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Analysis of Factors Related to Vasovagal Response in Apheresis Blood Donors and the Establishment of Prediction Model Based on BP Neural Network Algorithm

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Abstract: *Objective:* To analyze the factors related to vessel vasovagal reaction (VVR) in apheresis donors, establish a mathematical model for predicting the correlation factors and occurrence risk, and use the prediction model to intervene in high-risk VVR blood donors, improve the blood donation experience, and retain blood donors. *Methods:* A total of 316 blood donors from the Xi'an Central Blood Bank from June to September 2022 were selected to statistically analyze VVR-related factors. A BP neural network prediction model is established with relevant factors as input and DRVR risk as output. *Results:* First-time blood donors had a high risk of VVR, female risk was high, and sex difference was significant (P value < 0.05). The blood pressure before donation and intergroup differences were also significant (P value < 0.05). After training, the established BP neural network model has a minimum RMS error of 0.116, a correlation coefficient R = 0.75, and a test model accuracy of 66.7%. *Conclusion:* First-time blood donors, women, and relatively low blood pressure are all high-risk groups for VVR. The BP neural network prediction model established in this paper has certain prediction accuracy and can be used as a means to evaluate the risk degree of clinical blood donors.

Keywords: Vasovagal response; Related factors; Prediction; BP neural network

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1. Introduction

Donor safety has always been at the center of attention for the healthy development of the blood transfusion business. Caring for blood donors and enhancing the blood donation experience is the only way to retain donors and expand the pool of regular donors. The occurrence of adverse reactions to blood donation not only affects the donor experience but also causes donor turnover. Blood donation-related vasovagal reactions (VVR) are the most common adverse reactions to blood donation, which bring physical and psychological damage to them and are very detrimental to the expansion and maintenance of the pool of regular blood donors [1,2]. For this reason, the National Health Administrative Department organized the development and release of the health industry standard "Guidelines for the Prevention and Disposal of Blood Donation-Related Vascular Vagal Reaction" (WS/T595-2018), which puts forward recommendations for the prevention and disposal of VVR.

Some scholars have conducted ultrasound Doppler monitoring of blood donors who experienced VVR during blood donation and found that the blood pressure of blood donors in the occurrence of early VVR differed from that of donors who did not experience VVR [2,3], and that monitoring blood pressure of blood donors would play a preventive role in preventing the occurrence of VVR if it is done in conjunction with the relevant conclusions of the "Guidelines for the Prevention and Disposal of Blood Donation-Related Vaso-Vagal Nerve Reactions" (WS/T595- 2018)'s related conclusion that age, weight, blood donation history, and blood volume are correlated with the occurrence of blood donation-related vasovagal reaction [4]. In this paper, the age, gender, body mass index, and blood donation history of 316 component donors who donated blood from June 2022 to September 2022 were registered, and systolic blood pressure, diastolic blood pressure, and heart rate were recorded throughout the blood donation process, from which we analyzed the factors related to vasovagal reaction in mono-collected blood donors, established the predictive mathematical model of the related factors and the risk of occurrence, and gave interventions to the high-risk people at the same time, so as to reduce or even avoid the VVR can be reduced or even avoided by intervening in high-risk individuals.

2. Subjects and methods

2.1. Subjects

316 single blood donors from Xi'an Central Blood Station from June 2022 to September 2022 were selected as the study subjects. Of these, 44 cases of VVR occurred as the reaction group and 272 cases occurred as the control group.

2.2. Methods

2.2.1 Range of factor consideration

According to the available data, the gender of blood donors, blood donation experience, blood donation volume, blood collection duration, heart rate, systolic blood pressure, diastolic blood pressure, and body mass index (BMI) were included in the scope of consideration.

2.2.2 Data collection methods

In accordance with the Blood Donation Law of the People's Republic of China, the Measures for the Administration of Blood Stations, and the Health Examination Standards for Blood Donors, the study wore dynamic blood pressure monitors on 316 single blood donors during blood donation and recorded their systolic blood pressure, diastolic blood pressure, and heart rate every two minutes. The start time of blood collection and the termination time of blood collection were recorded, and the length of blood collection was calculated. The weight and height of blood donors were measured by weighing scale and height measuring tape, and the body mass index BMI = $(\text{weight}/\text{height})^2$, with weight unit kg and height unit m in the formula.

2.2.3 Diagnostic criteria

According to the Guidelines for the Classification of Adverse Reactions to Blood Donation, adverse reactions with predominantly systemic manifestations, i.e., vasovagal reactions, are manifested as generalized discomfort, weakness, pallor, sweating, anxiety, dizziness, and nausea. A few may experience transient loss of consciousness (syncope), convulsions, or loss of bowel movement [5].

