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Prediction of Acute Burn-Induced Coagulopathy Risk with Machine Learning Models

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Abstract

In burn patients, lipolysis, proteolysis, glycolysis and many severe hyperdynamic and hypermetabolic responses are seen with high fever. Patients who have these hypermetabolic reactions lose lean muscle mass, their immune systems deteriorate, their coagulopathy worsens, and they eventually die. Due to enhanced vascular permeability, fluid collection in the interstitial space is seen, especially in the first 24 hours following serious burns. If not treated, decreased intravascular volume has an impact on tissue perfusion. Acute burns also raise the risk of coagulopathy. Coagulopathy is one of the leading contributors to death in burn patients. Therefore, the use of machine learning-based decision support systems for quick coagulopathy pre-diagnosis may be crucial for physicians and healthcare executives. In this study, machine learning models were investigated for the estimation of the risk of coagulopathy due to acute burns, using a data set of 1040 burn patients and 35 different biochemical parameters of these patients. The Subspace KNN model showed the highest prediction success compared to other machine learning methods with 100% accuracy.
Keywords: burns; coagulopathy; machine learning

1. Introduction

Burn injuries are traumas that result from sources including fire, hot liquid, radiation, chemical, cold, or electricity and destroy skin and/or organic tissues as a result of energy transfer [1]. After falls, traffic accidents, and wars, burns are the fourth most frequent type of trauma in the globe. According to a 2004 survey, around 11 million people apply to medical facilities annually owing to burn injuries worldwide. The American Burn Association's research from 2016 highlighted the fact that 67% of burns only affect less than 10% of the total body surface area [TVSA] [2]. According to a 2019 study, more than 13,000 people experience severe burns that cover more than 20% of their body surface area every year [3]. Deeply catabolic and hypermetabolic reactions are triggered by burn injuries, and they can endure for weeks, months, or even years. In particular, lipolysis, proteolysis, glycolysis, high temperature, and several severe hyperdynamic and hypermetabolic responses are reported in burn patients who are impacted by more than 20% of TBSA. These hypermetabolic responses seen in patients cause a decrease in lean muscle mass, decrease in functional capacity, delay in wound healing, coagulopathy, and deterioration of fibrinolytic activity, leading to serious mortality [4,5]. After burning, muscle protein breaks down much faster than it is synthesized. Net protein loss leads to loss of lean body mass and severe muscle loss. Protein degradation can

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continue for up to 9 months after severe burn injury. Protein catabolism is associated with increases in metabolic rates. For severely burned patients, the resting metabolic rate at thermal neutral temperature [30°C] exceeds 140% of normal and increases to 130% after wounds are fully healed, then to 120% at 6 months and to 110% at 12 months. falls. These changes in metabolic rate vary according to the percentage of TBSA affected by the burn [6].

Burn-Induced Coagulopathy

Coagulopathy is frequently seen in patients with TBSA burns of 20% or more. The development of coagulopathy after burn injury further complicates treatment approaches in these patients. The inflammatory response that occurs after a burn has profound effects, affecting clot formation and leading to burn-induced coagulopathy. Coagulopathy seen in burn patients is similar to coagulopathy seen in patients with sepsis and/or post-traumatic and is characterized by disruption of natural anticoagulant systems, and procoagulant and antifibrinolytic changes [7-8].

Pathophysiology of Burn-Induced Coagulopathy

In patients with severe burns, coagulopathy may cause thromboembolic complications, multi-organ failure, and increased mortality and morbidity. Although there is no accepted definitive pathophysiology, it is thought that the hypermetabolism, inflammatory response, hypothermia and endothelial damage seen after burns cause coagulopathy and anti-fibrinolytic activities (Figure 1) [8].

