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Construction and Explanation Analysis of a Hypotension Risk Prediction Model in Hemodialysis Based on Machine Learning

Mingwei Zhang and Tianyi Zhang *

School of Health Sciences and Engineering, University of Shanghai for Science and Technology, Shanghai 200093, China; 221300167@st.usst.edu.cn
* Correspondence: 19117192540@163.com

Abstract: Objective. To establish a risk prediction model for intradialytic hypotension (IDH) in maintenance hemodialysis (MHD) patients and to analyze the explainability of the risk prediction model. Methods. A total of 2,228,650 hemodialysis records of 1075 MHD patients were selected as the research objects. Thirteen important clinical features including demographic features and clinical features were screened, the blood pressure measured before hemodialysis was collected, then an IDH risk prediction model during hemodialysis was established based on a machine learning algorithm. The contribution of each feature to the risk prediction of IDH was measured based on the Gini evaluation index. The TreeSHAP method was used to provide global and individual explanations for the IDH risk prediction model. Results. Hemodialysis duration, pre-dialysis mean arterial pressure, and pre-dialysis systolic blood pressure were the most important predictive variables for the occurrence of IDH during hemodialysis in MHD patients. The best IDH risk prediction model based on machine learning had an accuracy of 0.92 (95% CI 0.90–0.94) and an AUC of 0.95 (95% CI 0.94–0.96), indicating that machine learning has a good effect on the prediction of IDH during hemodialysis treatment. Our research innovatively achieved IDH risk prediction during the entire hemodialysis period based on blood pressure before the start of hemodialysis and other clinical features, thus enabling the medical team to quickly adjust hemodialysis prescriptions or initiate treatment for timely management and prevention of IDH. Global and individual explanations of the IDH risk prediction model can help hemodialysis medical staff understand the overall prediction mechanism of the model, discover prediction outliers, and identify potential biases or errors in the model. Conclusions. The IDH risk prediction model has definite clinical value in actual hemodialysis treatment.

Keywords: hemodialysis; intradialytic hypotension; machine learning; prediction model; explanation analysis

1. Introduction

In recent years, due to the increase in hypertension, diabetes, metabolic diseases, and the accelerating aging of the population, the incidence and prevalence of chronic kidney disease (CKD) have increased year by year, and it has become an important public health issue faced by the world. Cross-sectional survey data on the prevalence of chronic kidney disease in China in 2012 showed that the number of CKD patients was estimated to be approximately 119.5 (112.9–125.0) per million people, and the overall prevalence was 10.8% (10.2–11.3%) [1], with the number of patients with CKD and end-stage renal disease (ESRD) ranking first in the world. Patients with ESKD require long-term renal replacement therapy, such as hemodialysis and peritoneal dialysis.

Intradialytic hypotension (IDH) is one of the most common complications during hemodialysis [2,3] and an important risk factor for cardiovascular events, hospitalization, and death [4,5]. The usual clinical incidence is 20–30% [6], and IDH may accelerate the loss of residual renal function [7] and increase the risk of volume overload [8].

The exact mechanism of IDH is unclear, but possible mechanisms include increased left ventricular mass index, extracellular volume overload, sympathetic overactivity, dialysate sodium load, and antihypertensive drugs during hemodialysis [9–11]. Therefore, early evaluation and monitoring of MHD patients during hemodialysis is crucial for preventing and treating IDH. The prediction and prevention of IDH can greatly improve the quality of life of MHD patients. However, the occurrence of IDH depends on multiple risk factors, including demographic factors (age, gender), comorbidities (diabetes, coronary heart disease, left ventricular hypertrophy), hemodialysis characteristics, complications (year of hemodialysis, weight gain during hemodialysis, anemia), hemodialysis treatment prescription (ultrafiltration), drugs (antihypertensive drugs), etc. [12–14]. For patient safety, blood pressure is frequently measured during hemodialysis treatment. Since blood pressure in MHD patients has significant fluctuation trends before, during, and after hemodialysis, it remains challenging to develop an ideal IDH prediction model.

As a branch of artificial intelligence, machine learning has been increasingly used in the medical field in recent years. Compared with traditional rule-based model algorithms, machine learning algorithms can analyze complex and high-dimensional medical data, so they can be used for clinical diagnosis, prediction, and prognostic assessment [15–18]. The purpose of this study is to establish a prediction model for IDH events based on machine learning algorithms, considering that the first hour of hemodialysis is the peak period of IDH occurrence [19]. Therefore, the innovation of this study is that only one blood pressure measurement is required before the start of hemodialysis to predict IDH events throughout the dialysis period, which will enable medical staff to quickly adjust dialysis prescriptions or initiate treatment to manage and prevent IDH.

