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Comparison of Survival Predictions for Rats with Hemorrhagic Shocks Using an Artificial Neural Network and Support Vector Machine

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Abstract— **Hemorrhagic shock is the cause of one third of deaths resulting from injury in the world. Early diagnosis of hemorrhagic shock makes it possible for physicians to treat patients successfully. The objective of this study was to select an optimal survival prediction model using physiological parameters from rats during our hemorrhagic experiment. These physiological parameters were used for the training and testing of survival prediction models using an artificial neural network (ANN) and support vector machine (SVM). To avoid over-fitting, we chose the optimal survival prediction model according to performance measured by a 5-fold cross validation method. We selected an ANN with three hidden neurons and one hidden layer and an SVM with Gaussian kernel function as a trained survival prediction model. For the ANN model, the sensitivity, specificity, and accuracy of survival prediction were 97.8 ± 3.3 %, 96.3 ± 2.7 %, and 96.8 ± 1.7 %, respectively. For the SVM model, the sensitivity, specificity, and accuracy were 97.5 ± 2.9 %, 99.3 ± 1.1 %, and 98.5 ± 1.2 %, respectively. SVM was preferable to ANN for the survival prediction.**

I. Introduction

ACCORDING to The World Health Organization (WHO) in 2010 [1], death resulting from injury accounts for 14% of overall deaths in the world, and the cause of one third of these deaths directly due to injury is hemorrhagic shock [2], [3]. In South Korea, it was reported that the cause of 74% of multiple trauma patients' deaths in emergency rooms (ER) over the past eight years was hypovolemic shock [4]. Hemorrhagic shock is a clinical syndrome characterized by widespread inadequate oxygenation and supply of nutrients to the tissues and organs, resulting in cellular dysfunction [5], [6]. Failure of compensatory mechanisms in hemorrhagic shock can lead to death. It is not difficult to diagnose complications when patients are already in a state of shock, because the homeostatic response to hemorrhage involves obvious changes in many cardiovascular and biochemical variables.

On the other hand, the ability to rapidly and accurately triage and utilize appropriate interventions can be problematic in the early decision-making process of trauma care with insufficient information. An accurate diagnosis and treatment could be delayed because there are a few obvious symptoms. There have been many studies of early diagnosed patients with hemorrhagic shock through various hemodynamic indexes and blood tests [7], [8]. Also, statistical methods have recently been applied for prediction model of survival or mortality [9]-[11].

The aim of this study was to diagnose hemorrhagic shock in its early stage using various physiological parameters. Over the years, there have been several studies that suggested survival prediction models using an artificial neural network (ANN), logistic regression, and polynomial neural network (PNN) [10], [11]. However, most previous studies did not perform a validation process for model optimization. Thus, in this study, we constructed ANN and SVM models with 5-fold cross validation for selecting an optimal survival prediction model. Input parameters were heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), respiration rate (RR), and temperature (TEMP) from a hemorrhagic rat model.

II. Materials and Methods

A. Data Acquisition

Forty-five male Sprague-Dawley (S-D) rats were divided into three groups of each fifteen rats depending on the controlled blood volume loss. Three blood volumes of 2 ml/100 g, 2.5 ml/100 g, and 3 ml/100 g were withdrawn over 15 min for the three groups. HR, SBP, DBP, RR, and TEMP were measured as physiological parameters from the rats during the hemorrhagic experiment. We analyzed data for five min after "Bleeding end" (the shaded area) in Fig. 1. We selected this period because we simulated an emergency situation in which bleeding was treated. The five min data for each parameter were divided into five sets of data with one min averages. Thus, 225 (45 rats * 5 sets/rat) data sets were obtained in this study. When survival and death sets were determined 150 min after the start of the experiment, the numbers of survival and death sets were 95 and 130,

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respectively. The 225 data sets were then divided into 150 training sets and 75 testing sets as shown in Table I.

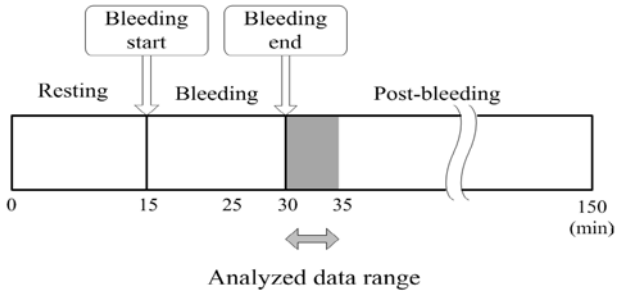

Fig. 1. Experimental protocol for rats with hemorrhagic shock.

