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Predicting endoscopic third ventriculostomy success in childhood hydrocephalus: an artificial neural network analysis

Clinical article

Parisa Azimi, M.D., and Hasan Reza Mohammadi, M.D.

Department of Neurosurgery, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Object. Artificial neural networks (ANNs) can be used as a measure for the clinical decision-making process. The aim of this study was to develop an ANN model to predict endoscopic third ventriculostomy (ETV) success at 6 months and to compare the findings with those obtained using traditional predictive measures in childhood hydrocephalus.

Methods. The ANN, ETV Success Score (ETVSS), CURE Children's Hospital of Uganda (CCHU) ETV (CCHU ETV) Success Score, and logistic regression models were applied to predict outcomes. The cause of hydrocephalus, patient age, whether choroid plexus cauterization (CPC) was performed, previous shunt surgery, sex, type of hydrocephalus, and body weight were considered as input variables for an established ANN model. Data from hydrocephalic children who underwent ETV were applied, and the computer program that analyzes the data was trained to predict successful ETV by using several input variables. Successful ETV outcome was defined as the absence of ETV failure within 6 months of follow-up. Then, sensitivity analysis was performed for the established ANN model to identify the most important variables that predict outcome. The area under a receiver operating characteristic curve, accuracy rate of the prediction, and Hosmer-Lemeshow statistics were measured to test different prediction models.

Results. Data for 168 patients (80 males and 88 females; mean age 1.4 ± 2.6 years) were analyzed. Data from patients were divided into 3 groups: a training group (n = 84), a testing group (n = 42), and a validation group (n = 42). The successful ETV outcome rate, defined as the absence of ETV failure within 6 months of follow-up, was 47%. Etiology, age, CPC status, type of hydrocephalus, and previous shunt placement were the most important variables that were indicated by the ANN analysis. Compared with the ETVSS, CCHU ETV Success Score, and the logistic regression models, the ANN model showed better results, with an accuracy rate of 95.1%, a Hosmer-Lemeshow statistic of 41.2, and an area under the curve of 0.87.

Conclusions. The findings show that ANNs can predict ETV success at 6 months with a high level of accuracy in childhood hydrocephalus. The authors' results will need to be confirmed with further prospective studies.
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Key Words • **prediction** • **endoscopic third ventriculostomy success** • **artificial neural network** • **hydrocephalus**

Childhood hydrocephalus is prevalent and is difficult to treat. Endoscopic third ventriculostomy (ETV) is a novel treatment that can be successful in some children and can avoid dependence on a lifelong ventricular shunt system. Indications for ETV and prediction of the chances of ETV success are, however, controversial, and deciding whether to perform ETV in these patients is very difficult. Thus, if a marker of success for ETV outcome could be established, it would be possible to create a better decision-making process based on each patient's status.[5–7,13,15,16] Medical informatics, such as logistic regression and artificial neural networks (ANNs), have been applied to develop models.

ANN History

The history of neural networking arguably began in the late 1800s as an effort to define how the human mind works. These ideas were initially applied to ANN models. In 1943, McCulloch and Pitts created a computational model for ANNs based on mathematics and algorithms; this model is still used today.[9] In 1959, Rosenblatt conceived of the first learning algorithm, creating a model known as the perceptron, which was then only a solution

Abbreviations used in this paper: ANN = artificial neural network; AUC = area under the curve; CCHU = CURE Children's Hospital of Uganda; CPC = choroid plexus cauterization; ETV = endoscopic third ventriculostomy; ETVSS = ETV Success Score; H-L = Hosmer-Lemeshow; MLP = multilayer perceptron; ROC = receiver operating characteristic.

This article contains some figures that are displayed in color online but in black-and-white in the print edition.

to simple linear problems using simple addition and subtraction. In 1974, the nonlinear processing of ANNs was introduced by Werbos. Subsequently, the interest of the scientific community steadily increased and was boosted in recent years by the introduction of new algorithms and by an increase in computational power associated with exponential advances in computer technology (http://library.thinkquest.org/C007395/tqweb/history.html).

