

Predicting ventriculoperitoneal shunt infection in children with hydrocephalus using artificial neural network

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Abstract

Objectives The relationships between shunt infection and predictive factors have not been previously investigated using Artificial Neural Network (ANN) model. The aim of this study was to develop an ANN model to predict shunt infection in a group of children with shunted hydrocephalus.

Materials and methods Among more than 800 ventriculoperitoneal shunt procedures which had been performed between April 2000 and April 2011, 68 patients with shunt infection and 80 controls that fulfilled a set of meticulous inclusion/exclusion criteria were consecutively enrolled. Univariate analysis was performed for a long list of risk factors, and those with p value < 0.2 were used to create ANN and logistic regression (LR) models.

Results Five variables including birth weight, age at the first shunting, shunt revision, prematurity, and myelomeningocele were significantly associated with shunt infection via univariate analysis, and two other variables (intraventricular hemorrhage and coincided infections) had a p value of less than 0.2. Using these seven input variables, ANN and LR models predicted shunt infection with an accuracy of 83.1 % (AUC; 91.98 %, 95 % CI) and 55.7 % (AUC; 76.5, 95 % CI), respectively. The contribution of the factors in the predictive performance of ANN in descending order was history of shunt revision, low birth weight (under 2000 g), history of prematurity, the age at the first shunt

procedure, history of intraventricular hemorrhage, history of myelomeningocele, and coinfection.

Conclusion The findings show that artificial neural networks can predict shunt infection with a high level of accuracy in children with shunted hydrocephalus. Also, the contribution of different risk factors in the prediction of shunt infection can be determined using the trained network.

Keywords Hydrocephalus · Shunt infection · Artificial neural network · Ventriculoperitoneal shunt

Introduction

Shunt infection has been an enduring concern in pediatric neurosurgery since the advent of ventricular shunts. The rates of shunt infection range from 10 to 22 % per patient and around 6.0 % per procedure, with 90 % of infections occurring within 30 days of surgery [8, 10]. Constituting a major source of morbidity and cost, shunt infections have not been eliminated despite considerable efforts. Numerous risk factors have been proposed for shunt infections, some of them are inherent with the patient's condition and some others seem to be modifiable [10, 22–25]. Accordingly, various protective measures and standardized protocols for shunt implantation have been suggested by some authors and institutes to reduce shunt infection occurrence [6, 11–13, 18, 25]. However, despite these advances, shunt infections remain the most significant complication associated with hydrocephalus treatment. Identification of predictive factors may improve current practice to prevent shunt infections. To our knowledge, relationships between predictive risk factors and shunt infection in children with shunted hydrocephalus have not been previously investigated using the artificial neural network (ANN) model.

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An artificial neural network is an information processing paradigm that is inspired by the way biological nervous systems process information. It is composed of a large number of highly interconnected processing elements (neurons or nodes) working in union to solve specific problems. Learning in biological systems involves adjustments to the synaptic connections that exist between the neurons. This is true for ANNs as well. Indeed, in AANs, a group of interrelated nodes (synaptic neurons) interact with each other and make the ANN to modify its structure via a learning process so that it will be able to estimate the input/output relationships and predict output for a given input.

Neural network was established before the advent of computers and has survived in computer era by being adapted as a computational model based on mathematics and algorithms [16]. The use of ANNs for clinical purposes began in the late 1980s, and afterward, ANN models were applied in medical fields for accurate diagnosis, classification, pattern recognition, and outcome prediction [9]. Even so, there has been limited use of this method in the field of neurosurgery [2]. Few studies have employed neural network models in pediatric neurosurgery; one of the most imperative one has applied ANN model for outcome prediction of endoscopic third ventriculostomy in childhood hydrocephalus [1]. However, ANN has not been used to estimate the risk of shunt infection so far. The aim of this study was to develop an ANN model to predict shunt infection in a group of children with shunted hydrocephalus.

Materials and methods

After approving by the Institutional Ethical Committee of Tehran University of Medical Sciences, a retrospective single center study was designed to make a comparison between an artificial neural network and conventional logistic regression (LR) model in predicting shunt infection in pediatric patients. From April 2000 to April 2011, more than 800 ventriculoperitoneal shunt procedures had been performed in Children's Medical Center on patients under the age of 12 years with different types of hydrocephalus. Applying a set of meticulous inclusion/exclusion criteria, 68 patients with shunt infection were consecutively enrolled to create a database for the purpose of training and validating the ANN and LR models. Afterward, 80 patients without shunt infection who had undergone shunting procedure in the same week as for each case, with the same protocol and inclusion/exclusion criteria, were matched as controls. The patients were included only if they had undergone ventriculoperitoneal shunting in an elective setting by the senior author via a standard protocol and had completed a follow-up period of at least 6 months. The method and time of surgery, prophylactic antibiotic, operation theater settings, and the number of staff inside the

theater were equal in all cases. Those with ventriculo-atrial shunting, first procedure in other centers, operation in an emergent setting, deviation from the protocol, incomplete or inaccessible medical data, and incomplete or missing follow-up were excluded from the study. Demographic and medical information including sex, parents' consanguinity, gestational age at birth, type of delivery, birth weight, prematurity, head circumference at birth, neonatal icterus, history of myelomeningocele (MMC), meningitis, intraventricular hemorrhage (IVH), head trauma, brain tumor, age at surgery time, duration of surgery, type of inserted shunt, other-site active infection within 30 days prior to shunt insertion, cerebrospinal fluid (CSF) leak after shunting, and numbers of previous shunt revisions were recorded for each patients. Initially, the association between these variables and shunt infection was evaluated by univariate analysis, and those with p value < 0.2 were used to create ANN and LR models.