TABLE I
DISTRIBUTION OF ALL DATA DIVIDED INTO TRAINING SET AND TEST SET, SURVIVAL SET AND DEATH SET

Group	Training data sets	Testing data sets	Total data sets
Survival data sets	65	30	95
Death data sets	85	45	130
Total data sets	150	75	225

Since the physiological parameters were obtained from each rat having different scales of each parameter, the whole data sets were normalized between zero and one using (1) to effectively train survival prediction models.

$$X_{norn}^{k} = ((x_1^k - \min_1)/(\max_1 - \min_1), \ldots, (x_i^k - \min_i)/(\max_i - \min_i)) \quad (1)$$

In equation (1), i is 5, which is the number of input parameters consisting of HR, SBP, DBP, RR, and TEMP. The $\max_i$ and $\min_i$ indicated maximum and minimum values of each physiological parameter in one min data. k is from one to five, meaning one min data length of total five min. We used MATLAB Version 7.6 (Mathworks Inc, Natick, USA) for analysis of ANN and SVM.

B. Artificial neural networks (ANN)

The architecture of the ANN in the study was based on a multi-layer perceptron which consisted of three layers: input, hidden, and output layers. Each layer of the network consisted of a number of elementary processing units called neurons [12].

In this study, the architecture of the ANN consisted of one input layer with five input neurons, one hidden layer with between two and ten hidden neurons, and one output layer with one output neuron as shown in Fig. 2(a). ANN with too few hidden neurons would be incapable of differentiating between complex patterns, leading only to a linear estimate of the actual trend. In contrast, if the ANN model had too many hidden neurons, it would follow the noise in the data due to over-fitting, leading to poor generalization for untrained data [13]. To obtain the optimal number of neurons in the hidden layer, we tried to train between two and ten hidden neurons to obtain the optimal ANN model. The ANN algorithm was based on Levenberg-Marquartd back-propagation to rapidly find an optimal solution.

C. Support vector machines (SVM)

SVM is an alternative training method of various statistical classifier methods and neural networks. A SVM model maps data patterns in high dimensional space. The data are divided into two groups by the training data called support vector. An optimal SVM model is determined using the best separation by the hyper-plane that has the longest distance to the support vector. Fig. 2(b) shows that a kernel function is generally able to linearly separate data patterns. Thus, the goal of the support vector machine is to improve the accuracy of a model by separating space using a kernel function. This study investigated survival prediction models using kernel function of non-kernel, quadratic, polynomial, and Gaussian radial basis.

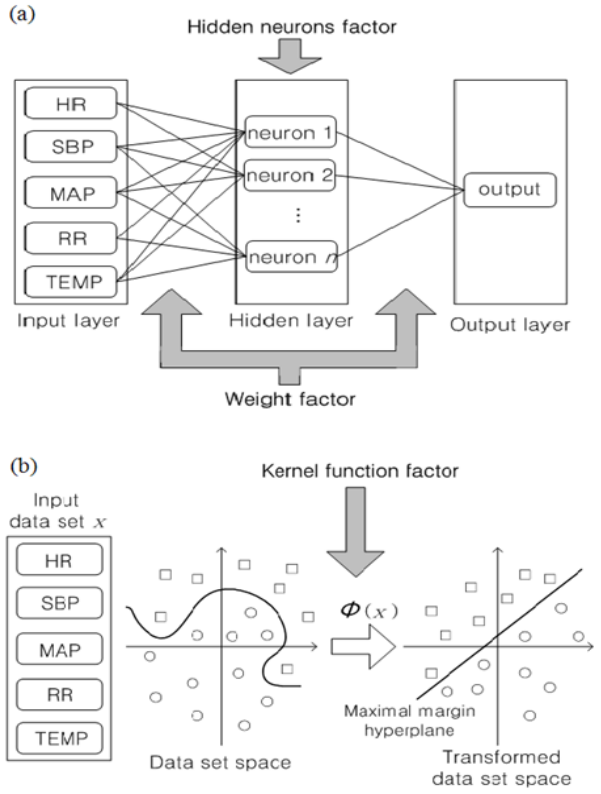

Fig. 2. Features in prediction models and their variables. Weight and hidden neurons factor of ANN (a), Kernel function factor of SVM (b).