ANN Theory

The ability to establish an accurate clinical diagnosis, appreciate clinical patterns (pattern recognition), analyze and interpret images to facilitate decision making, and ultimately predict optimal treatment is important in choosing the most appropriate management strategies for neurosurgery disorders. An ANN is a computational model based on the functioning of biological neural networks that can be used as a nonlinear statistical data modeling tool, with which the complex relationships between input and output (observed data) are modeled or patterns are revealed. Artificial neural networks attempt to simulate the learning process of human beings. In other words, they learn, as humans learn, through observing events. Actually, AANs are made of a group of interconnected nodes (artificial neurons) that are based on predefined computational rules. The nodes interact with each other. Based on these rules, passing sample data (pairs of observed input/output data) through ANNs causes the ANN to modify its structure so that it will be able to estimate the input/output relationship pattern of the system under study. At the end of this learning process, the results can then be used to estimate or predict output for new input. This capability makes ANNs a powerful tool for applications such as pattern recognition, medical diagnosis, financial assessments, data mining, and email spam filtering. The use of varying neuronal arrangements and learning methods facilitates the potential for creating a number of ANN types. The most common ANN type, the multilayer perceptron (MLP), consists of 3 layers: an input layer, a hidden layer, and an output layer (Fig. 1). With learning processes, sample data are fed into the input layer, and the network output is compared with the true expected output. The difference between the network's actual output and expected output equates to an error that is used to modify the interconnection of neurons that are weighted, based on a specific mathematical methodology. This methodology is termed "back propagation." It enables the network to optimally emulate the model of the system under study. The resulting trained network can be used to predict or estimate output for new input. One of the disadvantages of the ANN is that it does not allow an intuitive and transparent assessment of the effect of any 1 input variable in the model. As an investigative tool to understand relationships, the ANN is not very effective. In addition, it is possible to include too many input variables in the ANN, and therefore it does not force the developer to identify the truly important variables. Another issue is that the ANN does not produce a simple, transportable model. Rather, it is complex, but, given today's portable computing technology, that should not be great a barrier as it was in the past.[8,11] An ANN as a prediction technique has been in use for more than 20 years in clinical medicine for clinical diagnosis; prognosis and survival analyses; clinical outcome; and the medical domains of oncology, critical care, and cardiovascular medicine.[3,10] Artificial neural networks have also been successfully used in neurosurgery disorders such as prediction of death due to trauma, surgical decision making for patients who have suffered a traumatic brain injury,[3] surgical satisfaction in spine disorders,[1] and predicting survival in patients with brain metastases.[10]