AAN model

The ANN used in this model is called the "multilayer perceptron" (MLP), in which the structure of ANN is layered with the outputs of each layer connected to the inputs of another layer. The MLP has at least three layers of "nodes" or "neurons". The input layer accepts datasets from an external source and constitutes inputs to the next layer of neurons called hidden layer in which neuron values are not visible outside the net. The use of one or more hidden layers increases the net's learning abilities. The last layer is the output layer. Each single neuron is connected to the neurons of the previous layer through adaptable synaptic weights to make the neural networks learn the complex relationship between input and output through training. As this study is a pattern recognition type, we used "back propagation perceptron" model. Once the input is propagated to the output neuron, this neuron compares its activation with the expected training output. If the neuron finds an error, in a process called back-propagation, it goes backward through the network and adjusts the connection weights to compensate the error. By calculating the gradient vector of the error surface, the error gradually declines until all the expected outputs are correctly displayed.

In this MLP model, the input layer consists of seven *variables* which were theoretically related to shunt infection via the previous univariate analysis (p value < 0.2). These input variables included birth weight, age at first shunting procedure, numbers of shunt revision surgeries, history of premature birth, myelomeningocele, intraventricular hemorrhage, and coincided infections. Also, two *variables*, namely shunt infection vs. no shunt infection, were applied to the output layer. The dataset of 148 patients was randomly separated into a training set of 126 cases and a test set of 22 cases. To avoid the overfitting effect, the number of neurons in the hidden was designed to be 13 via statistical calculations. The

ANN model was then trained using the testing and training dataset, and these steps of randomized training of dataset for the same series were repeated 100 times and the best network was taken as the final ANN model.

In the next step, the individual effect of each single input variable on the network prediction was assessed. For this purpose, with the same training and testing dataset, each of the seven input variables were deleted once and the network prediction was calculated for each new setting. The more decrease in the network prediction accuracy after deleting a given variable, the more prominent effect of the considered variable on the whole network prediction and therefore on the shunt infection occurrence.

Logistic regression model

For the logistic regression model, the training and testing datasets were the same as those used with ANN models; thus, there was a logistic regression and an ANN model for each training and testing dataset.

Description of shunt infection

Shunt infection was defined as the identification of a bacterial pathogen in CSF culture. In children with negative CSF culture and clinical evidence of infection, shunt infection was considered if CSF parameters were abnormal, including positive smear, low glucose level (< 40 mg/dL), and high white blood cell count (> 10 cells/mm³) with polymorphonucleosis.

Statistical analysis

For the first statistical analysis, the association between shunt infection and each potential predictor variable was checked with univariate analysis using SPSS software package version 19. Continuous variables were compared using the Mann-Whitney *U* test and categorical variables were compared via chi-square testing, with Bonferroni correction to counteract the problem of multiple comparisons on univariate analysis. The *p* value of less than 0.05 was considered statistically significant, and variables with the *p* value of less than 0.2 in the univariate analysis were used to develop models.

In the second part, the artificial neural network was designed by the software MATLAB R2013b (MathWorks, Inc., MA, USA), and the logistic regression model was calculated via SPSS 19. The overall accuracy ($[\text{true positive} + \text{true negative}]/\text{total}$) of the final model was determined by comparing the predicted values with the actual events. For the comparison of ANN and logistic regression models, receiver operating characteristic (ROC) curves were created. The area under the curve (AUC) from the ROC analysis was used to compare the discriminatory capability of the models.

Results

A series of 148 patients (84 males and 64 females) were enrolled in the study. The age ranged from 3 days to 88 month, with the mean of 4.86 ± 10.38 months. The mean follow-up period was 3 years (ranging from 2 to 4 years). The etiology of hydrocephalus was as follows: congenital/idiopathic, for 80 patients (54 %); myelodysplasia, for 29 (19.6 %); intraventricular hemorrhage, for 25 (16.9 %); tumor/ mass lesion, for 8 (5.4 %); meningitis, for 4 (2.7 %); and trauma, for 2 (1.35 %). The etiologies of hydrocephalus in groups with and without shunt infection are presented in Table 1.

