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| RESEARCH ARTICLE

Machine Learning Models for Predicting Corticosteroid Therapy Necessity in COVID-19 Patients: A Comparative Study

Mujiba Shaima[1], Norun Nabi[2], Md Nasir Uddin Rana[3], Ahmed Ali Linkon[4], Badruddowza[5], Md Shohail Uddin Sarker[6], Nishat Anjum[7] ✉ and Hammed Esa[8]

[13]Department of Computer Science, Monroe College, New Rochelle, New York, USA
[2]Department of Information Technology, Washington University of Science and Technology, Alexandria, Virginia, USA
[4]Department of Computer Science, Westcliff University, Irvine, California
[56]Department of Computer & Info Science, Gannon University, Erie, Pennsylvania, USA
[7]Department of Computer Science, University of South Dakota, Vermillion, South Dakota, USA
[8]Department of Business Administration, International American University Los Angeles, California, USA

Corresponding Author: Nishat Anjum, **E-mail**: nishat.anjum@coyotes.usd.edu

| ABSTRACT

This study analyzes machine learning algorithms to predict the need for corticosteroid (CS) therapy in COVID-19 patients based on initial assessments. Using data from 1861 COVID-19 patients, parameters like blood tests and pulmonary function tests were examined. Decision Tree and XGBoost emerged as top performers, achieving accuracy rates of 80.68% and 83.44% respectively. Multilayer Perceptron and AdaBoost also showed competitive performance. These findings highlight the potential of AI in guiding CS therapy decisions, with Decision Tree and XGBoost standing out as effective tools for patient identification. This research offers valuable insights for personalized medicine in infectious disease management.

| KEYWORDS

Machine Learning; Corticosteroid Therapy; COVID-19

| ARTICLE INFORMATION

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1. Introduction

The COVID-19 pandemic has spurred urgent efforts to develop effective treatment strategies, particularly for patients experiencing severe respiratory symptoms. Corticosteroids (CS) have emerged as a potential therapeutic intervention for managing COVID-19-related pulmonary complications. However, determining which patients will benefit from CS therapy remains a challenge, necessitating the development of accurate predictive models. In this study, we investigate the efficacy of various machine learning algorithms in classifying the necessity of CS therapy based on initial patient assessments, including demographic information, blood tests, and pulmonary function tests.

The methodology employed in this study encompasses three key components: dataset collection and preprocessing, feature selection, and model evaluation. Initially, a cohort of 1861 COVID-19 patients was included in the analysis, with strict criteria excluding individuals without respiratory tract pneumonia. Through meticulous selection and assessment, 1580 patients were excluded, leaving only those deemed suitable for CS therapy based on clinical indications. The subsequent division of patients into CS therapy and non-therapy groups facilitated a comprehensive examination of treatment outcomes.

Feature selection was conducted utilizing advanced techniques such as SHapley Additive exPlanations (SHAP) and the k-best method, identifying key variables that significantly influence treatment necessity predictions. These features encompassed a range of clinical indicators, including CS dosage, SARS-CoV-2 antibody levels, and pulmonary function parameters, among others. The final feature set was meticulously curated to ensure relevance and efficacy in treatment decision-making.

To evaluate model performance, several metrics were employed, including accuracy, balanced accuracy, F1 score, sensitivity, and specificity. These metrics provided comprehensive insights into the predictive capabilities of each algorithm, facilitating informed comparisons and recommendations for clinical implementation. Notably, Decision Tree and XGBoost emerged as top-performing algorithms, demonstrating superior accuracy and balanced accuracy compared to other models.

2. Literature Review

In the Sayed et al. [2021] study, a predictive model was developed to assess severity risks for COVID-19 patients using X-ray images and machine learning techniques. The model combined the CheXNet deep pre-trained model with hybrid handcrafted techniques for feature extraction, utilizing PCA and RFE for feature selection. Merging PCA and RFE-selected features (PCA + RFE) resulted in the best outcomes across all classifiers. Notably, XGBoost achieved the highest performance with merged features, with 97% accuracy, 98% precision, 95% recall, 96% F1-score, and 100% ROC-AUC. SVM showed similar results with 97% accuracy, 96% precision, 95% recall, 95% F1-score, and 99% ROC-AUC. Additionally, for pre-trained CheXNet features, Extra Tree and SVM classifiers with RFE attained consistent scores of 99.6% across all evaluation measures.