D. 5-fold cross validation and testing

The k-fold cross validations that have been used in many studies are 10-fold or 5-fold cross validation. However, many studies didn't reveal any statistical advantages of 10-fold cross validation over 5-fold cross validation [14]. Therefore, the 5-fold cross validation was used because of the insufficient training data sets in this study. The training data sets were divided randomly into five subsets without overlapping as

shown in Fig. 3. Four of the five subsets were used for training and the fifth subset was used for validation during training. The entire validation process was repeated an additional four times by rotating the remaining subsets to be used as the validation set. The accuracy of each prediction model was computed and averaged. To obtain an optimal prediction, the survival prediction model that had accuracy closest to average was selected [15]. The selected survival prediction model represented producing five prediction models during 5-fold cross validation. After the training process, the selected model was tested with the remaining testing data sets from the original total data sets.

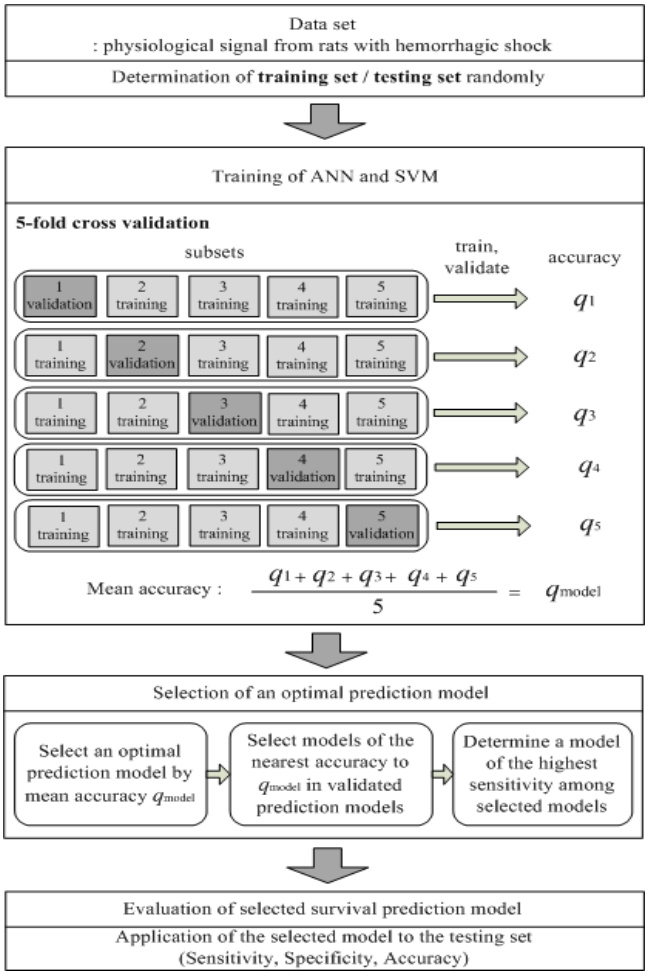

Fig. 3. Flowchart of determination for survival prediction model by 5-fold cross validation.

We utilized the following parameters in evaluating the performance of the prediction models: sensitivity, specificity, and accuracy.

$$Sensitivity = TP/(TP + FN) \quad (2)$$

$$Specificity = TN/(TN + FP) \quad (3)$$

$$Accuracy = (TP + TN)/(TP + TN + FP + FN) \quad (4)$$

True positive (TP): No. of survived rats correctly identified as surviving.
True negative (TN): No. of dead rats correctly identified as dead.
False positive (FP): No. of dead rats incorrectly identified as surviving.
False negative (FN): No. of survived rats incorrectly identified as dead.

When the training was performed, ANN set initial weights randomly and made different models, which had different sensitivity, specificity, and accuracy. Thus, we made up for this characteristic by suggesting an optimal survival prediction model based on mean sensitivity, mean specificity, and mean accuracy. These were determined through 10 repetitions with the ANN and SVM models.

III. Result

Tables II and III show the validation results of ANN and SVM models. It was determined by 10 times repetitions using the ANN and SVM models with a 5-fold cross validation method. ANN with three hidden neurons showed 97.9 ± 4.5% sensitivity, 94.8 ± 2.0% specificity, and 96.3 ± 1.1% accuracy, which was the best result. The mean accuracy decreased along with the increasing number of hidden neurons.