There were 68 cases of shunt infection including 54.7 % meningitis, 29.7 % distal infection, and 15.6 % wound infection leading to shunt external surface involvement accompanied with meningitis. In the primary univariate analysis, five variables including low birth weight, younger age at the first shunting procedure, numbers of shunt revision surgeries, history of premature birth, and myelomeningocele were significantly correlated to shunt infection with a *p* value of less than 0.05. Among the mentioned factors, history of myelomeningocele was associated with lower shunt infection rate and the other factors were related to higher rate of infection (Table 1). Moreover, two other variables namely; IVH and coincided infections were found to be marginally associated with a *p* value of less than 0.2. All these seven variables were used as input data in model planning. The results of the primary univariate analysis for these seven input variables are summarized in Table 2.

To develop the models, the dataset of 148 patients was randomly separated into a training set of 126 cases (85 %) and a test set of 22 cases (15 %). Interrelationships between predictor variables (7 input nodes), hidden variables (13 nodes in one hidden layer), and shunt infection or no infection (2 output nodes) were assessed using the artificial network. Calculating for the test dataset, the ANN predicted shunt infection with an accuracy of 86.4 %. Applying the calculation to the whole dataset, the accuracy rate for the prediction of shunt infection was 83.1 % with the MSE of 0.206. The confusion matrix showing the number of correct and incorrect predictions made by each set of data compared to the actual outcomes is displayed in Fig. 1. The accuracy of prognostic performance of LR model in predicting shunt infection with the same training and testing datasets was 55.7 %. The comparison of the accuracy rate and AUC of ANN and logistic regression models is presented in Table 3.

The accuracy of the beforehand trained network on the prediction of shunt infection was calculated with the same dataset, once deleting each of the seven input variables in turn. For this purpose, each time a new network with 6 input variables, 13 hidden nodes, and the same setting characters as the original network was developed and the best predictive performance of the new network was recorded. The more drop in

Table 1 The etiologies of hydrocephalus in patients with and without shunt infection

Etiology	Shunt infection		No shunt infection		Total	
	No.	%	No.	%	No.	%
Congenital/idiopathic	42	61.76	38	47.5	80	54
Myelomeningocele	6	8.82	23	28.75	29	19.6
Intraventricular hemorrhage	15	22.05	10	12.5	25	16.9
Tumor/mass lesion	3	4.41	5	6.25	8	5.4
Meningitis	2	1.94	2	2.5	4	2.7
Trauma	0	0	2	2.5	2	1.35
Total	68	100	80	100	148	100

the accuracy rate of the network means the more importance of the given deleted variable on the prediction of shunt infection. Based on this rational, the most important factor was the history of shunt revision, followed by low birth weight (under 2000 g.), history of prematurity, the age at the first shunt procedure, history of IVH, history of MMC, and coinfection. Table 4 shows the accuracy rate of the new seven networks in ascending order, representing the contribution of risk factors in the network prediction performance in descending order. Confusion matrix for each new network is demonstrated in Fig. 2.

Discussion

Shunt infections continue to be the main source of medical problems leading to unfavorable outcome in children with hydrocephalus. Many efforts have been made to eradicate the concerns of shunt infection. Kestle et al. and Choux et al. found that after the implementation of a standardized protocol, there was a significant lowering in shunt infection occurrence [6, 11, 12]. Similar results were found by Pirotte et al. following the implementation of a strict protocol for sterile shunt placement [19]. However, despite these advances, shunt infections remain the most significant complication associated with hydrocephalus treatment, posing a serious problem for children with hydrocephalus, their parents, and their caregivers. Because of the high morbidity associated with CSF shunt infection, it is critical for families and care providers to understand whether certain children undergoing CSF shunt placement are at higher risk for subsequent infection. The significance of different risk factors of shunt infection, related to either patients or surgical aspects, has been assessed in the previous published studies. However, data regarding clinical predictors of ventricular shunt infection in children are still controversial and limited.

We developed intelligent models that assessed the role of baseline patient factors (including age, birth weight, prematurity, MMC, and IVH) as well as revision surgery and coinfection in the prediction of shunt infection. Subsequently, the

contribution of each factor to the estimation of shunt infection risk was separately assessed using the trained network. While observed in clinical practice, no previous studies have used such network modeling to predict shunt infection risk.

As was found in the previous studies, applying artificial neural network models in different medical fields [1, 5], ANN was shown to have a better performance than the conventional logistic model, with the accuracy rate of 83.1 vs. 55.7 %, respectively. A potential drawback of ANN models, cited in the previous studies, is that ANNs were unable to calculate the weight of single variables on outcomes [5]. In this study, we introduced a method to assess the contribution of each single variable on the network function. Through one by one deleting variables from input layer and assessing the amount of drop in the network prediction accuracy, we could estimate the weight of each individual variable on network performance and established a hierarchy for the proposed risk factors of shunt infection.

