021-03580-y.

[16] Vincent JL, Moreno R, Takala J, Willatts S, De Mendonça A, Bruining H, et al. The SOFA (Sepsis-related organ failure assessment) score to describe organ dysfunc-tion/failure. On behalf of the working group on sepsis-related problems of the Eu-ropean society of intensive care medicine. Intensive Care Med 1996;22(7):707–10. doi:10.1007/BF01709751.

[17] Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA 2016;315(8):801–10. doi:10.1001/jama.2016.0287.

[18] Chen T, Guestrin C. XGBoost: a scalable tree boosting system. In: Proceed-ings of the 22nd ACM SIGKDD international conference on knowledge discov-ery and data mining. San Francisco California USA: ACM; 2016. p. 785–94. doi:10.1145/2939672.2939785.

[19] Cawley GC, Talbot NLC. On over-fitting in model selection and subsequent selection bias in performance evaluation. J Mach Learn Res 2010;11:2079–107.

[20] Melnick ER, Sinsky CA, Krumholz HM. Implementing measurement sci-ence for electronic health record use. JAMA 2021;325(21):2149–50. doi:10.1001/jama.2021.5487.

[21] Favaron E, Ince C, Hilty MP, Ergin B, van der Zee P, Uz Z, et al. Capillary leukocytes, microaggregates, and the response to hypoxemia in the microcircu-lation of coronavirus disease 2019 patients. Crit Care Med 2021;49(4):661–70. doi:10.1097/CCM.0000000000004862.

[22] Landstra CP, de Koning EJP. COVID-19 and diabetes: understanding the interrela-tionship and risks for a severe course. Front Endocrinol (Lausanne) 2021;12:649525. doi:10.3389/fendo.2021.649525.

[23] Cariou B, Hadjadj S, Wargny M, Pichelin M, Al-Salameh A, Allix I, et al. Phenotypic characteristics and prognosis of inpatients with COVID-19 and diabetes: the CORO-NADO study. Diabetologia 2020;63(8):1500–15. doi:10.1007/s00125-020-05180-x.

[24] COVID-19 host genetics initiative. Mapping the human genetic architecture of COVID-19. Nature 2021. doi:10.1038/s41586-021-03767-x.