2. Materials and Methods

2.1. Data Source

We used data from 1075 hemodialysis patients collected by Lin et al. [20] from the HD unit of MacKay Memorial Hospital, a tertiary medical center in Taiwan, where a total of 4,366,298 hemodialysis recordings were collected from these patients in 165,986 hemodialysis sessions. From the beginning to the end of hemodialysis treatment, blood pressure was measured every 30 min with an electronic sphygmomanometer, and body temperature was measured with an ear thermometer. Vital signs were measured at each time point, and hemodialysis settings, including blood flow, ultrafiltration rate, total ultrafiltration volume, dialysate temperature, and dialysate sodium concentration, were simultaneously recorded. Figure 1 shows the data collection process. Subjects received HD treatments two to three times per week, with each treatment lasting up to 240 min, and vital signs collected by the hemodialysis equipment were linked to hemodialysis patient demographic data stored in the hospital information system.
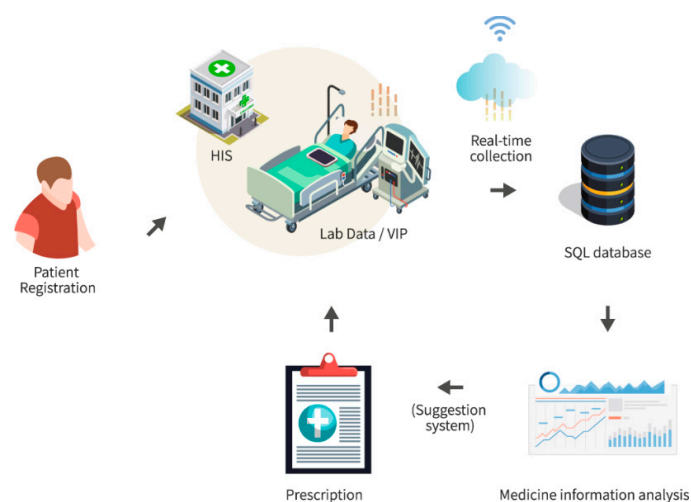

Figure 1. Schematic diagram of the data collection process [20].

2.2. Definition of IDH

IDH, which was set as the target output, was defined as a systolic blood pressure (SBP) drop = 20 mmHg, a mean arterial pressure drop = 10 mmHg during hemodialysis, or the occurrence of clinical hypotensive events requiring nursing intervention [21].

2.3. Data Preprocessing

Based on the hemodialysis patient ID number, we extracted the patient's physical data and recording time, hemodialysis start time, blood pressure measurement time, systolic blood pressure (SBP), diastolic blood pressure (DBP), dialysate temperature, dialysate sodium concentration (conductivity), ultrafiltration rate, the rate of blood flow through the hemodialysis equipment, and the dialysis duration. The data extracted above are the key patient information currently recorded in hemodialysis treatment. They are indicators recognized by clinicians and used to evaluate the dialysis patient's status.

Then multi-step calculation, time dimension alignment, and data preprocessing were performed to finally obtain the MHD patient demographic features and clinical features used in this study, with a total of 13 features, as shown in Table 1. This study finally included 2,228,650 hemodialysis recordings collected from 1075 MHD patients. IDH events accounted for approximately 27% of the total hemodialysis recordings. All recordings were divided into a training set of 1,782,920 recordings and a test set of 445,730 recordings at a ratio of 8:2 based on a stratified sampling method. The distribution of non-IDH and IDH events in the training set and test set is shown in Figure 2.

Table 1. MHD patient features used in this study.

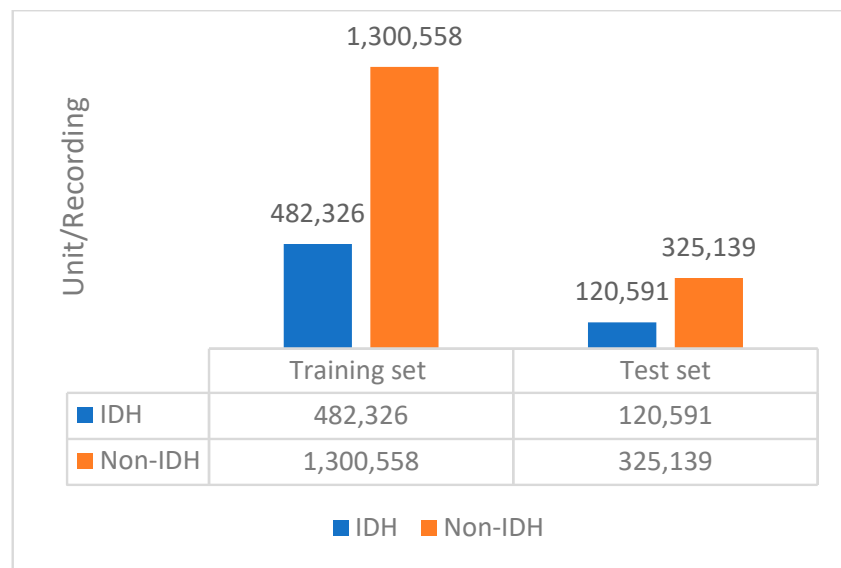| Category	Features
Demographic features	Age, Pre-dialysis weight, Dialysis age
Clinical features	
Comorbidities	Diabetes
Hemodialysis records	Dialysis duration, Temperature, Ultrafiltration rate, Pre-dialysis SBP, Pre-dialysis DBP, Pre-dialysis MAP, Dialysate temperature, Conductivity, Blood flow

	Training set	Test set
IDH	482,326	120,591
Non-IDH	1,300,558	325,139

Figure 2. Distribution of non-IDH and IDH events in the training set and test set.