Nurhakim et al. [2023] utilized machine learning techniques to analyze a dataset collected from regions including South Sudan and the Eastern Democratic Republic of the Congo. This dataset encompasses various factors such as sociodemographic characteristics, COVID-19 exposures, symptoms, health history, and laboratory test results. Through the application of advanced statistical models and data mining algorithms, we identify significant risk factors associated with COVID-19 mortality. The machine learning models employed include Logistic Regression, Decision Tree, Random Forest, and XGBoost. Among these models, Random Forest emerges as the highest performing one for predicting mortality risk in COVID-19-positive patients in the specified regions, achieving an accuracy rate of 87.01%, precision and recall rates of 86.67%, and an F1-Score of 86.67%. The SHAP model employed reveals that factors such as the patient's appearance at enrollment, nationality, and the presence of COVID-19-related symptoms significantly contribute to the mortality condition.

Panthakkan et al. [2020] focus on efficiently predicting COVID-19 positivity using advanced machine intelligence techniques applied to lung X-rays. The study introduces the VGG16 transfer learning model as a promising tool for accurate and rapid COVID-19 diagnosis. The system classifies lung X-ray images into two categories: COVID-19 positive and normal. Evaluation of the system's effectiveness is conducted using performance metrics such as accuracy, precision, recall, and F1 score. Experiments involved 2000 X-ray samples, and the proposed VGG16 model achieved an exceptional recognition accuracy of 99.5% for the two-class classification, surpassing existing methods in the literature. The proposed approach demonstrates high efficiency and precision, making it a valuable tool to assist radiologists and healthcare professionals in identifying COVID-19 positivity through lung X-rays.

Yaqin et al. [2022] study started from a situation that began to emerge in Indonesia towards the end of February 2020, leading to a notable increase in new COVID-19 patients. Despite researchers conducting various models and projections for COVID-19 cases in Indonesia, the results remain somewhat unreliable due to the fluctuating patterns observed. Predictions made at the national level must consider these pattern variations, as they likely correlate with unique patterns in each region. This study aims to predict COVID-19 cases in Indonesia using the Support Vector Regression (SVR) algorithm and mathematical models for predicting reproduction numbers. SVR analysis is employed to address the nonlinearity of data in model formation. The modeling process is based on the SIR model, with parameters estimated from available data. Testing results using three different kernels show variations, with the most accurate prediction achieved using the 'RBF' kernel with C = 1E3 and gamma = 0.1, resulting in a Mean Absolute Percentage Error (MAPE) of 4.5% and Mean Squared Error (MSE) of 4.2.

3. Methodology

This section outlines the approach employed in this study. Initially, it details the dataset, including patient enrollment criteria and the parameters assessed during the initial examination (refer to Section 3.1). Additionally, it discusses the machine learning algorithms and optimization methods utilized (see Section 3.2). Section 3.3 delineates the metrics employed for evaluation purposes.

3.1 Dataset collection and preprocessing

In this study, 1861 patients diagnosed with COVID-19 were included. Patients without respiratory tract pneumonia were excluded from the study, as pulmonary fibrosis in such cases is rare, making corticosteroid treatment unnecessary. Additionally, when necessary, individuals were assessed for signs of pre-existing interstitial lung disease using HRCT scans or biopsy, with only those demonstrating clear post-COVID lung damage being included for analysis. Consequently, 1580 patients were excluded, leaving only those for whom corticosteroid treatment was deemed appropriate. The selection process is illustrated in Figure 1.