2.2.4 Statistical methods

Data were statistically analyzed using SPSS 19.0 software. The Kolmogrov-Smirnov and Shapiro-Wilk normality tests were used for the measurement data, and the BMI, blood pressure, heart rate, and blood collection time indexes did not meet the normal distribution. The median and quartiles indicating M (P25, P75) can be described, and the differences between the two groups were compared using the nonparametric rank-sum test (Mann-Witney U). Differences were considered statistically significant at $P < 0.05$.

2.2.5 Modeling method

BP neural network is a multi-layer feed-forward neural network training based on the error back-propagation algorithm, which is suitable for correlation analysis of objects with non-explicit relationships so as to build complex models with strong nonlinear mapping capabilities. In this paper, the BP neural network algorithm was used to establish a BP neural network model using the MATLAB software toolbox with parameters such as gender, blood donation experience, pre-donation high pressure, and pre-donation low pressure as inputs, and whether or not the vagal nerve response is the output. A total of 76 samples, 38 samples with VVR and 38 samples without VVR, were randomly selected to build the neural network model. The BP neural network consists of an input layer, a hidden layer, and an output layer, and according to the empirical formula, a BP neural network model with 4 nodes in the input layer, 10 nodes in the hidden layer, and 1 node in the output layer was established, as shown in **Figure 1** below. The transfer function of the hidden layer is "tansig", and the transfer function of the output layer is "purelin."

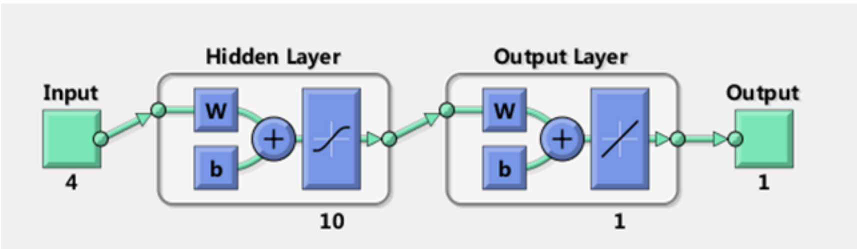

Figure 1. Schematic of BP neural network model.

3. Results

3.1. Significance analysis of VVR-related factors

Significance analysis of the situation of the reaction group and the control group from the three aspects of blood donation experience, gender, and donation volume. The difference in the factor of number of blood donations between the reaction group and the control group was significant $p < 0.05$, and the proportion of first-time donors in the reaction group was higher (84%), indicating that the risk of vagal reaction was high in first-time donors. The difference in gender factor was significant $p = 0.014$; there was a higher percentage of females (52.3%) in the response group, indicating a high risk of vagal nerve reaction in female blood donors. The difference in the effect of the donation volume factor on vagal reaction was not significant ($P = 0.534$).

Data on BMI, blood pressure, heart rate, and duration of blood collection were analyzed. Firstly, normality was analyzed using S-W test and none of them satisfied normal distribution ($P < 0.05$). Median and interquartile descriptions were used and a non-parametric rank sum test (Mann-Witney U) was performed for comparison between groups. The results showed insignificant differences between the vagal response group and the control group in terms of BMI, heart rate, and duration of blood collection ($P > 0.05$). Differences in pre-donation blood pressure including both high- and low-pressure groups were significant with p-values of 0.044 and 0.033, respectively. The analysis showed that pre-donation blood pressure had an effect on vagal response and that relatively low blood pressure was more likely to result in vagal response. The analyzed data are shown in **Table 1** below.

Table 1. Analysis of the VVR reaction group and control group

Projects		Reaction group (*n* = 44)	Control group (*n* = 272)	Statistic	*p*-value
Blood donation	Initial	37 (84%)	143 (52.6%)	c^2 = 15.346	8.95E-5
	Repeat	7 (16%)	129 (47.4%)		
	Total	44 (100%)	273 (100%)		
Sex	Male	21 (47.7%)	182 (66.9%)	c^2 = 6.068	0.014
	Female	23 (52.3%)	90 (33.1%)		
	Total	44 (100%)	273 (100%)		
Blood donation	1 Healing capacity	13 (29.5%)	93 (34.2%)	c^2 = 0.386	0.534
	2 Healing capacity	31 (70.5%)	178 (65.8%)		
	Total	44 (100%)	273 (100%)		
BMI (kg/m^2)		22.6 (21.43–24.68)	23.1 (21.03–25,20)	Z = -0.504	0.614
Systolic blood pressure (mmHg)		115 (110–123)	120 (111–120)	Z = -2.015	0.044
Diastolic blood pressure (mmHg)		70 (70–75)	75 (70–80)	Z = -2.133	0.033
Heart rate (beats/min)		82.5 (76–87)	83 (75.3–87)	Z = -0.285	0.775
Blood collection time (min)		67 (58–80)	65 (56–75)	Z = -0.718	0.473

3.2. Establishment of a prediction model based on BP neural network

From the above analysis, it can be seen that compared with the control group, there were significant intergroup differences in factors such as gender, blood donation experience, and blood pressure indexes (including systolic and diastolic blood pressure) before blood donation in the VVR reaction group ($p < 0.05$). Based on these factors, establishing a prediction model for the degree of risk of vagal reaction in blood donation is of great significance in guiding the prevention of vagal reaction during blood donation. In this paper, the BP neural network algorithm was used to establish the prediction model.