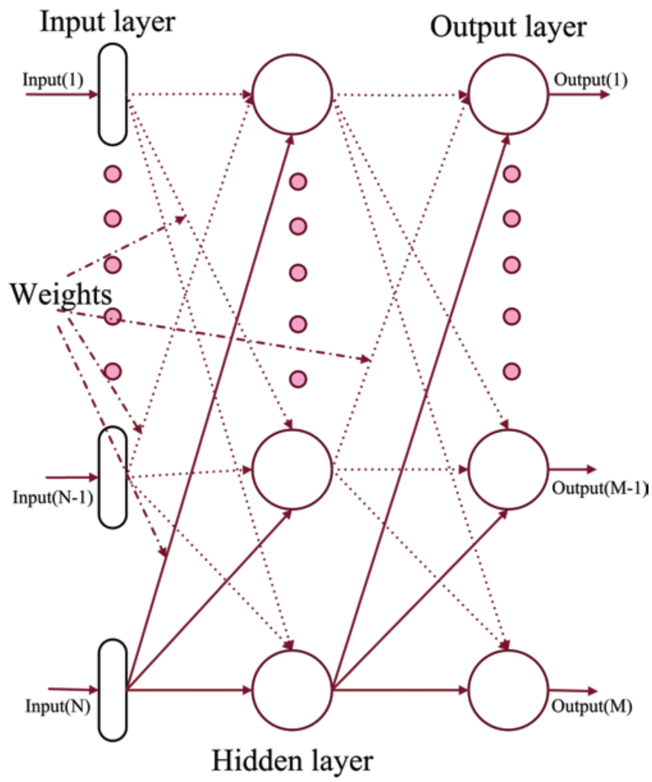

Fig. 1. Schematic showing the ANN. N is the number of input variables and M is the number of output data.

For neurosurgery disorder applications, due to the limited number of treatment options available, these prediction models can potentially improve diagnostic accuracy, treatment decisions, and efficiency. Relationships between prognostic factors and a successful ETV surgery outcome in children with hydrocephalus have not been previously investigated using the ANN model.

The aim of this study was to develop an ANN model based on etiology, age, whether choroid plexus cauterization (CPC) was performed, previous shunt placement, sex, type of hydrocephalus, and body weight in a group of children with hydrocephalus. We also sought to determine whether ANNs perform better at predicting a successful ETV outcome at 6 months in these patients compared with traditional predictive tools such as logistic regression, ETV Success Score (ETVSS), and the CURE Children's Hospital of Uganda (CCHU) ETV Success Score. We hypothesized that ANN analysis could predict the 6-month success rate for ETV in patients with hydrocephalus with an efficacy equal or superior to that of traditional models.

Methods

Patients and Data Collection

This study included a consecutive series of 168 patients (88 females and 80 males) who were referred to our hospital in Tehran, Iran, for treatment of hydrocephalus between January 2009 and January 2013. All patients were 15 years or younger, and the diagnoses were made based on clinical symptoms and imaging studies including cranial ultrasonography, CT scanning, and MRI. All patients had high-pressure hydrocephalus and were treated by pediatric neurosurgeons. The research was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences, Tehran, Iran.

For all cases, a standard ETV was performed as the primary or secondary treatment and was made through a frontal bur hole, with a fenestration made in the floor of the third ventricle and/or lamina terminalis by a flexible endoscope. There were no restrictions on patient inclusion with regard to age, disease etiology, or previous shunt surgery. The only exclusion criteria were inability to perform an ETV due to technical reasons. Demographic data, including age, type of hydrocephalus, sex, and body weight, were recorded.

Additional Measures

Additional measures were used to predict the 6-month ETV outcomes. The ETVSS was proposed by Kulkarni et al.[7] to determine which hydrocephalic children will benefit from an ETV compared with a shunt. It is a simple scoring system that predicts the chances of ETV success, based on patient age and etiology of hydrocephalus and previous shunt surgery. The ETVSS is calculated as the sum of 3 items ranging from 0 (extremely poor chance of ETV success) to 90 (extremely high chance of ETV success) (Table 1). The CURE Children's Hospital of Uganda (CCHU) ETV Success Score was introduced by Warf et al.[16] to predict the chances of ETV success. It is based on age, etiology of hydrocephalus, and whether CPC was performed and is calculated as the sum of 3 items, ranging from 0 to 9 with higher scores indicating higher levels of successful ETV (Table 2).

Development of the Logistic Regression Model

For the logistic regression model, the data set was randomly separated into a training set of 84 cases (50% of the overall data set) and a test set of 84 cases (50% of the overall data set). The training set was applied to make the logistic regression model. Etiology, age, whether CPC was performed, previous shunt, sex, type of hydrocephalus, and body weight were the independent variables, and outcome (successful ETV vs ETV failure) was the dependent variable. The logistic regression model was then tested using the testing data set. These steps (randomized division of data set and regression analysis considering the same variables) were repeated 1000 times. This resulted in 120 pairs of training and testing data sets (each group with half of the original data set), which were saved for further processing by the ANN, ETVSS, and CCHU ETV Success Score models.