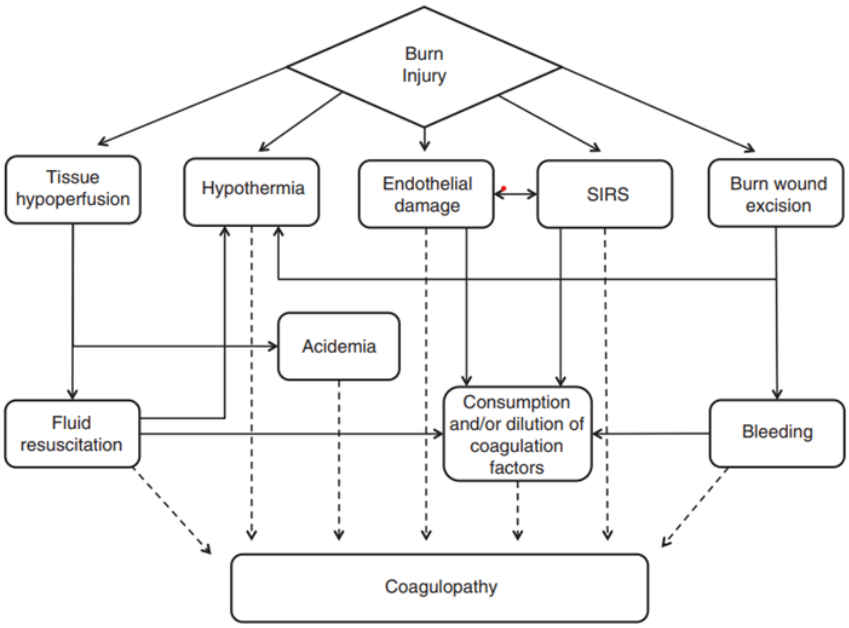

Figure 1. Pathophysiologic mechanisms impacting coagulation in patients with severe burns (The syndrome known as the systemic inflammatory response [8])

The changes that cause coagulopathy in burn patients are quite similar. These changes are:

- Increase in thrombin-antithrombin complex [TAT] levels and FVII [FVIIa] activation,
- Decrease in protein c, protein s levels,

- Seeing markers of thrombin activation such as fibrin degradation products and prothrombin fragment F1+2 [8].

Processes of Burn-Induced Coagulopathy

Very Early Stage After Burn – Before Hospitalization
It is unknown when coagulopathy first manifests in patients with severe burns, however it is generally accepted that coagulation indicators and systemic alterations appear soon after burn damage. Although there aren't any studies on coagulopathy in the very early stages following burns, it is believed that these changes start to occur right away and even before hospitalization [7-8].

First Days After Burn
On the first day following a serious burn, significant activation of both coagulation and fibrinolysis is observed. During this time, these patients are regarded as hyperfibrinolytic, and tissue-type plasminogen activator [t-PA] levels also rise [8].

Chronic Period After Burn
After a burn injury, coagulopathy is characterized by changes to the natural anticoagulation system that are procoagulant and antifibrinolytic in nature. Within 7 days following a burn injury, this hypercoagulation often returns to more stable levels, unless a condition that causes coagulopathy also manifests. At various stages in patients with severe burns, a number of potential pathophysiological factors, alone or in combination, may cause and/or exacerbate coagulopathy. Aggressive fluid resuscitation techniques used to prevent shock [burn-induced shock] that also trigger hypothermia in later days may exacerbate or induce coagulopathy. In the early stage, burn injury directly triggers coagulopathy through tissue hypoperfusion, hypothermia, endothelial damage, or a systemic inflammatory response. Coagulation disorder may also be brought on by burn-related complications such sepsis, bleeding from prolonged inactivity during the hospital stay, repeated wound excision, and other surgical procedures [8].

Treatment of Burn-Induced Coagulopathy
There are no specific suggestions or tested guidelines for the management of postburn coagulopathy. Most people are aware of how to avoid situations that will worsen or cause coagulopathy.These measures are can be listed as [8];

- Preventing tissue hypoperfusion
- Preventing hypothermia during fluid resuscitation
- Use of anticoagulants

The use of low-molecular heparin or antithrombin at a protective dose against increased coagulopathy in burn patients is part of the standard treatment, but has a low inhibitory effect on microvascular thrombus formation. The use of drugs such as steptokinase or urokinase may be more effective in preventing coagulopathy. However, these drugs are not suitable for use in traumas where there are many open wounds such as burns and where there is a risk of infection. In the literature, randomized controlled studies for the treatment of coagulopathy in patients with severe burns were described as insufficient [7-8].