Revision surgery

In the present study, revision surgery was shown to be the most vigorous factor in the prediction of shunt infection by neural network. Deleting the revision surgery from the input variables of the trained network, the predictive performance for shunt infection showed the most decrease in accuracy (dropped from 83.1 to 59.1 %). Also in the first univariate analysis, the rate of shunt infection had significantly raised by increase in the number of reoperations. Accordingly, Rogers et al. found shunt revision within the prior 90 days to be significantly associated with ventricular catheter infection with an adjusted odds ratio of [22]. In both single-center and multiple-center studies published by Simon et al., controlling for baseline factors, the risk of infection after shunt revision was significantly greater than initial placement, and this risk increased as numbers of revisions increased [23, 24]. Also, Reddy et al. demonstrated that the mean number of shunt revisions was significantly higher among patients with infection who had a median of four, compared with a median of zero among those without infection (p value; 0.001) [20].

Table 2 Primary univariate analysis of seven independent variables (subsequently being set as input variables for network)

Variables	Total	Shunt infection	No shunt infection	<i>p</i> value
Patients	148	68	80	
Birth weight (g)				0.003
≤2000	19	14	5	
2000–2500	10	4	6	
2500–3000	51	28	23	
3000–3500	50	13	37	
>3500	18	9	9	
Prematurity				0.008
Yes	39	25	14	
No	109	43	66	
Age at first shunting				0.000
<2 weeks	13	12	1	
>2 weeks	135	56	79	
Revision numbers				0.000
0	46	4	42	
1	67	37	30	
2	18	13	5	
3	10	8	2	
4	3	2	1	
5	1	1	0	
6	1	1	0	
7	1	1	0	
8	1	1	0	
History of MMC ^a				0.012
No	115	59	56	
Yes	33	9	24	
History of IVH ^b				0.189
No	125	55	70	
Yes	23	13	10	
Coinfection ^c				0.173
No	139	62	77	
Yes	9	6	3	

^a Myelomeningocele^b Intraventricular hemorrhage^c Active infection in another site of the body within 30 days prior to shunt insertion

Median shunt number and previous shunt infection were independent risk factors for shunt infection in McGirt's study [17]. In contrast, Choux et al. did not find an increased risk of infection following shunt reinsertion, but the number of patients who underwent reoperation was limited in their series [6]. Also in Renter's study, children with multiple procedures were not found to have a higher risk of infection [21].

The issue that shunt revision has been associated with increased infection in many studies is important to be considered, because an estimated of more than 50 % of patients with

a ventricular shunt requires at least one revision surgery following the first shunt insertion [29]. Each surgery likely represents an opportunity to introduce new organisms into the CSF and colonize onto the shunt hardware. So, to reduce the risk of infection, further work should focus on modalities to optimize revision procedures and reduce microbial exposure during reinsertion. As stepwise protocols of shunt insertion had been successful in reducing shunt infection; specific protocol for shunt revision procedure should be established as well.

Young age

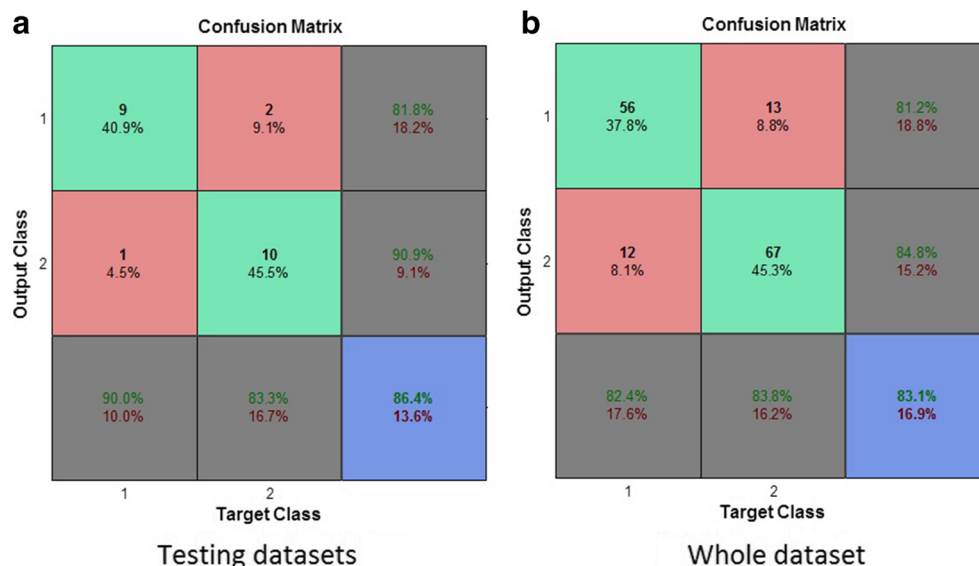
Multiple studies have shown inverse relationship between patients' age and shunt infection risk [8]. The mean number of infection episodes per patient has been shown to be considerably higher in pediatric patients than in adults [20]. More than one-half of the infections in the patients treated by Choux et al. occurred in children less than 2 years old [6]. Vinchon et al. also found a significantly higher incidence of infection in children less than 4 months (9.7 vs 5.6 %, $p = 0.008$) [27]. Some other investigators have reported an important association between child's age of less than 6 months and infection of the shunt system, with the frequency being 2.6 times higher than that in children older than 1 year in one investigation [3, 14, 24]. Multivariate analysis in the Korean study performed by Lee et al. demonstrated that shunt insertion on a patient under the age of 1 year was an independent risk factor of shunt infection [15]. Conversely, in a study by Braga and colleagues, analysis of the relationship between age and complications showed a significantly higher rate of infection among children older than 2 years ($p = 0.001$), a finding that is in contrast to literature data [3]. However, the small sample size was small in the latter study, and analysis was performed on 13 cases of shunt infection among a total of 46 shunted patients.