2.4. Models and Methods

Machine learning has powerful big data processing capabilities as well as high-dimensional and complex computing capabilities, so we used machine learning to establish the prediction model for this study. This study established a risk prediction model for IDH events during hemodialysis in MHD patients based on five machine learning algorithms, including Random Forest [22], XGBoost [23], ExtraTrees [24], KNN [25], and AdaBoost. Then the Random Forest algorithm was used to evaluate the importance of each feature for predicting IDH events. The Gini index evaluation index was used to measure the contribution of each feature. The principle is to calculate the contribution value of each feature on each tree in Random Forest and then take the average. The Gini index is a measure of data impurity, and its calculation formula is as shown in Equation (1):

$$Gini(D) = 1 - \sum_i^c p_i{}^2 \tag{1}$$

where c represents the number of categories in the data set, and p_i refers to the proportion of category i. When p_i is closer to 0 or 1, the smaller the coefficient is, which means the higher the purity of the data. When the data set D has only one data type, then the value of the Gini index is the lowest, 0. If the selected attribute is A, then the calculation of the Gini index of the split data set D is as shown in Equation (2), where k means that the data set D is split into k data sets.

$$Gini_A(D) = \sum_{j=1}^k \frac{|D_i|}{|D|} Gini(D_j) \tag{2}$$

We further used the TreeSHAP method for global and individual explanations of the IDH risk prediction model. Because it is an additive explanatory model based on cooperative game theory, considering all features as "contributors", this method assigns an individual Shapley value to each prediction, focusing on explaining how each prediction was generated and how each feature affects the model's decisions. The feature set of this study includes 13 features, and the original model is f (an extremely random tree). g is the post-explanation model in TreeSHAP (Equation (3)).

$$g(x) = \phi_0 + \sum_{i=0}^{24} \phi_i x_i = f(x) \tag{3}$$

A single hemodialysis period datum is expressed as $x = (x_1, x_2 \ldots x_{13})$, $f(x)$ is the predicted value of the original model, $g(x)$ is the predicted value of the explanatory model, and ϕ_i is the Shapley value of the i-th feature variable (Equation (4)).

$$\phi_i(f, x) = \sum kernel \times [f_x(S \cup i) - f_x(S)] \tag{4}$$

$$kernel = \frac{|S|!(13-|S|-1)!}{13!} \tag{5}$$

S is a subset of the feature set, and there are $2^{13} - 1$ possibilities. $|S|$ is the total number of elements in S, $f_x(S \cup i)$ indicating the predicted value of the model when there are only features in $S \cup i$. $f_x(S)$ indicates the predicted value of the model when there are only features in S. The subtraction of the two can be used as the marginal contribution of the i-th feature under the feature subset S. The overall framework of the models and methods is shown in Figure 3.
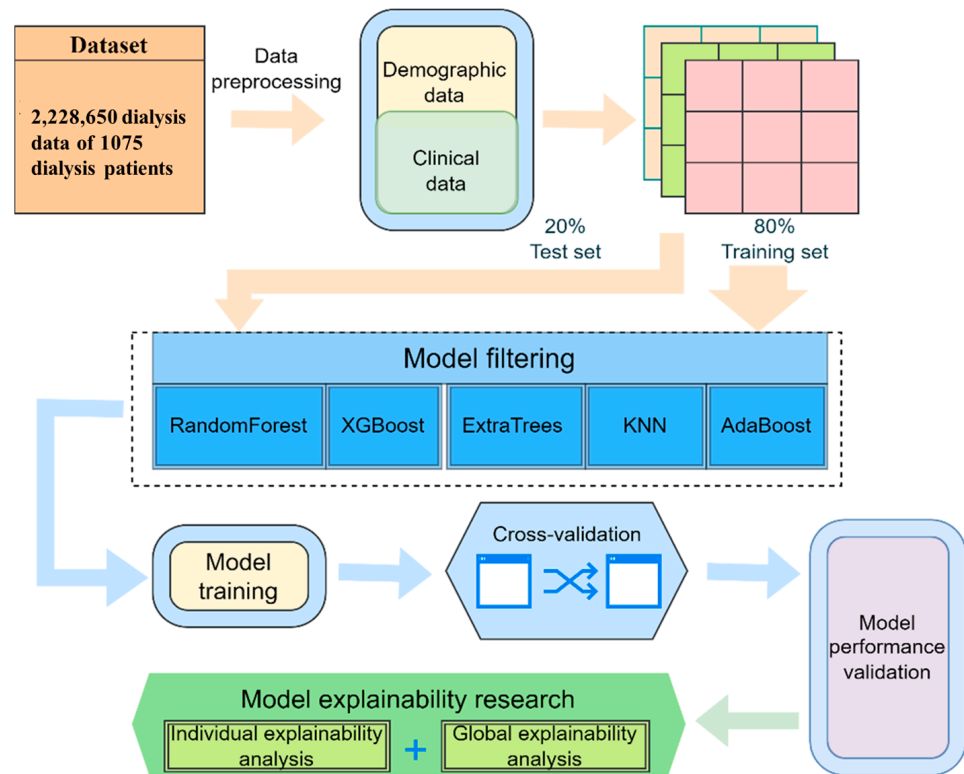
Figure 3. The overall framework of the models and methods.