Parameters Used in Monitoring Coagulation and Fibrinolytic System
Clinical coagulation tests are functional assays that evaluate the rate of clot formation from the moment the coagulation cascade is activated. Prothrombin time [PT], activated partial thromboplastin time [APTT], fibrinogen, thrombocyte, d-dimer tests are used.

These tests are commonly used to identify disorders in the intrinsic and extrinsic pathways of coagulation [9].

Prothrombin Time [PT]
This test, which gives information about the functions of the extrinsic pathways of coagulation, has been used since 1935. Following the addition of thromboplastin and calcium to the plasma, its normal values are stated as 10-14 seconds. It is a parameter generally used in the monitoring of anticoagulant treatments. It is generally used in the evaluation of acute coagulopathy in burn patients. [9-10]. It was determined that coagulopathy was observed in patients with a value above 14.6 sec [9-10].

Activated Partial Thromboplastin Time [APTT]
The APTT is a test used to evaluate the intrinsic and common pathways of coagulation. It is especially used in the evaluation of acute coagulopathy in burn patients. Reference values vary between 22.0-35.0 sec. A value >45.0 sec in burn patients indicates the risk of acute coagulopathy [11]. Coagulopathy may be an early indicator of mortality in patient groups with a very high mortality rate, such as burns. Therefore, the aim of this study is to predict the risk of coagulopathy associated with acute burns with machine learning models. Developing artificial intelligence-based interfaces that can be used by clinicians working in the field of burns and creating a sample data set needed for academicians who want to work in the field of artificial intelligence in burns are other purposes of the study.

2. Related Works

The incidence of coagulopathy associated with acute burns has been defined as 37% in the literature [12,13]. Although its incidence is low, a coagulopathy that starts within 24 hours increases the risk of mortality for burn patients and causes disruption of treatment processes. Although there are studies in the literature such as predicting mortality with machine learning models in burn patients, studies evaluating the risk of coagulopathy due to acute burns have not been found. Similar studies are seen in other patient groups other than burns.

Fengping et al. In 2020, they looked examined patients who had spontaneous intracerebral hemorrhages for coagulation abnormalities. Aspartate transaminase, alanine transaminase, hemoglobin, platelet count, white blood cell count, neutrophil percentage, systolic and diastolic pressure, albumin/globulin ratio, neutrophil count, lymphocyte percentage, aspartate transaminase, and aspartate transaminase were employed in this investigation. These figures indicate that the accuracy rate is 931%. They have developed models that have the predictive ability [14].

Another study conducted in 2021 developed machine learning models to dynamically predict the risk of sepsis-induced coagulopathy. In this study, in which open-access data was used, it was stated that two models were developed that could better predict the risk of coagulopathy in septic patients than Logistic Regression and SIC scores [15].

In 2020, Hasegawa et al. In another study, machine learning models that can predict sepsis-induced coagulopathy were compared. A total of 17 parameters in 1017 patients were included in the study. Machine learning methods such as random forests [RF], support vector machines [SVM] and neural networks [NN] are used. It was reported that the prediction accuracy of multiple linear regression, RF, SVM, and NN models were 63.7%, 67.0%, 64.4%, and 59.8%, respectively [16].

Kaiyuan et al. In a study in which they evaluated acute coagulopathy due to trauma in 2020, they used the data of 818 patients. They stated that traditional logistic regression models may be better than the predictive power of machine learning models [17].

When all these studies were examined, it was observed that machine learning models were tried to predict acute coagulopathy in cases such as trauma such as sepsis, but no such study was performed in burn patients. In addition, the data used in the studies in the literature are not as large as the data set in our study. We believe that we can make important contributions to the literature in this study, which can predict coagulopathy due to acute burns and uses more algorithms.

3. Materials Methods

3.1. Study Population

A total of 1040 patients hospitalized in the intensive care and/or service units between January 2016 and June 2023 in Turkey 25 December State Hospital Burn Center were included in the study. The data of the patients were obtained retrospectively from the web Karmed database of 25 December State Hospital. Demographic information of all patients and blood test results at the time they were first admitted to the hospital were recorded. Permission was obtained from Hasan Kalyoncu University Health Sciences Ethics Committee to conduct the study [ethical approval numbered 2023/65]. Informed consent form was signed, and consent was obtained in order to use the data of all patients included in the study. The Declaration of Helsinki was followed when conducting the study.