In agreement with other studies, univariate analysis in our study showed that the age of less than 2 weeks at the first shunting procedure was significantly associated with shunt infection. Also, this variable was found to have a meaningful contribution in the predictive performance of the trained neural network, so that with deleting it from the list of input variables, the accuracy of prediction dropped to 72.7 %. Overall, the higher rate of shunt infection in these young patients may be due to the poorly developed humoral and cellular immune systems, the immaturity of the skin barrier in early infants, and the features of residential bacterial flora in this age group.

Birth weight

Regardless of gestational age and the weight at shunting procedure, low birth weight has been proposed by Dallacasa and

Fig. 1 The confusion matrix showing the number of correct and incorrect predictions made by each set of data using testing datasets (a) and whole dataset (b)



coworkers as a risk factor for CSF catheter infection [7]. In a study by Bruinsma et al. on low birth weight infants (LBWI, 2000 g) and extremely low birth weight infants (ELBWI, 1000 g), LBWI had higher risk of CSF shunt infection [4]. Also, Simon et al. has found a significant association of shunt infection risk and lower weight of infants at initial CSF shunt placement, but conclusion about birth weight was limited in this cohort due to missing data [24].

In the current study, lower birth weight was significantly associated with shunt infection in univariate analysis ($p = 0.003$). As an input variable, this factor had a substantial contribution to the prediction accuracy of the network, ranking second in the hierarchy of importance for the prediction of shunt infection. It can be assumed that improvements in neonatal intensive care have reduced the mortality rates of neonates with an extremely low birth weight who are immunologically vulnerable and have a significantly higher risk of developing shunt infection.

Prematurity

Prematurity has been supposed as a potential risk factor of shunt infection for many years. Considering this concept,

Table 3 Comparison of the AUC and predictive accuracy of ANN and logistic regression models for predicting shunt infection in 148 children with ventriculoperitoneal shunt

Model	Accuracy rate (%)	AUC (%)	* p value
ANN (95 % CI)	83.1	91.98	0.001<
(95 % CI) LR	55.7	76.5	0.000

ANN artificial neural network, LR logistic regression, AUC area under the curve, CI confidence interval

*Significance on ROC curve analysis

strategies to lower infection risk in premature infants including temporary device or ventriculosubgaleal shunt or repeated lumbar puncture, with particular advantages and disadvantages of each of offers, have been employed [8]. Bruinsma et al. has demonstrated that especially patients with a postmenstrual age of less than 37 weeks at their initial shunt placement were at higher risk for ventricular catheter reservoir and ventriculoperitoneal catheter infections [4]. Premature birth was an independent risk factor for shunt infection in studies by McGirt [17], Spader [25], Kalkurni [14], and Moussa [18], as well. However, in contrary to the findings of the mentioned studies, only one out of 73 premature babies (1.4 %) shunted by Choux and colleagues developed shunt infection [6].

We also identified prematurity as a significant variable in univariate analysis ($p = 0.008$), and the role of this factor in the network prediction accuracy ranked third after revision surgery and birth weight. Plus with the immune system, skin barrier, and bacterial flora which were mentioned as potential causes of shunt infections in young infants, the often long hospitalization of premature neonates may result in more colonization with specific nosocomial microorganisms leading to higher risk of CSF device infection in this group.

Myelomeningocele

Newborns with open neural tube defects pose a special risk of shunt infection due to potential contamination of the CSF with skin or bowel organisms through the spinal defect. Simultaneous shunting with repair of spina bifida, although decreases the wound leakage, may theoretically increase the risk of shunt infection due to longer time of surgery and exposed hardware in more risky condition. Some studies have shown higher risk of shunt infection in long term follow-up of

Table 4 The accuracy of the trained network by deleting each of input variables

Ranking in the predictive performance	Deleted variable	New network accuracy (%)
1	The numbers of shunt revisions	59.1
2	Birth weight	63.3
3	History of prematurity	68.2
4	Age at the first shunting	72.7
	History of MMC ^a	72.7
	History of IVH ^b	72.7
5	Coinfection	81.8

The more decrease in the prediction accuracy, the more prominent effect of the considered variable on the whole network prediction and therefore on the shunt infection occurrence