TABLE 1: Calculation of the ETVSS*

Score	Age	Etiology	Previous Shunt
0	1 mo	postinfectious	yes
10	1 mo to <6 mos		no
20		myelomeningocele, IVH, nontectal brain tumor	
30	6 mos to <1 yr	aqueductal stenosis, tectal tumor, other	
40	1 yr to <10 yrs		
50	≥10 yrs		

* ETVSS = age score + etiology score + previous shunt score. A high ETVSS is ≥ 80, a moderate ETVSS is between 50 and 70, and a low ETVSS is ≤ 40. IVH = intraventricular hemorrhage.

ANN Model

The ANN used in this study is the most common type of ANN and is called the multilayer perceptron (MLP). Multilayer perceptron ANNs are composed of 3 layers of nodes arranged in series: an input layer, a hidden layer, and an output layer. The observed data consisted of input (etiology, age, whether CPC was performed, previous shunt, sex, type of hydrocephalus, and body weight) and output (successful ETV or ETV failure at the 6-month follow-up) that were applied to the input layer and output layer, correspondingly, to make the MLP ANN learn the complex relationship between input and output. Patients were grouped by a 2:1:1 ratio to generate training, testing, and validation samples, respectively. Based on a trial-and-error process, the training cycle is repeated until the number of the network layers and hidden neurons were determined. The learned network could then estimate output for the new sets of input data.[2,12]

The training, testing, and validation data sets were the same as those used with regression models; thus, there was a logistic regression and an ANN model for each training, testing, and validation data set.

Follow-Up

The reference points for this study were the date of the initial ETV procedure. Successful ETV outcome was defined as the absence of ETV failure within 6 months.

TABLE 2: Calculation of the CCHU ETV Success Score*

Score	Age	Etiology	CPC
0	<6 mos	other	none
1	6 mos to <1 yr	postinfectious	
2		myelomeningocele	partial unilat
3	≥1 yrs		
4			complete bilat

* CCHU ETV Success Score = age score + etiology score + CPC. A score of 7–9 indicates a high chance of success, a score of 3–6 indicates a moderate chance of success, and a score of 0–2 indicates a low chance of success.

Failure of ETV was defined as any surgical intervention for definitive CSF diversion or death due to hydrocephalus treatment within 6 months of the index procedure. We chose this definition because the majority of ETV failures occur within 6 months.[6,14,16]

Statistical Analysis

For parameters describing the patient population, continuous variables were compared using the Mann-Whitney U-test; categorical variables were compared using Pearson chi-square testing. In addition, on univariate analysis, the Bonferroni adjustment was used to calculate for multiple comparisons.

For each individual variable and for comparison of the ANN and logistic regression models, receiver operating characteristic (ROC) curves were created and were used to calculate specificities, the positive predictive value, and the negative predictive value at 95% sensitivity. The area under the curve (AUC) from the ROC analysis was evaluated to compare the discriminatory power of the models.[1,10]

The relative calibration (goodness-of-fit) of the models was assessed using the Hosmer-Lemeshow (H-L) statistic. The H-L statistic is a single summary measure of calibration and is based on comparing the observed and estimated success of ETV for patients grouped by estimated successful ETV.[4] The resulting statistic follows a chi-square distribution, with degrees of freedom ranging from the number of groups (10 in this study) minus 2 up to the number of groups. A lower H-L statistic value is associated with better fit.

A probability cut point of 0.5 was applied to classify observations as events or nonevents. The overall accuracy ([true positive + true negative]/total) of the final model was determined by comparing the predicted values with the actual events.

For each of the 120 pairs of the ANN, logistic regression, CCHU ETV Success Score, and ETVSS models, H-L statistics, AUC, and accuracy rate were calculated and compared using t-tests ($p < 0.05$). All statistical analyses were performed using the STATISTICA software program (version 10.0, StatSoft).