3. Experimental Results and Analysis

3.1. Evaluation Indicators

We used Accuracy, Precision, Recall, F1-score and the area under the receiver operating characteristic curve (AUC) as indicators to evaluate the risk prediction performance of the model. The definitions of each indicator are as shown in Equations (6)–(9).

$$Accuracy = \frac{TP + TN}{TP + TN + FP + FN} \tag{6}$$

$$Precision = \frac{TP}{TP + FP} \tag{7}$$

$$Recall = \frac{TP}{TP + FN} \tag{8}$$

$$F1score = \frac{2 \times Precision \times Recall}{Precision + Recall} \tag{9}$$

TP represents the number of successful predictions of IDH events. TN represents the number of successful predictions of non-IDH events. FP represents the number of failed predictions of non-IDH events. FN represents the number of failed predictions of IDH events.

3.2. Statistical Analysis

We used the Mann–Whitney U test method to analysis the differences between the features of the non-IDH and IDH groups. Because the Mann–Whitney U test is a non-parametric statistical test method, it can effectively compare whether there are significant differences between two independent samples that do not meet the normal distribution assumption. As shown in Table 2, the results showed that there were statistical differences ($p < 0.05$) in dialysate temperature, conductivity, ultrafiltration rate, dialysis duration, diabetes, pre-dialysis weight, temperature, dialysis duration, age, pre-dialysis SBP, pre-dialysis MAP, and pre-dialysis DBP. The features differences between the two groups are visually shown in Figure 4.

Table 2. Mann–Whitney U test analysis of non-IDH and IDH groups.

Features	non-IDH Group (n = 1,625,697)	IDH Group (n = 602,953)	p Value
Dialysate temperature	36.5 (33.3–39.0)	36.4 (39.5–34.2)	<0.001
Conductivity	14.0 (10.0–20.0)	14.1 (10.0–20.0)	<0.001
Ultrafiltration rate	0.5 (0–3.0)	0.5 (0–3.0)	<0.001
Blood flow	188.5 (0–400.0)	196.0 (0–400.0)	0.005
Dialysis duration	83.1 (0–284.0)	145.7 (0–370.0)	<0.001
Diabetes	36.8 (31.7–40.4)	36.8 (33.1–39.9)	<0.001
Pre-dialysis weight	60.2 (30.6–172.7)	61.8 (30.6–172.7)	<0.001
Temperature	36.4 (35.0–39.5)	36.4 (35.0–39.4)	<0.001
Dialysis age	80.0 (0–332.2)	79.5 (0–329.9)	<0.001
Age	66.5 (18.1-94.4)	66.7 (18.1–94.4)	<0.001
Pre-dialysis SBP	140.4 (46.0–200.0)	158.6 (70.0–200.0)	<0.001
Pre-dialysis MAP	92.0 (36.7–187.3)	103.9 (46.7–187.3)	<0.001
Pre-dialysis DBP	67.8 (30.0–184.0)	76.5 (30.0–184.0)	<0.001

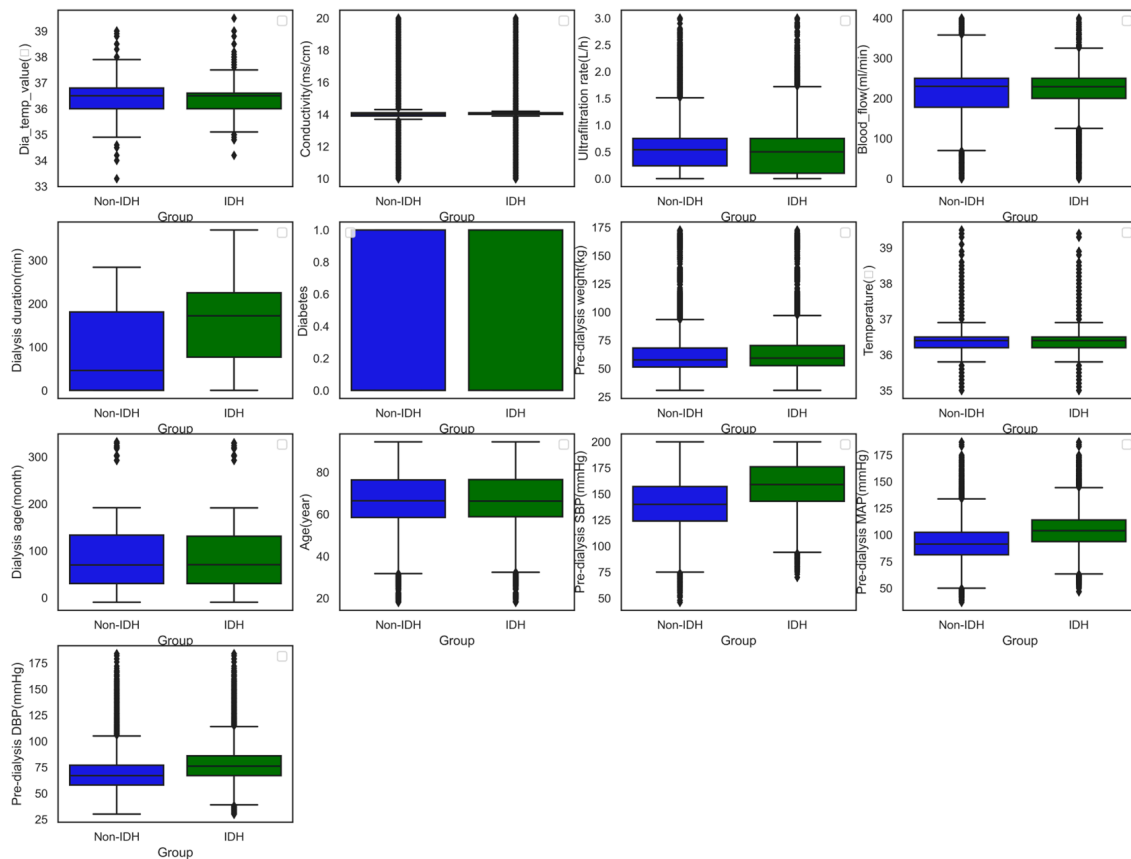$p < 0.05$, the difference between groups is statistically significant.