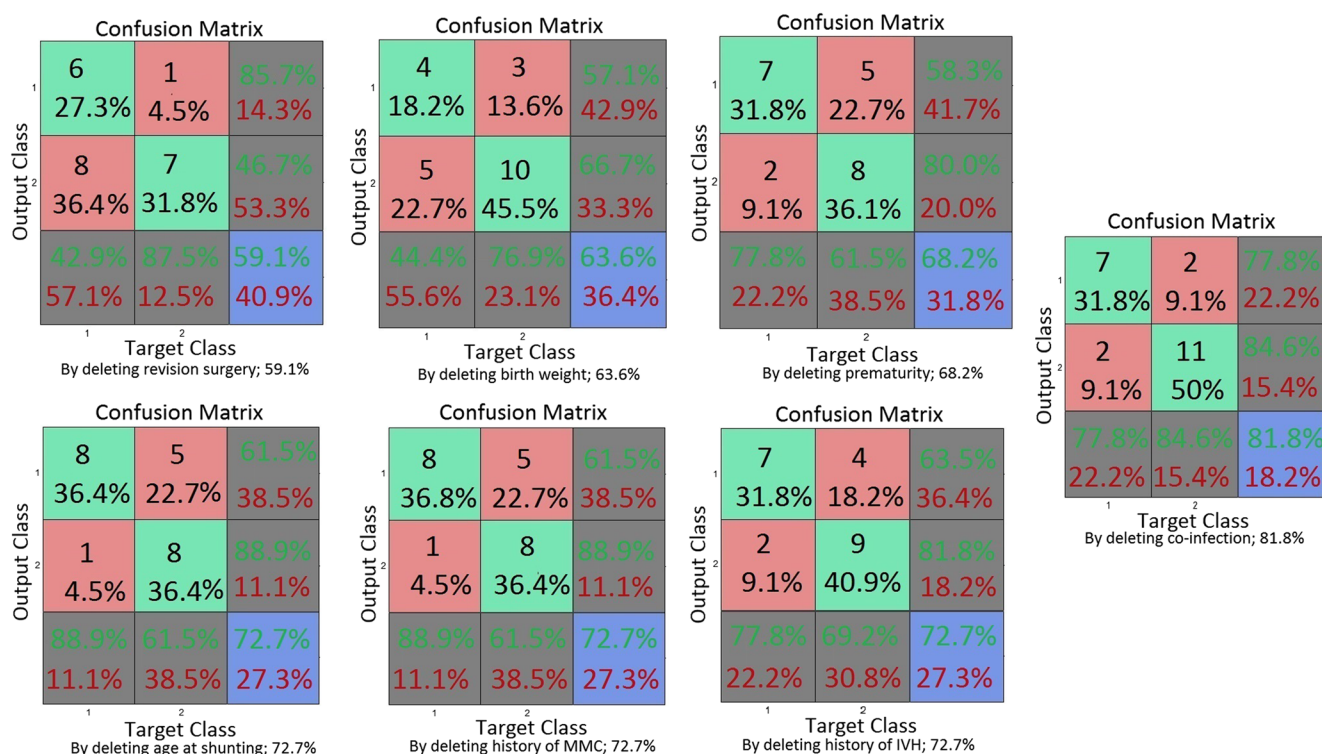
^a Myelomeningocele

^b Intraventricular hemorrhage

patients with MMC, while other studies found no increased risk [8]. For instance, in Braga's study, infection rate was much higher in MMC patients than in those with congenital hydrocephalus and the authors attributed this finding to the requirement of longer period of hospitalization [3]. Steinbok, Vinchon, and Reddy showed in separate studies that patients with myelomeningocele experienced higher rates of infection after ventricular shunting [20, 26, 27]. Even so, the condition was not correlated to shunt infection in McGirt study [17]. On the other hand, some other authors found MMC to be a protective factor [24]. In the single center study by Simon et al., myelomeningocele was significantly associated with a decreased risk of infection, and this protective effect was

attributed to the routine use of intravenous antibiotics in children with myelomeningocele [24]. The protective effect of myelomeningocele was not replicated in the larger multiple-center study by the same authors [23].

In the current study, univariate study revealed significant association between MMC and lower shunt infection ($p = 0.012$). Also, in neural network model, its contribution to the ANN prediction accuracy was exactly equal to that of IVH and age at first shunting. As an explanation for no increase in infection rate, it could be cited that we did not enroll patients with simultaneous shunting and MMC repair. All MMC patients in this cohort had been shunted with our routine protocol in the setting similar to others. Nonetheless, we

**Fig. 2** The confusion matrix for each new network developing after deleting each of the seven input variables

have no reasonable justification for the lower rate of infection in MMC patients. It seems that a specific study with enough sample size should be designed to evaluate shunt infection in myelomeningocele patients.

Intraventricular hemorrhage

Generally, neonates with post-hemorrhagic hydrocephalus are at high risk for infection [25]. The study by Lee et al. found that shunts which were performed on patients with hydrocephalus due to hemorrhagic events (IVH or subdural hematoma) demonstrated higher rate of infection [15]. In a clinical cohort by Vinchon, the rate of shunt infection per patient was significantly higher in patients with post-hemorrhagic hydrocephalus ($p = 0.002$) [27]. McGirt et al. found IVH to be an independent risk factor for CSF shunt infection ($p = 0.0053$) [17].