Results

Demographic data of the hydrocephalic patients, their ETVSSs and CCHU ETV Success Scores, and ETV outcomes at 6 months are shown in Table 3. A total of 168 patients (80 males and 88 females; mean age 1.4 ± 2.6 years) were divided into training (n = 84), testing (n = 42), and validation (n = 42) groups. Interrelationships between predictor variables (input nodes), hidden variables (3 in one hidden layer), and ETV outcomes (output nodes) are demonstrated in Fig. 2. The rate of successful ETV outcome, defined as the absence of ETV failure within 6 months' follow-up, was 47%.

The results of comparisons of the ANN, logistic regression, ETVSS, CCHU ETV Success Score models, and individual parameters are shown in Tables 4 and 5. The etiology, age, CPC status, type of hydrocephalus, and previous shunt surgery were important variables selected by the ANN. Compared with the ETVSS, CCHU ETV Success Score, and logistic regression models, the ANN model had a better accuracy rate (95.1%), a better H-L statistic (41.2), and a better AUC (0.87).

Discussion

Individual parameters such as cause of hydrocephalus, age, whether CPC was performed, previous shunt surgery, type of hydrocephalus, sex, and body weight can provide tools of prognostic benefit; however, the findings from this study showed that the combination of these parameters in the ANN model could be used to predict the rate for successful ETV in childhood hydrocephalus with a high level of accuracy. The full structure details of the resulting ANN can be saved and then be used as a software estimator or predictor for new cases with no need for further training. Although the ANN shows promise, the study sample was unique and very small, and therefore the technique will need to be repeated with larger, multicenter data sets to convincingly show its predictive power.

To date, no study has analyzed the outcome at 6 months in childhood hydrocephalus based on the ANN model. There are currently only 2 measures designed to predict ETV outcome: the ETVSS and the CCHU ETV Success Score.[7,16] Although these measures are simple and easy to use in clinical practice, they do not include some prognostic factors and need to be optimized. Therefore, we developed and validated an ANN model to predict the chances of ETV success. Finally, it should be noted that the models in our study were developed, tested, and validated within the same population, using subsets of data from that population, while the ETVSS and CCHU ETV Success Score were subjected to external validation, a much more rigorous standard. These models were developed using completely different data sets (ETVSS from patients in North America and Europe and CCHU ETV Success Score from patients in Uganda). Therefore, it is to be expected that the internal validation of ANN and logistic regression will outperform the external validation of the ETVSS and CCHU ETV Success Score.

The prediction parameters in Table 5 are very similar to what has been published in the literature before for these models. This was surprising since the models were developed and intended for use in very different populations. The ETVSS, for example, did not take into account the effects of CPC status. However, some might argue that there was external validation of models of the ETVSS and CCHU ETV Success Score models in different populations. In the current study, the relatively homogeneous patient population was also found based on the 2 scores: the ETVSS and CCHU ETV Success Score. In addition, the ANN theory can be considered along with the other methods.

For the first time, ANNs have been used to predict 6-month ETV success in patients with hydrocephalus. In fact, we describe here a third index for predicting the success rate of ETV in childhood hydrocephalus. The results obtained from the sensitivity analysis suggest that combinations of variables of ETVSS and CCHU ETV Success Score in the input layer of the ANN model are useful

TABLE 3: Demographic data and postoperative status of 168 children with hydrocephalus for neural network analysis*