3.2. Data Collection

A data set was created with hemogram and biochemistry parameters of all patients: age, gender, burn type, burn percentage, presence of inhalation burn, duration of hospitalization in intensive care unit, length of hospital stay, total hospitalization time (Table-1).

Table 1. Biochemical parameters and abbreviations

Name	Abbreviation	Name	Abbreviation
White Blood Cell	WBC	Creatine Kinase	CK
Hemoglobin	HGB	Sodium	-
Hemorectitis	HCT	Aspartate Aminotransferase	AST
Platelet	PLT	Phosphorus	-
Neutrophil	NEU%	C-Reactive Protein	CRP
Lymphocyte	LYM%	Alanine Aminotransferase	ALT
Monocyte	MONO%	Very Low Density Lipoprotein	VLDL
Urea	-	Potassium	-
Blood Urea Nitrogen	BUN	T-Protein	-
Creatinine	-	Glucose	-
Triglyceride	-	Albumin	-
Albumin	-	Egfr	-
Calcium	-	Active Partial Thromboplastin Time	APTT
Magnesium	-	Alkaline Phosphatase	-
Bilirubin	-		

Among the patients, those with PT tests over 14.6 seconds were considered as coagulopathy due to acute burn [12]. Patients with values between 10-14.5 were recorded as normal. While coagulation due to acute burn was observed in 334 of the

patients, this did not occur in 706. The data set was randomly divided into two separate clusters, 70% to be used in ANN training and 30% to test model success. The data set consisting of 40 input variables and 1 outcome variable for each patient is given in Table 2

Table 2. Dataset of features collected from patients.

Features and Outcome
Sex
Age
Nationality
Type of Burn
Percentage of Burn
Inhalation Burn
Duration of Intensive Care Unit
Duration of Ward Hospitalization
Length of Hospitalization [total]
WBC-1
HGB-1
HCT-1
PLT-1
NEU%-1
LYM%-1
MONO%-1
Ure-1
BUN-1
Kreatinin-1
Trigliserit-1
Albumin-1
Kalsiyum-1
Magnezyum-1
Bilurubin-1
ALP-1
CK-1
Sodyum-1
AST-1
Fosfor-1
CRP-1
ALT-1
VLDL-1
Potasyum-1
T-protein-1
Glukoz-1
Albumin[g/L]-1
eGFR-1
Procalsitonin-1
Discharge (ex or recovery)
APTT-1
Outcome- Acute Burn-Induced Coagulopathy

3.3. Machine Learning Algorithms

By creating algorithms that effectively describe a dataset, machine learning focuses on the learning component of artificial intelligence. Or, to put it another way, machine learning algorithms are algorithms that employ a range of statistical, probabilistic, and optimization techniques to draw lessons from the past and identify insightful patterns in huge, complicated datasets [18]. These days, research is done on the issue and these algorithms are commonly utilized in the early diagnosis of disease or in the calculation of risk factors. [18,19].

3.3.1. Artificial neural networks

One of the most popular machine learning techniques, artificial neural networks (ANNs), are made up of a network of simple information processing units called neurons. High-level relationships can be recognized and nonlinear relationships between variables can be learned using ANNs. Instead of using intricate mathematical models to represent complicated relationships, artificial neural networks (ANNs) make use of an interactive construction of many basic neurons. Algorithms for supervised, unsupervised, and reinforcement learning can all be completely implemented using ANNs. [20].

3.3.2. Decision Tree

Decision trees are a supervised classification method that produces a model in the form of a tree data structure consisting of decision-making nodes that direct the classes according to the characteristics of the data used and the classes of the classification to be made, and leaf nodes marked as class information. The algorithm that creates the decision tree model is divided into small pieces of the data set to be analyzed and the tree model is developed. In the decision tree model, a black decision node may contain a single or more than one sub-branch [21-27].