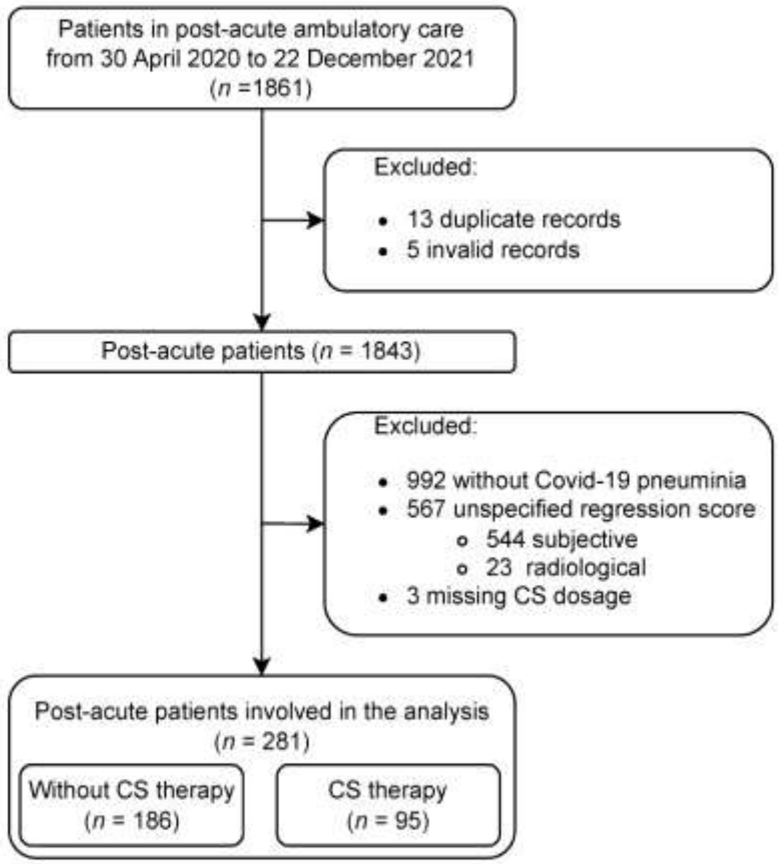


Fig 1: Patients were included in the analysis based on specific criteria, while reasons for exclusion were also provided.

The patients were divided into two groups: those who underwent corticosteroid (CS) therapy as part of post-COVID treatment (95 patients) and those who did not (186 patients). CS therapy was administered to individuals experiencing persistent pulmonary interstitial damage caused by COVID-19 pneumonia. The prescribed dose was 0.5 mg of prednisolone per kilogram of body weight for 2 weeks, followed by 4 weeks of 20 mg of prednisolone treatment, gradually tapering off until withdrawal. Notably, CS treatment was contraindicated for patients with bacterial or other infections. Each patient underwent an initial examination approximately 3 weeks after the onset of acute COVID-19 symptoms. Data collected for the study encompassed various aspects, including demographic information (age, BMI, smoking status, comorbidities), details of acute-phase treatment, pulmonary function tests, and blood test results (e.g., IgG, IgM levels). Additionally, data on treatment outcomes approximately 3 months post-acute treatment initiation were recorded, assessing improvements based on objective radiological findings (X-ray, CT) and subjective patient feedback. Efforts were made during treatment selection to minimize potential biases and overfitting risks by removing certain attributes from the dataset. The complete dataset, including detailed attribute information, was made available to facilitate future integration with other datasets. This paper elaborates only on the parameters deemed significant.

3.2 Feature Selection

In this study, we assessed nine machine learning algorithms designed for a classification task: predicting whether corticosteroid (CS) treatment should be recommended for a patient. The initial step involved selecting a set of features to be used in the algorithms. To accomplish this, we utilized SHapley Additive exPlanations (SHAP), which gauges the impact of features on algorithm output. In our case, we focused on the Decision Tree algorithm. Among the crucial features identified were the amount of CS administered during treatment and IgM values from blood tests. Additionally, we employed a method involving the selection of k-highest scores based on p-values.

Subsequently, a subset of features was extracted from the results of both methods. The features common to both approaches included the amount of CS administered, SARS-CoV-2 IgM (quantitative), and Mo % from blood tests. Using the k-best method, we further identified the following features: corticosteroid usage, duration of CS treatment in weeks, total CS dosage, olfactory loss, RDW from blood tests, absolute values of VC, FEV1, and PEF (% predicted). Additionally, we incorporated additional features deemed medically significant in treatment decisions, such as pneumonia, comorbidities, post-COVID disability, SARS-CoV-2 IgG (qualitative), % predicted values of FVC, DLCOc SB, KCO SB, MEF25, persistent cough, and persistent dyspnea.