According to the conclusions of the aforementioned statistical analysis, a neural network model can be established with four parameters: gender, blood donation experience, systolic blood pressure before blood donation, diastolic blood pressure before blood donation as inputs, and whether or not the vagal nerve reaction is the output. The parameterization definitions are as follows in **Table 2**. To improve the accuracy of the model analysis, the blood pressure indexes are input after normalization, and the input values are between 0 and 1.

Table 2. Parameterization definitions

Parameter	Define
Sex	Female = 1, Male = 0
Blood Donation Experience	First time = 0, again = 1
Vagal response	Occurs = 1, Does not occur = 0

In this paper, there were 44 cases of vasovagal reaction and 38 cases of no vasovagal reaction recorded. 38 cases of no vasovagal reaction were randomly selected to build the neural network model in consideration of data balance. Six cases of each were reserved, and a total of 12 cases were used for model validation. The BP neural network toolbox of MATLAB software was used to train the model, and the training method was Levenberg-Marquardlt. 76 samples were randomly divided into training sets, validation sets, and test sets, and the proportion of division was 70%, 15%, and 15%, respectively. **Figure 2** below shows the graph of the number of iterations of the neural network training process versus the mean square error MSE. The three curves from top to bottom are the MSE error curves of the test set, validation set, and training set, respectively. As can be seen in the figure, the model converges in 14 iterations, the MSE of the root mean square error of the validation set is minimized to 0.116 in the 8th iteration, and the neural network stops training to avoid overfitting, affecting the accuracy of the prediction model.

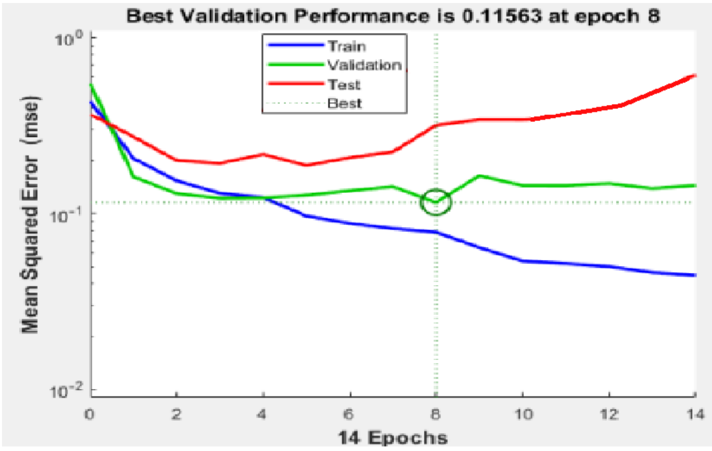

Figure 2. Number of iterations vs. mean square error.

In the constructed neural network model, after training, the predicted output of all the data is compared with the target output as shown in the following **Figure 3**. From the figure, it can be seen that the scatter points of the target value and the predicted value are approximately dispersed on both sides of the straight line with slope 1, and the correlation coefficient R = 0.75, which is highly correlated, and the fitting effect of the data has some significance. The constructed BP neural network model has some predictive value.

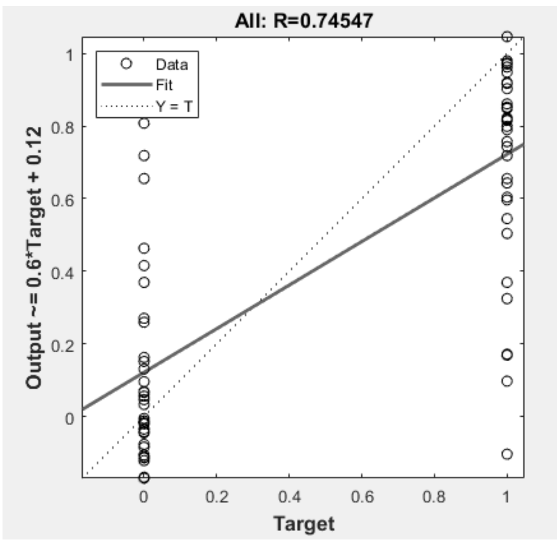

Figure 3. Correlation of data target values with input values.