Parameter	Total	Successful ETV†	ETV Failure	p Value
no. of patients	168	79 (47.0)	89 (53.0)	
mean body weight in kg	12.8 ± 12.8	14.5 ± 13.1	11.2 ± 9.9	0.81
sex				
male	80 (47.6)	38 (47.5)	42 (52.5)	0.67
female	88 (52.4)	41 (46.6)	47 (53.4)	0.72
mean age in yrs	1.4 ± 2.6	2.2 ± 1.8	0.7 ± 1.1	0.02‡
previous shunt	36 (12.5)	10 (27.7)	26 (72.3)	0.02‡
etiology				
postinfectious	12 (7.1)	4 (33.3)	8 (66.7)	0.06
myelomeningocele, IVH, & nontectal brain tumor	57 (33.9)	31 (54.4)	26 (45.6)	0.12
myelomeningocele	21 (12.5)	11 (52.4)	10 (47.6)	0.13
nontectal brain tumor	13 (7.7)	7 (53.8)	6 (46.2)	0.12
IVH	23 (13.7)	13 (56.5)	10 (43.5)	0.10
aqueductal stenosis & tectal tumor	47 (28.1)	33 (70.2)	14 (29.8)	0.04‡
aqueductal stenosis	37 (22.02)	27 (72.9)	10 (27.02)	0.02
tectal tumor	10 (5.9)	6 (60.0)	4 (40.0)	0.05
other	52 (30.9)	11 (21.2)	41 (78.8)	0.01‡
CPC				
none	99 (58.9)	34 (34.3)	65 (65.7)	0.02‡
partial unilat	9 (5.4)	5 (55.5)	4 (44.5)	0.09
complete bilat	60 (35.7)	40 (66.7)	20 (33.3)	0.02‡
type of hydrocephalus				
communicating	53 (31.5)	19 (35.8)	34 (64.2)	0.03‡
noncommunicating	115 (68.5)	60 (52.2)	55 (47.8)	0.07
ETVSS				
≥80	22 (13.1)	19 (86.4)	3 (13.6)	0.02‡
50–70	77 (45.8)	48 (62.3)	29 (37.7)	0.04‡
≤40	69 (41.1)	12 (17.4)	57 (82.6)	0.01‡
CCHU ETV Success Score				
7–9	16 (9.5)	14 (87.5)	2 (12.5)	0.01‡
3–6	75 (44.7)	50 (66.7)	25 (33.3)	0.03‡
0–2	77 (45.8)	15 (19.5)	62 (80.5)	0.02‡

* Values are the number of patients (%) unless indicated otherwise. Mean values are presented as the mean ± SD. The Mann-Whitney U-test and Pearson chi-square test with Bonferroni correction were used to test for significant differences between groups. IVH = intraventricular hemorrhage.

† Successful ETV outcome was defined as the absence of ETV failure within 6 months.

‡ Significantly different within 6-month successful ETV categories.

parameters for selecting patients with hydrocephalus for ETV. The use of this simple software program is recommended to increase the success of ETV in these patients, especially in teaching hospitals. In addition, the predictive ability of the ANN model increased based on each new prognostic factor.

Maximizing the accuracy of the ANN for optimal clinical efficacy is an achievable end point that will be tracked in a multicenter study with a large sample size based on global databases and sufficient statistical power to determine the value of variables for the input layer of the ANN model. Finally, this should lead to an even finer prediction of results. The ANN model presented in our study is an acceptable test for predicting the 6-month ETV success in childhood hydrocephalus. However, our results will need to be confirmed by further prospective studies.

There were some limitations in this study. First, we were unable to identify all effective parameters that influence the success of ETV and need to be fed into the input layer of an ANN model, for example the presence of residual membranes and arachnoid adhesions. Further prospective multicenter studies are needed to examine these other factors to establish a more complete model. Second, the study is retrospective in nature, so we could not evaluate outcome tools. Third, the main weakness of this study is the small sample size, especially in the valida-