The final feature set comprises the following variables: pneumonia status, presence of comorbidities, corticosteroid usage, olfactory loss, post-COVID disability, qualitative SARS-CoV-2 IgG levels, quantitative SARS-CoV-2 IgM levels, amount and total dosage of corticosteroids administered, duration of corticosteroid use in weeks, RDW from blood tests, absolute VC, percentage predicted FVC, absolute FEV1, Mo % from blood tests, percentage predicted PEF, absolute DLCOc SB, absolute KCO SB, persistent cough, persistent dyspnea, and absolute MEF25.

3.3. Evaluation Metrics

We chose several metrics to assess and compare the outcomes of the experiments detailed in the preceding section. These metrics consist of accuracy (as per Equation (1)), balanced accuracy (refer to Equation (5)), $F1$ score (defined in Equation (2)), sensitivity (calculated using Equation (3)), and specificity (determined through Equation (4)). To describe these metrics, the following abbreviations were utilized: TP for the number of true positive cases, TN for true negative cases, and FN for false negative cases.

Accuracy measures the ratio of correctly predicted labels over total number of evaluated samples [9]:

Acc=TN+TP TP+TN+FP+FN. (1)

$F1$ score is a combination of precision and recall metrics, which capture properties of both [9]:

$F1$=TP / TP+12(FP+FN). (2)

Sensitivity measures, how the model can correctly predict positive samples [9]:

Sen=TP / TP+FN. (3)

Specificity measures how the model can correctly predict negative samples [9]:

Spe=TN / TN+FP. (4)

Balanced Accuracy is average value between sensitivity and specificity [9]:

AccBAL=Spe+Sen/ 2. (5)

4. Result

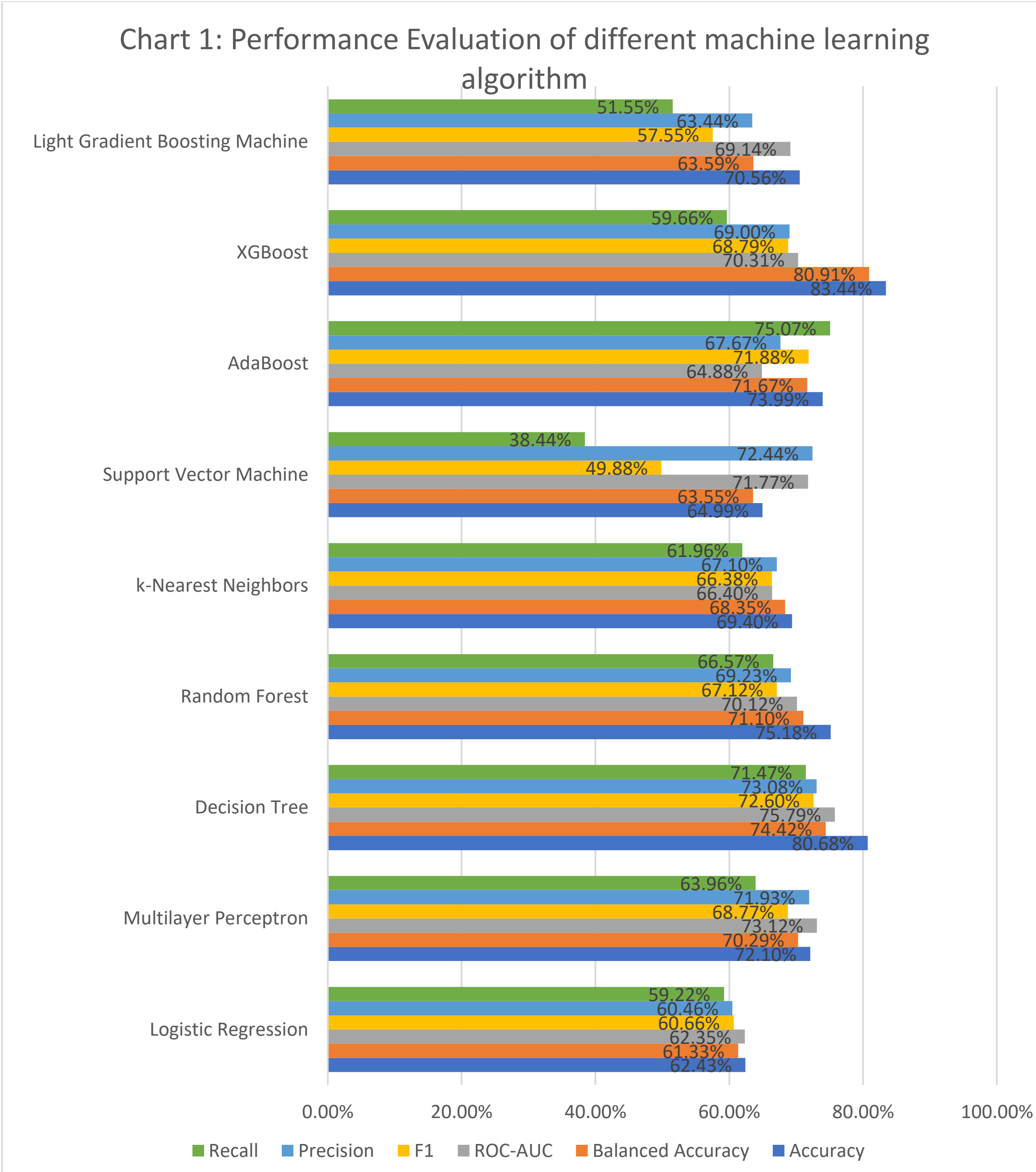
The objective of this study is to create artificial intelligence algorithms capable of categorizing the requirement for corticosteroid (CS) therapy based on the initial assessment of patients. This assessment comprises blood tests, pulmonary function tests, and data regarding ongoing health concerns, including considerations for treatment administration, potential dosage, and duration.