3.3. Modification of the BP neural network prediction model

The BP neural network model constructed above has an output value of a number between (-1,1), and we are actually concerned with the magnitude of the risk of developing a vasovagal response. To further improve the prediction accuracy of the model, the output can be categorized into two values, 0 and 1, with 0 indicating low risk and 1 indicating high risk. Comparing the initial output y1 with 0 and 1, close to 0 is equal to 0, and close to 1 is equal to 1. The model output Y1 is corrected according to the following equation:

$$\mathrm{Y1} = \begin{cases} 0, & |\mathrm{y1}| < |\mathrm{y1} - 1| \\ 1, & |\mathrm{y1}| \geq |\mathrm{y1} - 1| \end{cases}$$

According to the corrected model, 12 data used for testing were inputted into the constructed neural network model, and the predicted outputs were corrected according to the equation. 8 out of 12 predicted output data were consistent with the target value, and the model predicted correctly by 66.7%. The model has a certain prediction accuracy, which can be further improved by increasing the sample size for training.

4. Discussion

Compared with the control group, there was a significant difference between the groups in terms of gender, blood donation experience, and blood pressure indexes (including systolic and diastolic blood pressure) before blood donation ($P < 0.05$). First-time blood donors and some female blood donors are not psychologically mature enough, and some of them are not clear about the blood donation process or are too nervous. They will have insufficient autonomic function tension regulation and are relatively prone to VVR. Some scholars have found that blood donors with a fear of donating blood have a 13.6% higher probability of experiencing VVR than those who do not have any fear of donating blood [6–9]. In July 2018, China released the health industry standard WS/T595-2018 (Guidelines for the Prevention and Management of Blood Donation-related Vasovagal Reactions), listing female, first-time blood donors as a vulnerable population for VVR [3]. VVR is more likely to be induced in blood donors whose blood pressure is at the low limit of the normal range before blood donation. When the vagus nerve is excited, there will be a decrease in heart rate, a decrease in cardiac contractility, a decrease in cardiac output, a dilation of peripheral vasculature, and a decrease in resistance, and it can inhibit the release of renin and inhibit the hypothalamus to make it synthesize less vasopressin thus blood pressure decreases, so blood donors who have a low blood pressure should be paid special attention to or intervene in advance [10]. The three factors of blood donation history, gender, and blood pressure before blood donation are the indicators of routine examination before blood donation and are easy to obtain. Compared with the use of electrocardiograms, ambulatory blood pressure monitoring, or other means of predicting the occurrence of VVR in blood donors, the prediction model in this study is more likely to achieve better social and economic benefits.

In the BP neural network prediction model established in this paper, after training, the mean square error MSE is minimized to 0.116, the correlation coefficient R = 0.75, and the correct rate of the model reaches 66.7%, which has a certain predictive value. Blood pressure of donors can be collected in advance during blood collection, and gender, whether it is the first time to donate blood, and blood pressure indexes before blood donation can be input into the prediction model to carry out risk assessment and intervene in advance for high-risk people. Appropriate sugar/saline supplementation before blood donation can increase blood pressure and replenish blood volume, and its physiological mechanism is that saline can activate the human renin-angiotensin system [11]. This is a measure and tool that has long been used in most blood collection and supply organizations to prevent or alleviate VVR. Coffee stimulates the body to produce higher amounts of epinephrine and norepinephrine, which acts as a blood pressure booster. It has been stated in the literature that applied muscle tension

(AMT) exercise can increase central blood volume and blood oxygenation and increase venous return by repeatedly tensing muscle groups such as the buttocks and legs and emptying large-volume veins, all of which have preventive effects on vasovagal reactivity induced by hypovolemic factors [12,13]. For high-risk donors predicted by the model can be supplemented with sugar saline or coffee before blood donation, together with muscle tone exercise, coupled with the patient, warm and professional service of the blood station staff can greatly reduce the incidence of VVR, which can improve the donor experience, increase the willingness of donors to donate blood again, and play a role in the retention of blood donors [11,14].

There are more studies on the prediction of adverse reactions to blood donation with different modeling methods. This paper adopts the prediction method of the BP neural network, which is somewhat innovative, giving full play to the characteristics of the algorithm's strong nonlinear mapping ability, and facilitating the establishment of complex models with unknown multifactor correlation. From the results of the model prediction, it has a potential application value. Because of the limited number of samples in this study, the factors included in the consideration are not comprehensive enough, and the prediction accuracy is not high enough. The follow-up can be increased by increasing the sample size, increasing the consideration factors, further optimization of the network, and training to improve the model prediction accuracy so that it can play a greater socio-economic benefit.

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Disclosure statement

The authors declare no conflict of interest.

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