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Prediction of 6 months endoscopic third ventriculostomy success rate in patients with hydrocephalus using a multi-layer perceptron network

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ABSTRACT

Objective: Discrimination between patients most likely to benefit from endoscopic third ventriculostomy (ETV) and those at higher risk of failure is challenging. Compared to other standard models, we have tried to develop a prognostic multi-layer perceptron model based on potentially high-impact new variables for predicting the ETV success score (ETVSS).

Methods: Clinical and radiological data of 128 patients have been collected, and ETV outcomes were evaluated. The success of ETV was defined as remission of symptoms and not requiring VPS for six months after surgery. Several clinical and radiological features have been used to construct the model. Then the Binary Gravitational Search algorithm was applied to extract the best set of features. Finally, two models were created based on these features, multi-layer perceptron, and logistic regression.

Results: Eight variables have been selected (age, callosal angle, bifrontal angle, bicaudate index, subdural hygroma, temporal horn width, third ventricle width, frontal horn width). The neural network model was constructed upon the selected features. The result was AUC:0.913 and accuracy:0.859. Then the BGSA algorithm removed half of the features, and the remaining (Age, Temporal horn width, Bifrontal angle, Frontal horn width) were applied to construct models. The ANN could reach an accuracy of 0.84, AUC:0.858 and Positive Predictive Value (PPV): 0.92, which was higher than the logistic regression model (accuracy:0.80, AUC: 0.819, PPV: 0.89).

Conclusion: The research findings have shown that the MLP model is more effective than the classic logistic regression tools in predicting ETV success rate. In this model, two newly added features, the width of the lateral ventricle's temporal horn and the lateral ventricle's frontal horn, yield a relatively high inter-observer reliability.

1. Introduction

The inadequate cerebrospinal fluid (CSF) passage within the brain leads to hydrocephalus (HCP) and abnormal ventricular system distension. If left untreated, HCP would end in a catastrophic comatose state [1,2]. The precise incidence of HCP in the pediatric population is challenging to estimate. This is due to the diverse spectrum of etiologies of HCP in the pediatric population. Approximately 400,000 new cases of pediatric hydrocephalus occur annually in the world, of which the highest incidence is in Africa and South America [3]. HCP is conceivably the most common disorder to be treated by pediatric neurosurgeons. HCP costs over 2 billion US dollars in the united states annually [4,5]. The management of HCP remains a quandary in the pediatric population. HCP is implanted to an immense spectrum of conditions. It can occur at any age, as a co-occurrence with ventriculomegaly or even in the state of slit ventricles [6]. Recognition of miscellaneous underlying conditions of HCP in progress is a paramount subject that neurosurgeons are dealing with in order to differentiate patients with intracranial fluid

Abbreviations: ETV, endoscopic third ventriculostomy; ETVSS, endoscopic third ventriculostomy success score; VPS, ventriculo-peritoneal shunt; BGSA, Binary Gravitational Search algorithm; AUC, area under the ROC curve; ROC, receiver operating characteristic; ANN, artificial neural network; PPV, positive predictive value; MLP, multi-layer perceptron.

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collection from an etiologic perspective. Hence, a more individualized therapeutic approach is being used in HCP.

There are two foremost neurosurgical approaches in treating the HCP: inserting a CSF diversion device (Ventriculo-Peritoneal Shunt; VPS) or utilizing endoscopic procedures. Each of these two approaches has its pros and cons. Picking out the aptest treatment plan in each patient addressing the least short-term and long-term side effect profile remains a momentous dispute.

Recently, the University of British Columbia gave both patients and care givers out a questionnaire about the odds upon choosing the endoscopic third ventriculostomy (ETV) over VPS. Eighty percent of responders returned “minimizing repeat surgery” as a priority when deciding on a treatment plan as well as “the need to implant a permanent device” [7]. More compelling were the answers of the majority of respondents who choose a procedure even with higher presumed surgical risk yet without permanent device implantation even if that procedure fails several times.