Table 1: Matrices evaluation of different machine learning algorithm

Method	*Accuracy*	*Balanced Accuracy*	*ROC-AUC*	*F1*	*Precision*	*Recall*
Logistic Regression	62.43%	61.33%	62.35%	60.66%	60.46%	59.22%
Multilayer Perceptron	72.10%	70.29%	73.12%	68.77%	71.93%	63.96%
Decision Tree	**80.68%**	**74.42%**	**75.79%**	**72.60%**	**73.08%**	71.47%
Random Forest	75.18%	71.10%	70.12%	67.12%	69.23%	66.57%
***k*-Nearest Neighbors**	69.40%	68.35%	66.40%	66.38%	67.10%	61.96%
Support Vector Machine	64.99%	63.55%	71.77%	49.88%	72.44%	38.44%
AdaBoost	73.99%	71.67%	64.88%	71.88%	67.67%	**75.07%**
XGBoost	83.44%	80.91%	70.31%	68.79%	69.00%	59.66%
Light Gradient Boosting Machine	70.56%	63.59%	69.14%	57.55%	63.44%	51.55%

When comparing the performance of various machine learning algorithms in predicting the necessity of corticosteroid (CS) therapy for COVID-19 patients, several key observations emerge. Decision Tree and XGBoost notably outperform other algorithms in terms of accuracy, achieving 80.68% and 83.44%, respectively. This suggests that these models are better at correctly classifying patients who require CS therapy based on the initial examination data, including blood tests, pulmonary function tests, and health history. Additionally, XGBoost demonstrates superior balanced accuracy (80.91%), indicating its effectiveness in handling imbalanced datasets and providing more reliable predictions across different classes.

Multilayer Perceptron (MLP) also presents a competitive performance with an accuracy of 72.10%, highlighting its potential utility in classifying patients' CS therapy needs. However, it falls short compared to Decision Tree and XGBoost in terms of accuracy and balanced accuracy. Nevertheless, MLP showcases strong precision (71.93%) and recall (63.96%), indicating its ability to accurately identify positive cases (patients requiring CS therapy) while minimizing false positives.



Support Vector Machine (SVM), despite achieving a moderate accuracy of 64.99%, demonstrates lower precision (72.44%) and recall (38.44%) compared to other algorithms. This suggests that SVM may struggle with accurately identifying patients in need of CS therapy, particularly in scenarios where false negatives (missing patients who need treatment) are costly.