In the univariate analysis of this study, IVH was not found to have a significant association with shunt infection ($p = 0.189$). However, as an input variable of the ANN, IVH had a contribution as much as those of significant risk factors like age and MMC in the prediction performance of the network (accuracy dropped from 83.1 to 72.7 by deleting each of these three variables).

Coinfection

Although most infections are known to be induced at the time of surgery from skin contact, hematogenous contamination may occasionally play as a source of infection. Few studies have assessed the role of other sources of infection in the shunt infection. Reddy et al. and Vinchon et al. have demonstrated the role of blood-borne contamination, appendicitis, bowel perforation, peritonitis, contamination during abdominal surgery or trauma, and accidental wound in the occurrence of late shunt infection [20, 28]. However, the role of recent infection before shunting procedure as a risk factor for CSF catheter infection is hardly ever evaluated. In this study, the number of patients with other-site infections within 30 days prior to shunting surgery was twice in patients with shunt infection vs. those without shunt infection (six vs. three), though the condition was not statistically significant in univariate analysis. In the same line, coinfection as an input variable for neural network did not have an important role in the network predictive function, and by deleting this variable, the network accuracy did not changed substantially (just dropped from 83.1 to 81.8 %).

Clinical message

From the results of this study, it appears that four interrelated conditions including low birth weight, prematurity, young age, and IVH constituted substantial parts of the predictive performance of the trained network in

descending order. Moreover, there would be correlations between these bundles of variables with shunt revision, as more shunt revision might be needed in premature and low birth weight patients [4]. Since none of the factors in this and some previous studies was as strong as shunt revision, and this risk increased as numbers of revisions increased, future research efforts should focus on modalities to reduce microbial exposure during the perioperative period to optimize revision procedures and reduce risk of subsequent infection. For instance, standardized protocol regarding cranial scar opening that allows access to the valve and its connections, avoiding skin incision to be over the valve and catheters, the way of manipulating the implanted cranial catheter, and reinserting distal catheter through a new parietal incision within the previous skin opening can be of help.

In addition, further studies are necessary to determine whether longer courses of antimicrobial therapy or implanting antibiotic-coated catheters in patients who are considered high risk, based on the current and previous studies, can actually reduce the risk of infection without further risk for multidrug resistant or gram-negative infections.

Limitations

This study is subject to a number of important limitations inherent to retrospective methodology that relies on medical record review. Many patients had to be excluded from the first enrolment because of failed to capture qualified medical data. Some other limitations were presented by conducting a single center study; these include small sample size and the heterogeneity of the clinical presentations in a tertiary referral center. Although a uniform technique for VP shunt placement was used, the overall treatment for comorbidities was chosen based on the individualized condition. The findings of this study must be validated with further prospective studies in a larger cohort of patients involving more surgeons and centers.

Conclusion

The findings show that artificial neural networks can predict shunt infection with a high level of accuracy in children with shunted hydrocephalus. Also, the contribution of different risk factors in the prediction of shunt infection can be determined using the trained network. Identification of predictive factors may improve current practice to prevent shunt infections.

Compliance with ethical standards

Conflict of interest The authors have no conflict of interest.