In Table III, SVM with Gaussian kernel function as trained survival prediction model resulted in 98.7 ± 2.7% sensitivity, 97.8 ± 2.9% specificity, and 98.0 ± 1.7% accuracy, which was the best result among the kernel functions. SVM showed better accuracy than ANN because SVM converges into the global minima to train an optimal model, whereas ANN converges into the local minima to perform regional over-fitting.

TABLE II
Validation results of ANN with hidden neurons between 2 and 10 (Mean ± S.D.)

Number of hidden neurons	Sensitivity (%)	Specificity (%)	Accuracy (%)
2	98.5 ± 3.2	93.1 ± 4.1	95.3 ± 2.3
3	97.9 ± 4.5	94.8 ± 2.0	96.3 ± 1.1
4	99.3 ± 2.1	90.1 ± 2.8	94.0 ± 1.4
5	100.0 ± 0.0	91.0 ± 4.6	94.7 ± 2.8
6	99.2 ± 2.6	90.6 ± 4.8	94.7 ± 1.7
7	100.0 ± 0.0	89.2 ± 3.8	93.7 ± 2.5
8	96.9 ± 5.4	89.8 ± 5.4	92.7 ± 3.4
9	98.4 ± 3.4	86.6 ± 8.1	92.0 ± 3.6
10	99.4 ± 2.0	86.8 ± 6.7	92.3 ± 3.9

S.D. = standard deviation

TABLE III
Validation results of SVM model with several kernel function (Mean ± S.D.)

Kernel function	Sensitivity (%)	Specificity (%)	Accuracy (%)
Non-kernel	99.1 ± 2.9	96.4 ± 3.2	97.7 ± 1.6
Quadratic	98.3 ± 3.6	96.5 ± 4.1	97.3 ± 2.1
Polynomial	98.4 ± 3.4	94.1 ± 2.9	95.7 ± 1.6
Gaussian	98.7 ± 2.7	97.8 ± 2.9	98.0 ± 1.7

Each selected model was evaluated for the test set (n=75) to compare its performance. Table IV presents mean and standard deviation of receiver operating characteristic-area under curve (ROC-AUC), sensitivity, specificity, and accuracy of the selected ANN and SVM models. Mean and S.D. of ROC-AUC of the ANN models with three hidden neurons and SVM model with Gaussian kernel function were 0.97 ± 0.02 and 0.98 ± 0.01, respectively. For ANN, 97.8 ± 3.3% sensitivity, 96.3 ± 2.7% specificity, and 96.8 ± 1.7% accuracy were obtained. For SVM, 97.5 ± 2.9% sensitivity, 99.3 ± 1.1% specificity, and 98.5 ± 1.2% accuracy were obtained. Therefore, SVM was better than ANN in terms of ROC-AUC, specificity, and accuracy.

TABLE IV
SURVIVAL PREDICTION TESTING RESULTS BY SELECTED ANN AND SVM MODEL (MEAN ± S.D.)

Model	ANN 3 hidden neurons	SVM Gaussian radial basis
ROC-AUC	0.97 ± 0.02	0.98 ± 0.01
Sensitivity (%)	97.8 ± 3.3	97.5 ± 2.9
Specificity (%)	96.3 ± 2.7	99.3 ± 1.1
Accuracy (%)	96.8 ± 1.7	98.5 ± 1.2

ROC-AUC = receiver operating characteristic – area under curve

IV. DISCUSSION AND CONCLUSION

There have been many studies predicting survival animal studies with hemorrhagic shocks. However, most studies did not perform a validation process. Also because training group and testing group were classified randomly once, training group could be over fitted by biased training data. To make up for this shortcoming, we used 5-fold cross validation to evaluate survival prediction models for ANN and SVM. Consequently, we confirmed that a SVM model with 5-fold cross validation had excellent performance for survival prediction. ANN has a disadvantage of local minima when creating models. However, because the SVM model is based on the structural risk minimization, it can create a model which converged to a global minima.

However, the survival prediction model suggested in this study would be difficult to apply to clinical situation because the model was obtained using data from the rats with controlled hemorrhagic shock. Therefore, further studies are warranted to suggest survival prediction models using data from a state of uncontrolled hemorrhagic shock for rats first, and then for humans. If further studies make it possible to predict the survival rate for patients with hemorrhagic shock, it would be useful to give preferential emergency treatment to patients who are more in danger.

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