On the other hand, AdaBoost presents competitive performance with an accuracy of 73.99% and balanced accuracy of 71.67%. While its precision (67.67%) and recall (75.07%) are balanced, they fall slightly short compared to Decision Tree and XGBoost. Nevertheless, AdaBoost remains a viable option for predicting the necessity of CS therapy in COVID-19 patients.

Overall, the results suggest that Decision Tree and XGBoost are the top-performing algorithms for predicting the need for CS therapy in COVID-19 patients, showcasing superior accuracy and balanced accuracy compared to other models. However, Multilayer Perceptron and AdaBoost also present promising results and can be considered viable alternatives, especially in scenarios where interpretability or computational efficiency is prioritized.

5. Result and Discussion

In conclusion, this study aimed to develop AI-based algorithms for accurately classifying the necessity of corticosteroid (CS) therapy in COVID-19 patients based on their initial examination data. Through rigorous methodology involving dataset collection, preprocessing, feature selection, and evaluation metrics, the performance of nine machine learning algorithms was analyzed. The findings indicate that Decision Tree and XGBoost outperformed other algorithms, achieving high accuracy and balanced accuracy rates. These models demonstrated robustness in correctly identifying patients requiring CS therapy, showcasing the potential for their implementation in clinical settings to assist healthcare professionals in treatment decision-making.

While Multilayer Perceptron and AdaBoost also exhibited competitive performance, they fell slightly short compared to Decision Tree and XGBoost. Nevertheless, these models present viable alternatives, especially considering their balanced precision and recall rates. However, it's worth noting that the Support Vector Machine (SVM) exhibited lower precision and recall rates, suggesting limitations in accurately identifying patients in need of CS therapy. This highlights the importance of selecting appropriate algorithms tailored to specific clinical contexts to ensure optimal patient care.

In the broader context, the successful development and validation of AI-based algorithms for predicting CS therapy necessity in COVID-19 patients represent significant progress in leveraging machine learning techniques to enhance clinical decision-making. These algorithms have the potential to streamline treatment processes, improve patient outcomes, and alleviate the burden on healthcare systems, particularly during times of public health crises such as the COVID-19 pandemic. Moving forward, further research and validation studies are warranted to assess the scalability, generalizability, and real-world implementation of these algorithms across diverse patient populations and healthcare settings. Additionally, ongoing advancements in machine learning methodologies and healthcare data collection will continue to drive innovation in AI-driven healthcare solutions, ultimately benefiting patients and healthcare providers alike.

6. Conclusion

In conclusion, this study represents a significant step forward in harnessing the power of artificial intelligence to enhance clinical decision-making in the context of COVID-19 management. Through a meticulous process of dataset collection, preprocessing, feature selection, and rigorous evaluation, we identified Decision Tree and XGBoost as top-performing machine learning algorithms for predicting the necessity of corticosteroid (CS) therapy in COVID-19 patients.

The robust performance of Decision Tree and XGBoost, with accuracy rates of 80.68% and 83.44%, respectively, underscores their potential as effective tools for guiding CS therapy decisions based on initial patient assessments. These findings hold valuable implications for personalized medicine in infectious disease management, offering insights that can optimize treatment strategies and improve patient outcomes.

While Multilayer Perceptron and AdaBoost demonstrated competitive results, Decision Tree and XGBoost stood out with superior accuracy and balanced accuracy rates. The study emphasizes the importance of selecting appropriate algorithms tailored to specific clinical contexts, considering factors such as interpretability, precision, and recall rates.

Furthermore, the successful development and validation of AI-based algorithms for predicting CS therapy necessity highlight the potential for machine learning to streamline treatment processes, improve patient outcomes, and alleviate healthcare system burdens, particularly during public health crises like the COVID-19 pandemic. Moving forward, continued research and validation studies will be crucial to assess the scalability, generalizability, and real-world implementation of these algorithms across diverse patient populations and healthcare settings.

As advancements in machine learning methodologies and healthcare data collection persist, the integration of AI-driven healthcare solutions is poised to revolutionize clinical practices, ultimately benefiting both patients and healthcare providers. This study sets the stage for future endeavors in the intersection of artificial intelligence and infectious disease management, paving the way for innovative approaches to enhance healthcare delivery and patient care.

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