References

1. Azimi P, Mohammadi HR (2014) Predicting endoscopic third ventriculostomy success in childhood hydrocephalus: an artificial neural network analysis. *J Neurosurg Pediatr* 13(4):426–432
2. Azimi P, Mohammadi HR, Benzel EC, Shahzadi S, Azhari S, Montazeri A (2015) Artificial neural networks in neurosurgery. *J Neurol Neurosurg Psychiatry* 86(3):251–256
3. Braga MH, Carvalho GT, Brandão RA, Lima FB, Costa BS (2009) Early shunt complications in 46 children with hydrocephalus. *Arq Neuropsiquiatr* 67(2 A):273–277
4. Bruinsma N, Stobberingh EE, Herpers MJ, Vles JS, Weber BJ, Gavilanes DA (2000) Subcutaneous ventricular catheter reservoir and ventriculoperitoneal drain-related infections in preterm infants and young children. *Clin Microbiol Infect* 6(4):202–206
5. Caooci G, Baccoli R, Vacca A, Mastronuzzi A, Bertaina A, Piras E, et al. (2010) Comparison between an artificial neural network and logistic regression in predicting acute graft-vs-host disease after unrelated donor hematopoietic stem cell transplantation in thalassemia patients. *Exp Hematol* 38(5):426–433
6. Choux M, Genitori L, Lang D, Lena G (1992) Shunt implantation: reducing the incidence of shunt infection. *J Neurosurg* 77(6):875–880
7. Dallacasa P, Dappozzo A, Galassi E, Sandri F, Cocchi G, Masi M (1995) Cerebrospinal fluid shunt infections in infants. *Childs Nerv Syst* 11(11):643–648
8. Duhaime AC (2006) Evaluation and management of shunt infections in children with hydrocephalus. *Clin Pediatr (Phila)* 45(8):705–713
9. Edwards DF, Hollingsworth H, Zazulia AR, Diringier M (1999) Artificial neural networks improve the prediction of mortality in intracerebral hemorrhage. *Neurology* 53(2):351–357
10. Gutierrez-Murgas Y, Snowden JN (2014) Ventricular shunt infections: immunopathogenesis and clinical management. *J Neuroimmunol* 276(1–2):1–8
11. Kestle JR, Holubkov R, Douglas Cochrane D, Kulkarni AV, Limbrick DD Jr, Luerssen TG, et al. (2016) A new Hydrocephalus Clinical Research Network protocol to reduce cerebrospinal fluid shunt infection. *J Neurosurg Pediatr* 17(4):391–396
12. Kestle JR, Riva-Cambrin J, Wellons JC 3rd, Kulkarni AV, Whitehead WE, Walker ML, et al. (2011) A standardized protocol to reduce cerebrospinal fluid shunt infection: the Hydrocephalus Clinical Research Network Quality Improvement Initiative. *J Neurosurg Pediatr* 8(1):22–29
13. Konstantelias AA, Vardakas KZ, Polyzos KA, Tansarli GS, Falagas ME (2015) Antimicrobial-impregnated and -coated shunt catheters for prevention of infections in patients with hydrocephalus: a systematic review and meta-analysis. *J Neurosurg* 122(5):1096–1112
14. Kulkarni AV, Drake JM, Lamberti-Pasculli M (2001) Cerebrospinal fluid shunt infection: a prospective study of risk factors. *J Neurosurg* 95:201
15. Lee JK, Seok JY, Lee JH, Choi EH, Phi JH, Kim SK, et al. (2012) Incidence and risk factors of ventriculoperitoneal shunt infections in children: a study of 333 consecutive shunts in 6 years. *J Korean Med Sci* 27(12):1563–1568
16. McCulloch WS, Pitts WH (1943) A logical calculus of the ideas immanent in nervous activity. *Bull Math Biophys* 5:115–137
17. McGirt MJ, Zaas A, Fuchs HE, George TM, Kaye K, Sexton DJ (2003) Risk factors for pediatric ventriculoperitoneal shunt infection and predictors of infectious pathogens. *Clin Infect Dis* 1;36(7):858–862
18. Moussa WM, Mohamed MA (2016) Efficacy of postoperative antibiotic injection in and around ventriculoperitoneal shunt in reduction of shunt infection: a randomized controlled trial. *Clin Neurol Neurosurg* 143:144–149
19. Pirotte BJ, Lubansu A, Bruneau M, Loqa C, Van Cutsem N, Brotchi J (2007) Sterile surgical technique for shunt placement reduces the shunt infection rate in children: preliminary analysis of a prospective protocol in 115 consecutive procedures. *Childs Nerv Syst* 3(11):1251–1261
20. Reddy GK, Bollam P, Caldito G (2012) Ventriculoperitoneal shunt surgery and the risk of shunt infection in patients with hydrocephalus: long-term single institution experience. *World Neurosurg* 78(1–2):155–163
21. Renier D, Lacombe J, Pierre-Kahn A, Sainte-Rose C, Hirsch JF (1984) Factors causing acute shunt infection. Computer analysis of 1174 operations. *J Neurosurg* 61:1072–1078
22. Rogers EA, Kimia A, Madsen JR, Nigrovic LE, Neuman MI (2012) Predictors of ventricular shunt infection among children presenting to a pediatric emergency department. *Pediatr Emerg Care* 28(5):405–409
23. Simon TD, Butler J, Whitlock KB, Browd SR, Holubkov R, Kestle JR (2014) Risk factors for first cerebrospinal fluid shunt infection: findings from a multi-center prospective cohort study. *J Pediatr* 164(6):1462–1468
24. Simon TD, Whitlock KB, Riva-Cambrin J, Kestle JR, Rosenfeld M, Dean JM, et al. (2012) Revision surgeries are associated with significant increased risk of subsequent cerebrospinal fluid shunt infection. *Pediatr Infect Dis J* 31(6):551–556
25. Spader HS, Hertzler DA, Kestle JR, Riva-Cambrin J (2015) Risk factors for infection and the effect of an institutional shunt protocol on the incidence of ventricular access device infections in preterm infants. *J Neurosurg Pediatr* 15(2):156–160
26. Steinbok P, Thompson GB (1976) Complications of ventriculovascular shunts: computer analysis of etiological factors. *Surg Neurol* 5:31–35
27. Vinchon M, Dhellemmes P (2006) Cerebrospinal fluid shunt infection: risk factors and long-term follow-up. *Childs Nerv Syst* 22(7):692–697
28. Vinchon M, Lemaitre MP, Vallée L, Dhellemmes P (2002) Late shunt infection: incidence, pathogenesis, and therapeutic implications. *Neuropediatrics* 33(4):169–173
29. Wells DL, Allen JM (2013) Ventriculoperitoneal shunt infections in adult patients. *AACN Adv Crit Care* 24(1):6–12