ETV is carried out under direct visualization of the path. In addition to being device-free, this fact makes ETV a safe alternative to avert VPS-related long-term issues [8].

There are situations in which ETV is almost always superior to other methods, for instance, in noncommunicating hydrocephalus cases due to acquired aqueductal stenosis or posterior fossa tumors. However, this preference is not clear-cut for other cases, and patients must be carefully selected [9]. Kulkarni’s Toronto group efforts to introduce Endoscopic Third Ventriculostomy Success Score (ETVSS) is by far the most apposite predictive tool in the hands of the pediatric neurosurgeons (Table 1) [10]. Different institutes have outlined different systems to evaluate the upshots of the ETV. However, there are no tangible or incontestable systems to be used by a pediatric neurosurgeon so far, and several constituents have come up with the success of the ETV amongst them is carefully picking the best possible candidates based on clinical and radiological features [11]. Finding these features takes a substantial effort that current literature has not addressed adequately so far.

In 2011, IBM’s question-answering system "Watson" won the quiz show "Jeopardy!" by beating former human champions. But the idea of robots coming to life as intelligent creatures has been around for as long as ancient Greeks. However, since 1956 that the term A.I was coined in New Hampshire, no neurosurgeon is found to imagine a decision-making machine carrying his work as early as pre-op predictions [12]. To our knowledge and based on a thorough review of available literature, the most widely used supervised model of machine learning in means of ANN is used in neurosurgical entities so far. This idea was used to predict the outcome of patients suffering Traumatic Brain Injury (TBI). The algorithm aimed to improve the predictive ability of ground truth, which is the ability of neurosurgeons to predict the 30 days mortality [12,13]. Based on a recent review of all expert opinions (both neurosurgeons and neurosurgery residents in the US), the mean predictive ability of the aforementioned staff when facing a TBI patient regarding the outcome is about 37% [12].

This study tries to develop and validate a robust prognostic model for predicting the ETVSS using artificial neural networks on potentially high-impact new variables.

Table 1
Kulkarni’s ETVSS. A combination of age, etiology and history of previous shunt as predictors utilized in a logistic regression model to forecast the success percentage.

Score	Age	Etiology	Previous Shunt
0	< 1 month	Postinfectious	Yes
10 20	1 month to < 6 month	Myelomeningocele, IVH, nontectal brain tumor	No
30	6 months to < 1 year	Aqueductal stenosis, tectal tumor, other	
40	1 year to < 10 years		
50	≥ 10 years		

2. Materials and methods

2.1. Participants

Data of 128 patients referred to Namazi hospital, a tertiary center in the south of Iran, from March 2014 until September 2018 who suffered from hydrocephalus were collected. Patients were selected from all age groups of children and adults (72 males). Imaging investigations were used to confirm HCP. Data were collected during the six months follow-up of the patients. The success of ETV in these patients was assessed based on the remission of symptoms and not requiring VPS for at least six months after surgery. The radiologic endpoint was defined as at least a 24% reduction in the size of the bicaudate diameter on brain computed tomography (CT) scan or magnetic resonance imaging (MRI) one or more months after the operation. However, no significant change in the bicaudate diameter or ventricular size does not indicate ETV failure. The patients who met the mentioned endpoints criteria were labeled as successful.

2.2. Ethical approval

Written informed consent was obtained from all the patients or their caregivers. The ethical approval to embark on the study was taken from the ethics committee of Shiraz University of medical sciences.

2.3. Feature selection

Ten Features have been selected based on the perspective of the senior author (M.S.Masoudi) and previous studies [10]. Variables that did not reach statistical significance (p-value <0.05) were excluded from the dataset (backward elimination). Variable inflation factor (VIF) was calculated to avoid multicollinearity; values greater than ten or less than one exhibit interrelation among predictors.