3.3.3. K-Nearest Neighbor [KNN]

KNN Nearest Neighbor Algorithm is a supervised and non-parametric classification method that classifies data based on the proximity of training samples in the data set. The algorithm maintains its popularity among machine learning methods for years with its advantages such as not requiring training, being easy to implement, adaptable to local information and being resistant to noisy training data. In order to classify a new data, the algorithm operates by looking at the closeness of k of the training data known to belong to which class. The k value is defined intuitively at the beginning of the algorithm. For the proximity calculation, distance equations such as Manhattan, Hamming, Euclid and Minkowski are used [21-27].

3.3.4. Naive Bayes

Naive Bayes Classifier, named after British mathematician Thomas Bayes, is a simple probabilistic classification method with high performance in diagnosis based on Bayesian decision theory. In the Naive Bayes classifier, it is accepted that all the features are equally important and that all the features are independent of each other. For the Bayesian classifier using a tutorial learning method, taught data with known classes is presented to the system. Probability calculations are made on the taught data. According to the probability values obtained, it is tried to calculate how probable the test data is included in which class [21-27].

3.3.5. Support Vector Machine

Vladimir Vapnik created the Support Vector Machines [SVM] approach in 1992. It is based on statistical learning theory. Problems involving classification, regression analysis, and nonlinear function approaches are resolved using SVM, a supervised learning method. It offers strong classification and high generalization performance in text, voice, text, object, and image recognition difficulties when handling bioinformatics challenges [21-27]. For a small set of learning patterns, SVM seeks to achieve good generalization. It uses a helpful learning algorithm to identify patterns in challenging-to-analyze complex data sets. The approach uses classification learning to separate

samples for classification estimation from previously unobserved data. The objective of SVM is to construct an n-dimensional hyperplane that optimally separates the data into various [21-27].

3.4. Success Evaluation Criteria

The current dataset is split into two groups in order to assess the system's effectiveness in each group. One is used for training, and the other serves as a test set to simulate potential examples that the system is completely unaware of. With the chosen training algorithm, the system gains knowledge from the training set. The trained system's performance is then measured against the test set. [28-29].

3.4.1. Confusion Matrix

Machine learning and especially those with statistical classification problems A complexity matrix is a tabular layout that visualizes the performance of an algorithm.
If the predicted variable (dependent variable, target, target, output, output) is in binary format, the accuracy is evaluated with the evaluation complexity matrix [28-29].

Using this matrix, sensitivity, specificity, precision, negative predicted value, Many performance measures such as 24 npv), accuracy (accuracy) and f1-score (f1 score) can be calculated. In the evaluation of the success of the prediction model, it is generally accuracy formula is used [28-29].

3.4.2. ROC (Receiver Operating Characteristic) Curve

It allows the determination of appropriate cut-off points to determine the optimum sensitivity and optimum specificity of a medical test. A reference is needed to determine the appropriate cut-off point via the ROC curve. The ROC curve method uses values such as Sensitivity, Specificity, Accuracy Rates. Quantitative data of the variable measured in clinically or pathologically ill or healthy individuals are used to determine the appropriate cut-off point. In order to create the ROC curve, the variable values measured from patients and healthy individuals and used in diagnosis are ranked in order of magnitude. Each value from the sorted array is taken as the cutoff point in sequence. If the height of the measured quantitative variable indicates the disease, if the value above this value is below the patient, the categories are determined as robust.
is created [28-29]. The number of patients and healthy individuals in these categories is 2x2. displayed in the tables. According to the value determined as the cut-off point in these tables, rates are determined such as how many of the real patients are qualified as sick, how many of them are determined as healthy even though they are sick, and they are considered sick according to the cut-off point even though they are healthy.
Sensitivity ratios y obtained from the 2x2 tables created by taking each value as the cutoff point to obtain the ROC curve. axis, a coordinate axis is created to show 1-Specific ratios on the x-axis. The ratios calculated for each cut point are marked on the coordinate. A curve is obtained by connecting the points. This is a concave curve and is called the ROC curve. The area under the curve (AUC) is an important indicator in evaluating the accuracy of the test. How much is the ROC AUC
The higher the discriminative power of the medical test, the higher the discriminative power will be [28-29].