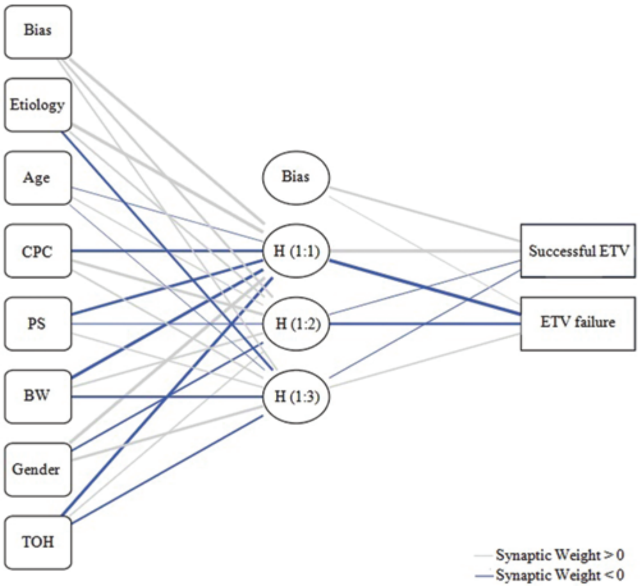

Fig. 2. Artificial neural network output diagram with insets for each layer. Output figure generated by PASW Statistics (version 18, SPSS, Inc.). The input layer variables are shown on the left, the hidden layer is shown in the center, and the output layer is shown on the right. BW = body weight (kg); H = hidden layer (with the first number after H designating the layer and the second, the node [artificial neuron] in that layer); PS = previous shunt; TOH = type of hydrocephalus.

tion group, which must be considered in future studies to enhance the comparability of research. Last, more studies are necessary to explore the differences between long- and short-term follow-up of the success of ETV in the ANN model for these patients.

Conclusions

These findings show that, for the first time, ANNs can predict 6-month successful ETV with a high level of accuracy in childhood hydrocephalus. Such information is of use in the clinical decision-making process.

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Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Azimi. Acquisition of data: Azimi. Analysis and interpretation of data: Mohammadi. Drafting the article: Azimi. Critically revising the article: both authors. Reviewed submitted version of manuscript: both authors. Approved the final version of the manuscript on behalf of both authors: Azimi.

TABLE 4: Comparison of the AUC and predictive values of ANN and logistic regression models, and individual parameters for predicting 6-month ETV outcomes in 168 children with hydrocephalus*

Parameter/Model	AUC (%)	p Value†	Specificity (%)‡	PPV (%)‡	NPV (%)‡
ANN	0.86	0.001	45	69	89
LR	0.79	0.001	34	65	82
etiology	0.68	0.01	29	60	74
age	0.65	0.02	28	59	73
CPC	0.64	0.03	26	59	72
previous shunt	0.63	0.04	25	58	70
type of hydrocephalus	0.60	0.046	23	56	69
sex	0.49	0.84	6	52	20
body weight (kg)	0.46	0.79	5	51	18

* LR = logistic regression; NPV = negative predictive value; PPV = positive predictive value.
† Asymptotic significance on ROC curve analysis.
‡ Specificity and predictive values at 95% sensitivity.

TABLE 5: Comparison of 120 pairs of the different models to predict 6-month ETV outcomes in children with hydrocephalus in the validation group

Parameter	Accuracy Rate (%)	AUC	H-L Statistic
ANN (95% CI)	95.1 (93.7–97.6)	0.87 (0.85–0.89)	41.2 (36.1–47.2)
LR (95% CI)	89.2 (85.8–92.3)	0.80 (0.75–0.80)	54.1 (51.2–57.3)
CCHU ETV (95% CI)	84.4 (82.5–89.2)	0.78 (0.71–0.78)	56.5 (51.3–59.3)
ETVSS (95% CI)	82.2 (81.7–89.2)	0.76 (0.71–0.76)	57.4 (53.2–60.4)
p value	<0.001	<0.001	<0.001

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Address correspondence to: Parisa Azimi, M.D., Shohada Tajrish Hospital, Functional Neurosurgery Research Center of Shohada Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Sharadari Street, Tajrish Square, Tehran 1989934148, Iran. email: parisa.azimi@gmail.com.