The Binary Gravitational Search algorithm (BGSA) was used to extract the best set of features that can accurately predict the patients’ prognosis [14].

2.4. Predictive model

Multi-layer perceptron (MLP), one of the most widely used ANN types, is carried out to predict outcomes. MLP has a high capability to solve nonlinear biomedical problems. There are three main layers in our model. The input layer consists of clinical predictors and imaging findings. Ten neurons construct the hidden layer; Softmax and hyperbolic tangent are set for the activation function of the hidden layer and output layer, respectively. The optimization algorithm was stochastic gradient descent.

2.5. Model validation

We divided the dataset into training (70%) and validation sets (30%) and utilized fivefold cross-validation to assess ANN’s performance in the training phase.

2.6. Statistical Analysis

The continuous variables were compared using the Mann-Whitney *U*-test, and categorical variables were compared using Pearson chi-square testing. The Bonferroni adjustment was used to measure multiple comparisons for univariate analysis, while the Hosmer-Lemeshow goodness of fit test was applied to the logistic regression model. The model’s discriminative power was assessed by the area under the receiver operating characteristic curve (AUC and ROC curve); the closer the ROC gets to the top left corner, the better it discriminates the outcome. The procedures were implemented in MATLAB R2018a environment (Math Works, Inc., Natick, Massachusetts) and SPSS version 26 (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp). The codes are attached to the supplementary materials.

2.7. Results

From March 2014 until September 2018, data of 128 patients were collected. Eight patients were excluded from the study due to missing data. Of 120 patients included in this study, ETV was unsuccessful in 32 cases (26.7%), while 88 cases (73.3%) had a favorable outcome at the 6-month follow-up. There were no deaths during the follow-up.

In the first feature selection step, eight variables were selected based on statistical significance: age, callosal angle, bifrontal angle, bicaudate index, subdural hygroma, temporal horn width, third ventricle width, frontal horn width (Table 2).

Then, the ANN model was constructed based on the variables. The model resulted in the accuracy of 0.859 (95% CI 0.589 ± 0.07), the sensitivity of 0.919 (95% CI 0.919 ± 0.07), the specificity of 0.695 (95% CI 0.695 ± 0.07), the positive predictive value of 0.890 (95% CI 0.890 ± 0.07), the negative predictive value of 0.762 (95% CI 0.762 ± 0.07), and area under curve of 0.913. The Hosmer-Lemeshow statistic was not significant (P = 0.595).). The ROC curve of the model is depicted in Fig. 1. Age, frontal horn width and temporal horn width were the most important variables.

In the next step, the BGSA algorithm was applied to the data. Four variables were selected to construct the simplified model: age ($p < 0.001$), temporal horn width ($p < 0.001$), frontal horn width ($p < 0.001$) and bifrontal angle ($p < 0.001$). Subdural hygroma, callosal angle, third ventricle width, and bicaudate index were removed by the BGSA algorithm. To check for collinearity, the VIF was calculated. The VIF between 1 and 2 was achieved for all of the variables.

The Hosmer-Lemeshow statistic of the ANN model was not significant (P = 0.555). Overall accuracy of 0.84, the Positive predictive value (PPV) of 0.92 (95% CI 0.92 ± 0.07), negative predictive value (NPV) of 0.625 (95% CI 0.625 ± 0.07), and AUC of 0.858 were achieved. In the logistic regression model, the Hosmer-Lemeshow statistic was not significant (P = 0.432). Overall accuracy of 0.80, PPV of 0.89 (95% CI 0.89 ± 0.07), NPV of 0.53 (95% CI 0.53 ± 0.07) and AUC of 0.819 were achieved. ROC was higher in the MLP model compared to the logistic regression. (Fig. 2 and Fig. 3). In general, the neural network model in all statistical evaluations showed better performance than the logistic regression model. The confusion matrix of the model is demonstrated in Tables 3 and 4.