3.4.3. Cross Validation

A common technique to gauge a classification algorithm's performance or compare the performance of two classification algorithms in a dataset is cross-validation. A dataset is randomly divided into k parts of roughly equal size, and each piece is used to test a classification technique and the model made up of the other pieces.
By averaging the k accuracies from cross validation, the classification algorithm's performance is assessed [28-29].

4. Experimental Study

In this study, 25 different machine learning methods (have been used. Here, each algorithm has utilized different activation functions, optimization algorithms, and loss functions, the details of which are provided below (with or without PCA) (Table-3). All these algorithms are developed using the machine learning toolbox of the MATLAB programming language. On a Windows 10 computer with an Intel processor, MATLAB R2021b was used to produce all results.

Table 3. Machine learning techniques for comparison (accuracy %)

Machine	**TV**		**3-Fold CV**		**5-Fold CV**		**10-Fold CV**	
Learning Models	**PCA Disable**	**PCA Enable**	**PCA Disable**	**PCA Enable**	**PCA Disable**	**PCA Enable**	**PCA Disable**	**PCA Enable**
Fine Tree	**99.9%**	80.5%	**99.9%**	61.3%	**99.9%**	62.9%	**99.8%**	63.8%
Medium Tree	**99.9%**	70.9%	**99.9%**	66.2%	**99.9%**	65.5%	**99.8%**	66.1%
Coarse Tree	**99.9%**	68.7%	**99.9%**	66.9%	**99.9%**	67.7%	**99.8%**	67.1%
Linear Discriminant	87.2%	68.0%	85.4%	67.9%	84.4%	67.9%	85.6%	67.9%
Quadratic Discriminant	79.1%	67.7%	64.3	66.77%	69.4%	67.6%	failed	67.4%
Logistic Regression	**93.4%**	68.0%	91.71%	67.9%	90.0%	67.9%	90.5%	67.9%
Gaussian Naive Bayes	72.3%	67.4%	89.2%	67.23%	69.6%	67.4%	69.8%	67.2%
Kernel Naive Bayes	**91.75%**	70.1%	62.6%	67.5%	85.19%	67.5%	82.9%	66.7%
Linear SVM	**91.00%**	68.0%	87.7%	67.6%	83.1%	64.3%	89.3%	66.2%
Quadratic SVM	**93.2%**	47.2%	87.1%	53.6%	88.7%	53.7%	88.2%	52.5%
Cubic SVM	**93.4%**	41.8%	85.3%	91.71%	87.2%	48.3%	85.9%	49.1%
Fine Gaussian SVM	**93.4%**	68.00%	69.7%	50.1%	70.1%	67.9%	70.3%	67.8%
Medium Gaussian SVM	**91.1%**	68.00%	83.7%	67.9%	85.4%	67.9%	85.3%	67.9%
Coarse Gaussian SVM	77.4%	68.00%	72.9%	67.9%	74.4%	67.9%	75.4%	67.9%
Fine KNN	**93.4%**	**93.4%**	73.7%	64.2%	73.0%	62.5%	73.7%	63.6%
Medium KNN	78.8%	70.2%	74.1%	65.1%	75.3%	64.5%	75.2%	66.6%
Coarse KNN	72.6%	67.9%	69.9%	67.9%	71.2%	67.9%	70.8%	67.9%
Cosine KNN	79.1%	67.0%	74.6%	56.6%	74.6%	59.0%	74.7%	62.1%
Cubic KNN	77.5%	70.2%	72.6%	65.4%	72.0%	64.7%	73.7%	66.6%
Weighted KNN	**93.4%**	**93.4%**	76.3%	64.5%	76.5%	64.1%	77.8%	65.5%
Boosted Trees	67.9%	71.3%	67.9%	66.8%	67.9%	68.3%	67.9%	67.9%
Bagged Trees	**99.7%**	**93.1%**	**96.6%**	65.0%	**99.7%**	64.6%	**99.7%**	66.3%
Subspace Discriminant	86.7%	68.0%	85.7%	67.9%	84.9%	67.9%	85.6%	67.9%
Subspace KNN	**100%**	**93.4%**	70.6%	62.2%	71.6%	64.3%	72.3%	65.5%
RUS Boosted Trees	**90.9%**	74.4%	89.3%	60.6%	80.8%	61.6%	77.4%	59.2%