Figure 4. Distribution visualization of characteristic variables of non-IDH group and IDH group based on median and interquartile range.

3.3. Feature Importance Assessment

The tree structure of the Random Forest algorithm has powerful result interpretation capabilities. So, we used the Random Forest algorithm to evaluate the importance of each feature for predicting IDH events during hemodialysis, and the Gini index evaluation was used to measure the contribution of each feature. As can be seen from Figure 5, the importance of each feature is ranked from high to low for dialysis duration, pre-dialysis MAP, pre-dialysis SBP, age, pre-dialysis DBP, pre-dialysis weight, dialysis age, dialysis blood flow rate, ultrafiltration rate, dialysate temperature, conductivity, temperature,

diabetes. The dialysis duration, pre-dialysis MAP, and pre-dialysis SBP are much more important than other features in predicting IDH events during hemodialysis.
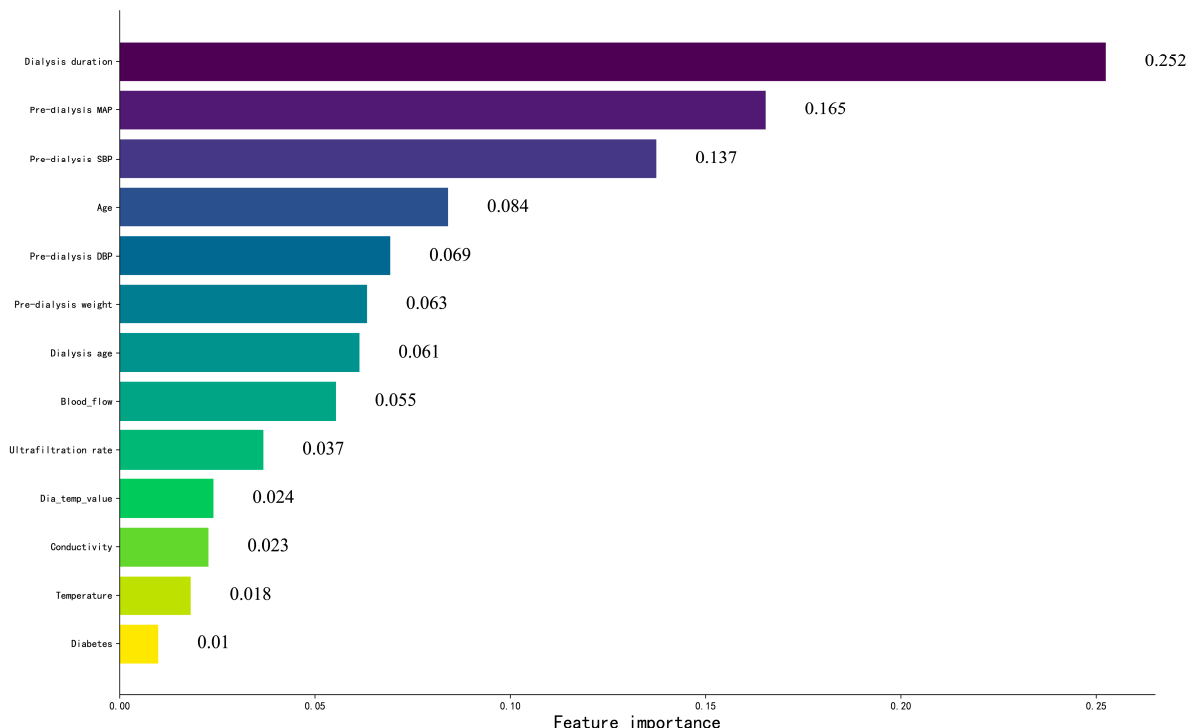

Figure 5. The result of the feature importance assessment based on Gini index evaluation.

3.4. Model Prediction Results

We established 5 machine learning models based on the training set, performed hyperparameter tuning through the grid search method and AUC indicator, and finally determined the optimal model hyperparameters. The accuracy, precision, recall, F1-score, and AUC comparison of the IDH risk prediction model during hemodialysis are shown in Tables 3 and 4 and Figure 6. The AUC of models based on KNN, Random Forest, XGBOOST, ExtraTrees, Adaboost, and Logistic reached 0.87 (0.86–0.88), 0.90 (0.88–0.92), 0.94 (0.92–0.95), 0.95 (0.93–0.97), 0.81 (0.79–0.84), and 0.79 (0.77–0.82) in the test set, respectively. Compared with the traditional Logistic method, the prediction effect of the machine learning method is better. Compared with other models, the accuracy of the IDH risk prediction model based on the ExtraTrees algorithm reached 0.99 (95% CI 0.98–1.00), the precision reached 1.00 (95% CI 0.99–1.00), the recall reached 0.98 (95% CI 0.97–0.99), the F1-score reached 0.99 (95% CI 0.98–1.00), and the AUC reached 1.00 (95% CI 0.99–1.00) in the train set. And the accuracy of the IDH risk prediction model based on the ExtraTrees algorithm reached 0.92 (95% CI 0.90–0.94), the precision reached 0.87 (95% CI 0.85–0.89), the recall reached 0.81 (95% CI 0.79–0.83), the F1-score reached 0.84 (95% CI 0.82–0.86), and the AUC reached 0.95 (95% CI 0.94–0.96) in the test set.