3. Discussion

Our research shows that the combination of clinical and radiological findings is able to predict ETV outcomes with high accuracy and can be practical in the clinical context. Age, temporal horn width, frontal horn width, and bifrontal angle are prognostic features that need to be confirmed by further studies. The MLP model could surpass the logistic regression model with respect to performance. Age, temporal horn width, and frontal horn width had the highest predictive values. Despite great endeavors, the development of prognostic models is still open-ended because the exact pathophysiology of hydrocephalus is still unclear. A closer look at the previous works shows that many attempts have been dedicated to precisely predicting ETV procedures' outcomes in different populations. In [15], a meta-analysis of 16 infants cases less than one-year, younger age and secondary etiologies were factors

Table 2
List of features used to develop the model.

Predictor	Significance	Mean Difference	95% Confidence Interval of the Difference	
			Lower	Upper
Subdural hygroma	0.000	1.9750	1.938	2.012
Age	0.000	1.9917	1.858	2.125
Callosal angle	0.000	1.192	1.12	1.26
Third ventricle width	0.000	1.458	1.37	1.55
Temporal horn width	0.000	1.492	1.40	1.58
Bicaudate index	0.000	1.483	1.39	1.57
Bifrontal angle	0.000	1.525	1.43	1.62
Frontal horn width	0.000	1.458	1.37	1.55

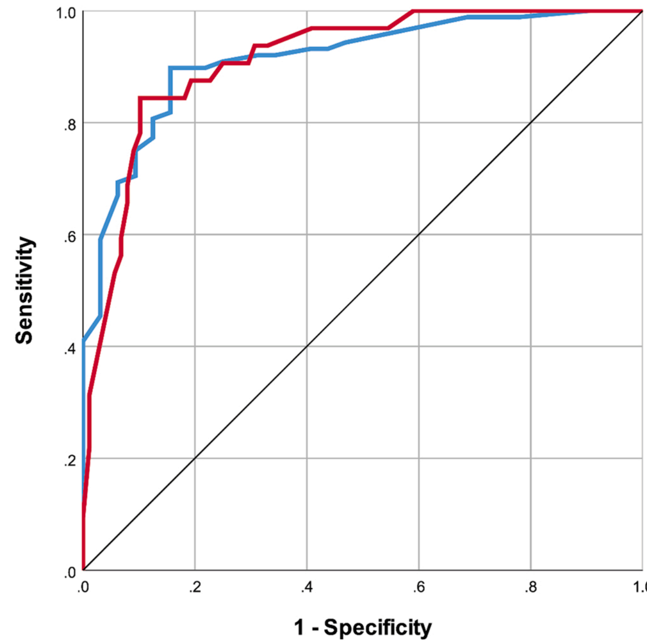

Fig. 1. ROC curve for ANN model based on 8 variables. The AUC is 0.913. The blue line indicates successful ETV and the red line indicates the unsuccessful endoscopic surgery. ETVRS indicates ETV surgery result.

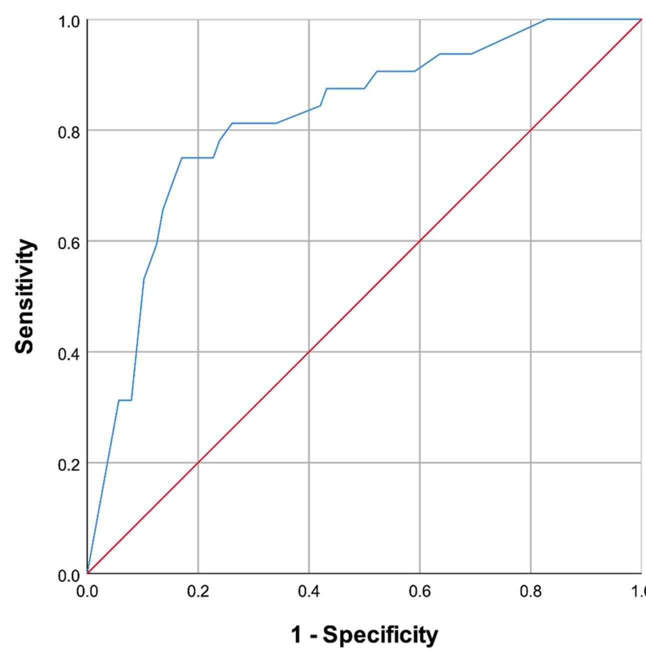

Fig. 2. ROC curve of Logistic Regression model. AUC is equal to 0.819.