Subspace KNN [1009%, Fine Tree, Medium Tree, Coarse Tree [99%]] showed the best performance in estimating the risk of coagulopathy due to acute burns.In addition, the PCA method was used to test different parameter variations and the best results were found in Table-3. A confusion matrix represents the most successful and unsuccessful algorithms implemented Machine learning uses a confusion matrix to interpret the performance of the classification model used Figure 2 and 3 show a confusion matrix comparing the predicted and actual values of the target feature.

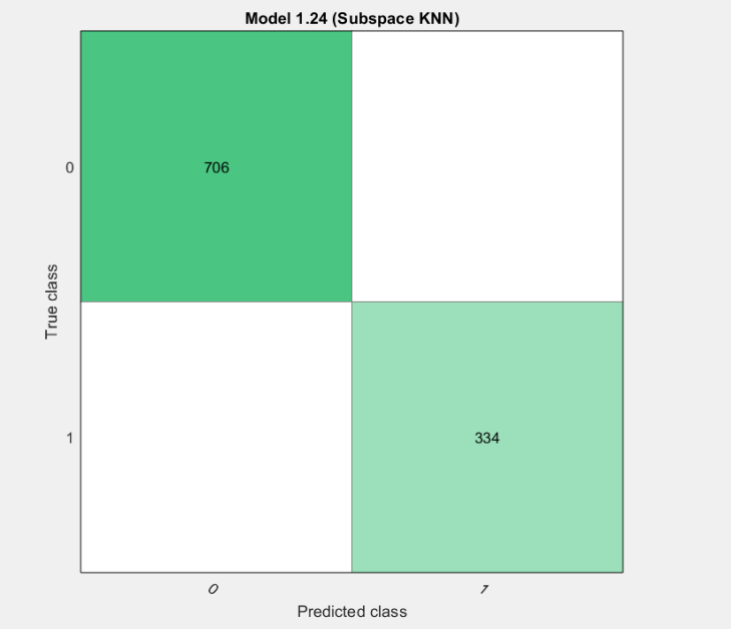

Figure 2. Confusion matrix for the most successful subspace KNN algorithm

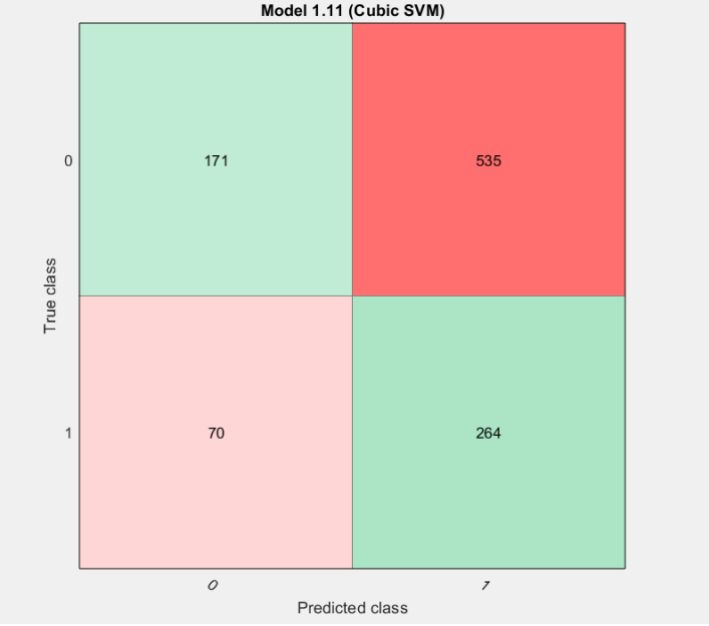

Figure 3. Confusion matrix for the worst successful cubic SVM algorithm

An illustration of a binary classifier system's classification performance as the discrimination threshold varies is the receiver operating characteristic (ROC) curve. ROC curve obtained after evaluating the effectiveness of the algorithm. Figures 4 and 5 illustrate, respectively, the ROC curves for the best-performing Subspace KNN method and the worst-performing Cubic SVM technique.