Table 3. Prediction effect of IDH risk prediction model established by machine learning in train set.

Models	Accuracy	Precision	Recall	F1 Score	AUC
ExtraTrees	0.99 (0.98–1.00)	1.00 (0.99–1.00)	0.98 (0.97–0.99)	0.99 (0.98–1.00)	1.00 (0.99–1.00)
XGBOOST	0.90 (0.88–0.92)	0.88 (0.87–0.90)	0.75 (0.73–0.77)	0.81 (0.80–0.82)	0.96 (0.94–0.97)
KNN	0.88 (0.86–0.90)	0.83 (0.81–0.85)	0.74 (0.73–0.75)	0.78 (0.76–0.80)	0.95 (0.94–0.97)
Random Forest	0.87 (0.85–0.89)	0.85 (0.84–0.87)	0.61 (0.59–0.63)	0.71 (0.69–0.73)	0.93 (0.91–0.95)
AdaBoost	0.79 (0.77–0.81)	0.66 (0.65–0.68)	0.44 (0.42–0.46)	0.53 (0.52–0.54)	0.81 (0.79–0.82)
Logistic	0.78 (0.76–0.80)	0.65 (0.63–0.67)	0.40 (0.38–0.42)	0.50 (0.49–0.51)	0.79 (0.78–0.81)

Table 4. Prediction effect of IDH risk prediction model established by machine learning in test set.

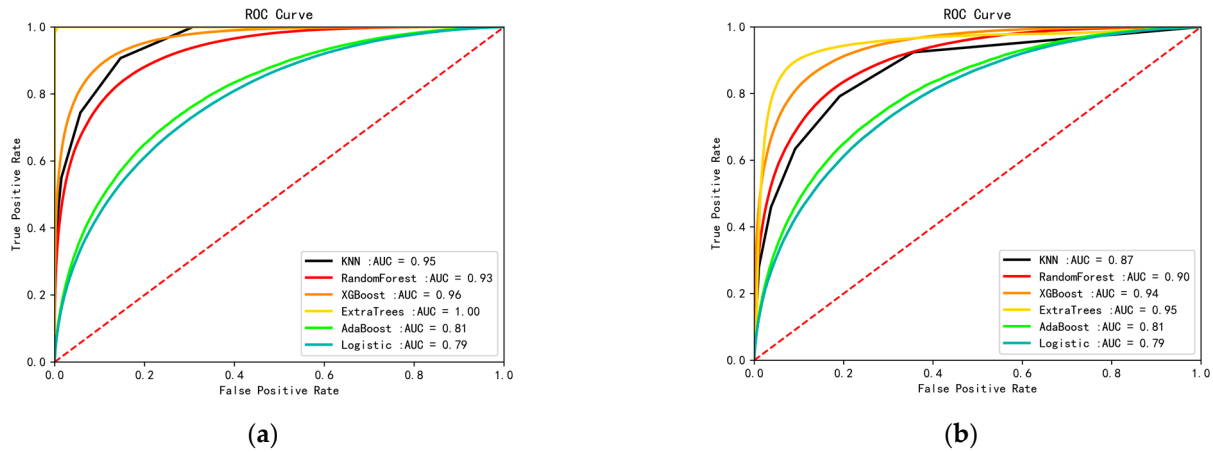| Models	Accuracy	Precision	Recall	F1 Score	AUC
ExtraTrees	0.92 (0.90–0.94)	0.87 (0.85–0.89)	0.81 (0.79–0.83)	0.84 (0.82–0.86)	0.95 (0.94–0.96)
XGBOOST	0.89 (0.87–0.91)	0.84 (0.82–0.86)	0.71 (0.70–0.73)	0.77 (0.75–0.79)	0.94 (0.92–0.96)
KNN	0.84 (0.82–0.86)	0.72 (0.71–0.73)	0.64 (0.63–0.65)	0.68 (0.67–0.69)	0.87 (0.85–0.89)
Random Forest	0.85 (0.83–0.87)	0.81 (0.80–0.83)	0.57 (0.56–0.58)	0.67 (0.65–0.69)	0.90 (0.88–0.91)
AdaBoost	0.79 (0.78–0.81)	0.66 (0.65–0.67)	0.44 (0.42–0.45)	0.53 (0.51–0.55)	0.81 (0.80–0.83)
Logistic	0.78 (0.76–0.79)	0.65 (0.64–0.67)	0.39 (0.37–0.41)	0.49 (0.47–0.51)	0.79 (0.78–0.81)

(**a**)

(**b**)

Figure 6. (**a**) ROC curve of IDH risk prediction model in hemodialysis constructed by machine learning in train set: KNN: 0.95 (0.94–0.96), Random Forest: 0.93 (0.91–0.95), XGBOOST: 0.96 (0.94–0.98), ExtraTrees: 1.00 (0.99–1.00), AdaBoost: 0.81 (0.79–0.83), Logistic: 0.79 (0.77–0.82); (**b**) ROC curve of IDH risk prediction model in hemodialysis constructed by machine learning in test set: KNN: 0.87 (0.86–0.88), Random Forest: 0.90 (0.88–0.92), XGBOOST: 0.94 (0.92–0.95), ExtraTrees: 0.95 (0.93–0.97), AdaBoost: 0.81 (0.79–0.84), Logistic: 0.79 (0.77–0.82).