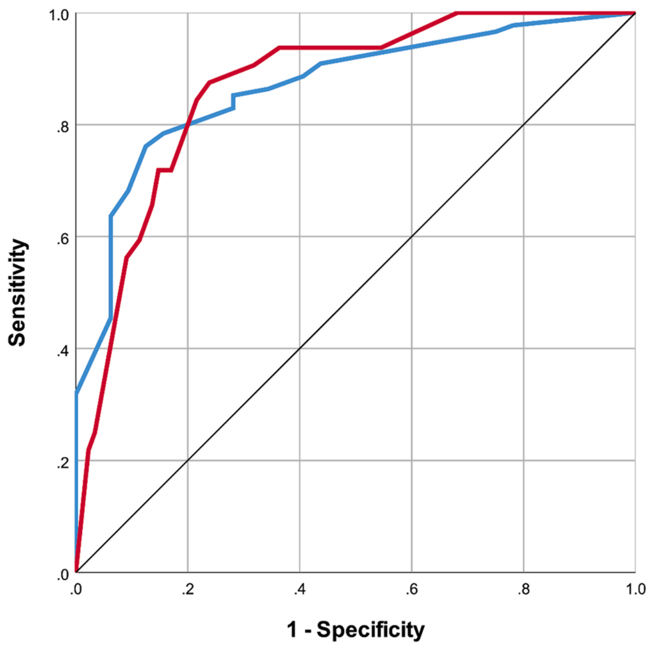

Fig. 3. ROC curve for ANN model based on 4 features. The AUC is 0.858. The blue line indicates successful ETV and the red line indicates the unsuccessful endoscopic surgery.

Table 3
Comparison of predicted and actual ETV success in the logistic regression model. The number of patients is provided in the table. ETRES indicates the actual result of ETV procedure.

Observed	Predicted			
		successful	unsuccessful	Percentage correct
ETVRES	successful	79	9	89.8
	unsuccessful	15	17	53.1
Overall accuracy Percentage	80.0			

Table 4
Comparison of predicted and actual ETV success for ANN model based on four variables. The table is divided into two parts, (i.e., training and test phase) and the number of patients in each group, the accuracy, sensitivity and specificity percentages are provided.

Classification				
		Predicted		
Sample	Observed	successful	unsuccessful	Percentage correct
Training	successful	49	4	92.5%
	unsuccessful	7	10	58.8%
	Overall Percent	80.0%	20.0%	84.3%
Testing	successful	32	3	91.4%
	unsuccessful	5	10	66.7%
	Overall Percent	74.0%	26.0%	84.0%

influencing the outcome of ETV. In [16], a prospective study has been carried out on 24 pediatric patients, and optic nerve sheath diameter (ONSD) change in MRI pre and post-operation is presented as a predictor of response to ETV. In [17], a combination of 139 pediatric and adult patients was assessed retrospectively for shunt independence after secondary ETV. They found that age at first VPS placement did not affect ETV results, and in patients younger than six months, the cause effects seemed to disappear. In [18], a new morphologic index, Third Ventricular Morphology Index (TVMI), has been developed to quantitively assess the third ventricle's structural form. A post-operation decrease in TVMI was associated with a better outcome. Similarly, Dlouhy et al. [19] found that preoperative third ventricle bowing was correlated with successful ETV. In [20], intraoperative factors such as pulsation of the third ventricle floor and the presence of scar membranes in the subarachnoid space have been considered to create an intraoperative prognostic scale range from 0 to 6. In a recent retrospective multicenter study [21], a prognostic model is being developed for adults suffering from hydrocephalus undergoing ETV.