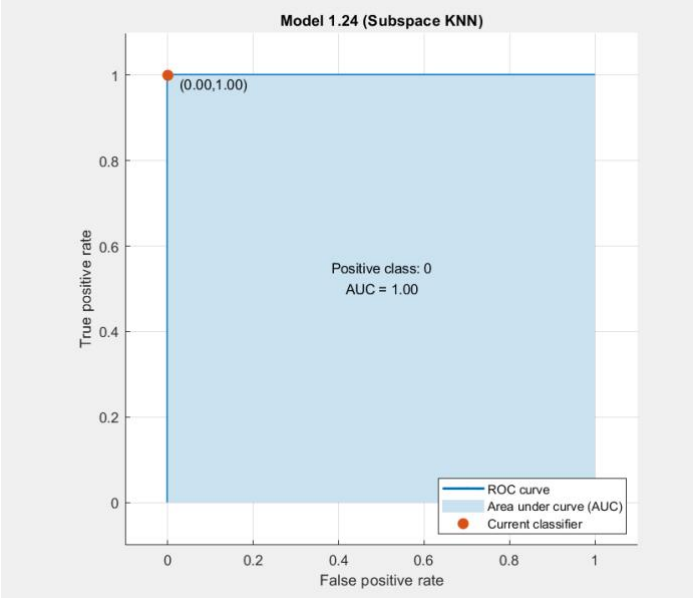

Figure 4. ROC curve for the best performing subspace KNN algorithm.

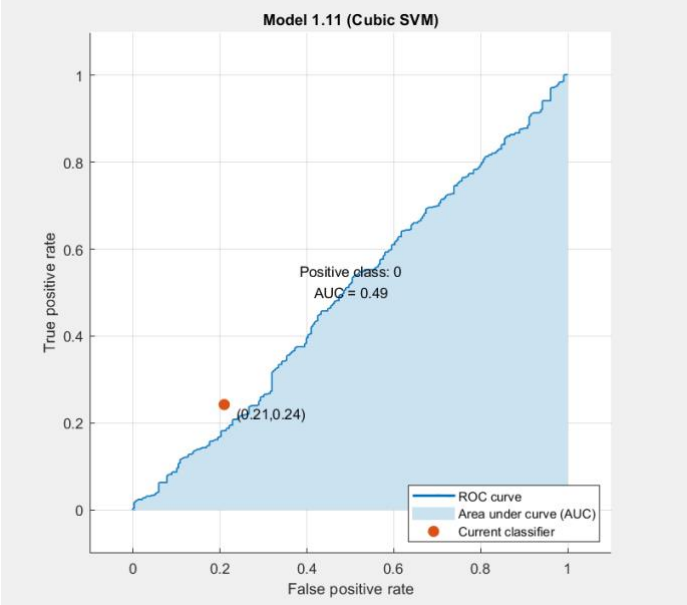

Figure 5. ROC curve for the worst-performing cubic SVM algorithm.

5. Conclusion

In this study, we developed an innovative clinical decision support system that can be used in various processes for clinicians. The Subspace KNN model proposed in this study showed the highest prediction success with 100% accuracy compared to other machine learning methods. We believe that this model, which was created by using 35 different biochemical markers, which predicts the risk of coagulopathy, which can be seen in the first 24 hours in burn patients and is difficult to diagnose, will contribute to the literature.

In this study, the application of machine learning-based decision support systems for rapid pre-diagnosis of coagulopathy in burn patients may be important for clinicians and healthcare administrators. By using these systems, healthcare providers can improve the efficiency and accuracy of the initial assessment and treatment process, especially in non-burn clinics. This can lead to better allocation of resources, including medical personnel, equipment and treatments. In addition, such systems can contribute to the standardization of care in different healthcare facilities, ensuring that patients receive consistent, high-quality care regardless of their location. Ultimately, the integration of these decision support systems into burn care management can help improve patient outcomes, reduce the burden on healthcare professionals, and guide policy makers in developing well-informed strategies to address the challenges associated with burn injuries. We also state that multicenter studies can contribute more to the literature.

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