3.5. Model Interpretability Analysis

We used the TreeSHAP method for individual and global explanations of the IDH risk prediction model. Figure 7 shows the individual explanation of the model predicting the occurrence of IDH risk in an MHD patient during hemodialysis. Each of its features makes a corresponding contribution. Red represents the positive impact on the occurrence of IDH, and blue represents the negative impact on the occurrence of IDH. The results showed that the MHD patient's pre-dialysis SBP = 166 mmHg, age = 86.04 years old, pre-dialysis MAP = 108.67 mmHg, and dialysis duration = 195 min were the main correlates of IDH during hemodialysis.
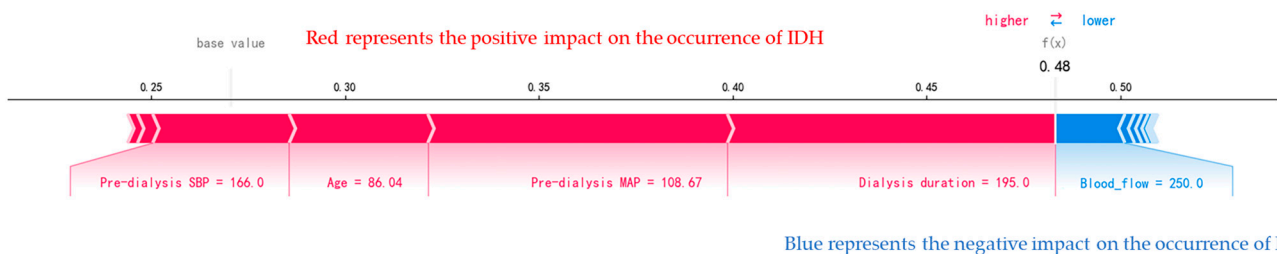

Figure 7. Individual explanation of the IDH risk prediction model.

Figure 8 shows the global explanation of the IDH risk prediction model. Plotting the contribution of each feature provided a better understanding of the model's overall prediction pattern and can identify predictive outliers. Each row represents a feature, the abscissa is the contribution value, and the color represents the feature value (red means high, blue means low). This global explanation method calculates the contribution of each

feature to the prediction and visualizes these contributions. As shown in the first row of the figure, excessive dialysis duration increases the risk of the occurrence of IDH. Analyzing the contribution of these features to predictions will help identify potential biases or errors in the model.
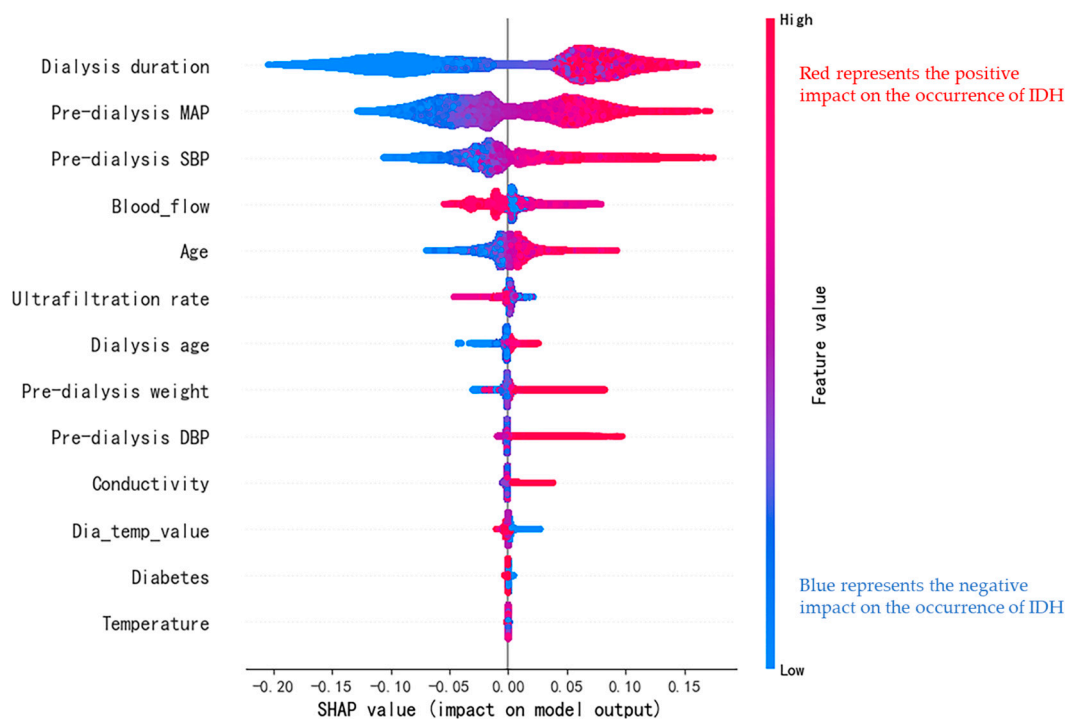

Figure 8. Global explanation of the IDH event prediction model.