In a study conducted by Labidi et al. on 128 patients of different age groups, including adults, they found that the ETV success score in the adult age group did not have significant predictive power as opposed to children younger than two years old [22]. Gianaris et al. revealed treatment failures in patients with the highest possible scores and suggested that new parameters should be considered predictors of success [23]. CURE Children's Hospital of Uganda (CCHU) ETV success score is a modified version of ETVSS, which takes choroid plexus cauterization into account and is unique for the large sub-Saharan African population. It shows that ethnicity may play an essential role in survival [24]. Artificial intelligence in medicine is growing day by day, and neurosurgery is not an exception. As Azimi et al. mentioned, ANN accuracy was higher than other standard approaches, and their results need to be confirmed by future studies [25]. BGSA is a robust met-heuristic algorithm that tries to find the optimal combination of features explaining much of the variations in outcomes.

Briefly, the BGSA algorithm is based on Newtonian gravity law and is rendered randomly by generating and multiplying the data matrix by zero and one vector. The model's performance is then calculated, and if it did not get the desired response, this process was continued until the best features were gradually achieved. The process is demonstrated in Figure 4. BGSA algorithm enabled us to speed up the calculation process by squeezing the dataset's dimension and removing predictors with less explanatory power. Utilizing BGSA, our model became simpler and remained reliable, which is necessary for application in the clinical setting. Our study also shows that ANN results were more fruitful than logistic regression. Age, frontal horn width, and temporal horn width were the most critical variables. There is no collinearity among predictors. The Hosmer-Lemeshow statistic of the ANN model indicates a good model fit, which means ANN has a higher discriminative power.

The major limitations of our work are its relatively small sample size and being a single center study. Because our research dataset is relatively undersized, it makes sense to view and compare our results in the context of other results in the field. As the ethnicity may play a crucial role in the predicting the outcome of ETV, it would be of great importance for future studies to consider this issue. Expanding our understating of the disease and forming sizable datasets could make the prediction of prognosis more accurate, and fewer patients will suffer from an ETV failure.

4. Conclusion

The predictive ability of our MLP model for the success rate of an ETV was higher than the classic logistic regression tools. The width of the temporal horn of the lateral ventricle and the frontal horn of the lateral ventricle are two newly added features to the MLP model. They are both measured in the brain CT plain of the foramina of the Monroe. Therefore, these two features yield a relatively high inter-observer reliability.

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Disclosure

The authors claim there was no conflict of interest for this issue.

Limitations

The relatively small sample size was an obvious limitation for our study.

CRediT authorship contribution statement

The data of this article was based on dissertation of Dr. Elahe Rezaei, entitled as "Demographic and radiologic factors correlaton with success rate of ETV surgery in hydricephalos patients in Shiraz university of medical science" as a part of fullfilment of Neurosurgery residency studies which was done under supervision of Dr MS Masoudi in Shiraz University of Medical Science. Patient selection and operations were done by Dr. M.S. Masoudi & Dr E. Rezaei. Radiologic Indices and Data were described and collected by Dr. E. Rezaei. Designation of the study was made by Dr. Masoudi Dr. Sousan Taleghani, Amirhossein Tahmouresi and Dr. Elahe Rezaei. Statistical analysis was done by Dr. E. Rezaei and Masoud Rezaei. AI analysis was done by A. Tahmouressi and M. Rezaei, and the manuscript was drafted by M. Rezaei and Dr. S. Taleghani. Furthermore, the manuscript edited and finalized by Dr. S. Taleghani, Dr. Sina Zoghi and Dr. Reza Taheri and M. Rezaei.

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