4. Discussion

IDH is common in MHD patients during hemodialysis, and relevant studies show that approximately 20–30% of patients developed IDH during hemodialysis [6], and 75% of MHD patients experienced IDH at least once [26]. In this study, IDH events accounted for approximately 27% of the hemodialysis recording set, indicating that the recording set used in this study was consistent with clinical reality. Since the blood pressure of MHD patients fluctuates significantly during hemodialysis, for the safety of hemodialysis patients, blood pressure needs to be measured frequently, it is of great significance to develop an ideal IDH risk prediction model during hemodialysis. Given the limitations of traditional statistical methods in highly complex multifactor analysis (multidimensional and nonlinear) problems, machine learning and deep learning can play an important role in IDH prediction. Gabutti et al. [27] conducted a retrospective and prospective observational study in two Swiss dialysis centers (80 chronic hemodialysis patients, 480 months of clinical observation and biochemical test results), and compared the performance of artificial neural networks (ANN) in predicting the risk of hypotension during dialysis with that of experienced nephrologists. ANN showed better results in predicting the incidence of hypotension in terms of sensitivity and specificity. Lin et al. [28] developed an intelligent system with the ability to predict IDH based on time-related logistic regression analysis, using 55,516 dialysis data from 653 hemodialysis outpatients. The model results showed that the prediction sensitivity of the systolic blood pressure nadir (SBP) < 90 mmHg was 86% and the specificity was 81%. Gómez-Pulido et al. [29] used clinical information from 98,015 treatments of 758 patients and used DT and SVM classifiers to construct a model for predicting hypotension during dialysis, taking into account up to 22 clinical parameters during treatment. The model prediction success rate reached 80%. Lee et al. [30] used data from more than 260,000 hemodialysis sessions and obtained a model for predicting intradialytic hypotension based on recurrent neural network training. The AUC of the

model reached 0.94. Huang et al. [31] used a linear regression model, LASSO, a tree-based ensemble machine learning model (Random Forest and Extreme Gradient Boosting) and Support Vector Regression to predict SBP based on 9245 blood pressure records of 248 maintenance hemodialysis patients. The comparison showed that the machine learning model had better prediction performance.

We used blood pressure data measured before the start of hemodialysis treatment and equipment information during hemodialysis treatment to screen a total of 13 modeling parameters including demographic features and clinical features, then established an IDH risk prediction model based on machine learning algorithms, making it possible to predict IDH events throughout the entire hemodialysis period by completing only one blood pressure measurement before the start of hemodialysis, allowing the medical team to manage and prevent IDH promptly during hemodialysis.

The best IDH risk prediction model's accuracy based on machine learning algorithms reached 0.92 (95% CI 0.90–0.94) and the AUC reached 0.95 (95% CI 0.94–0.96). The results show that the machine learning model has a good effect in predicting IDH events during hemodialysis. At the same time, this study measured the contribution of each feature to the prediction of IDH based on the Gini evaluation index. The results showed that dialysis duration, pre-dialysis MAP, and pre-dialysis SBP were much more important than other features in predicting IDH events during hemodialysis. Finally, we used the TreeSHAP method to perform individual and global explanations of the IDH risk prediction model. By plotting the contribution value of each feature, it will be helpful to better understand the overall prediction mechanism of the model, discover prediction outliers, and identify potential biases or errors in the model. At the same time, for the IDH risk prediction of a single sample, the TreeSHAP method can show how each feature drives the model prediction in a positive or negative direction, which helps explain individual model prediction, helps medical staff understand the model prediction mechanism and to explain how each patient's features affect the model's prediction results.

The IDH event prediction model established in this study only requires demographic information, equipment information, and blood pressure values measured before hemodialysis, and then the IDH risk prediction of the entire hemodialysis process can be performed, which greatly simplifies the threshold for model use. Therefore, the model is completely feasible in a real clinical environment. At the same time, the prediction model has non-invasive, simplicity, and low-cost clinical value, confirming the broad application prospects of machine learning in the task of predicting IDH during hemodialysis. However, this model also has certain limitations. It can only determine whether IDH will occur but cannot predict the accurate blood pressure value. At the same time, the model has not been verified by multi-center data, and its reliability and generalizability need to be further verified. Prospective studies still need to be conducted in larger multi-center cohorts in the future.

5. Conclusions

To further promote the application of artificial intelligence models in the field of hemodialysis, it is necessary to strictly evaluate the effectiveness and safety of artificial intelligence tools in actual clinical trials in the future. Secondly, it is necessary to pay attention to the implicit and explicit biases that occur during artificial intelligence model training. At the same time, medical staff in hemodialysis centers need to understand the explanation methods of artificial intelligence models. These measures will help improve the application of artificial intelligence models in the field of hemodialysis treatment. In the future, innovative hemodialysis equipment will integrate microelectronics technology and artificial intelligence technology, and its development trend will inevitably be miniaturization and intelligence.By being equipped with real-time hemodialysis parameter monitoring modules and high-throughput intelligent computing modules, the safety of hemodialysis patients will be effectively ensured. At the same time, by constantly adjusting hemodialysis prescriptions based on changes in the physical parameters of hemodialysis patients, the

quality of life and medical experience of hemodialysis patients can be improved, and medical costs can be reduced.

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