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Development of Machine Learning–Based Predictor Algorithm for Conversion of an Ommaya Reservoir to a Permanent Cerebrospinal Fluid Shunt in Preterm Posthemorrhagic Hydrocephalus

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■ BACKGROUND: **An Ommaya reservoir can be used to treat posthemorrhagic hydrocephalus secondary to intraventricular hemorrhage of prematurity until an acceptable weight can be obtained to place a permanent shunt. Identifying newborns at higher risk of developing shunt conversion may improve the management of these patients. This study aimed to develop a predictive algorithm for conversion of an Ommaya reservoir to a permanent shunt using artificial intelligence techniques and classical statistics.**

■ METHODS: **A database of 43 preterm patients weighing ≤1500 g with posthemorrhagic hydrocephalus (Papile grades III and IV with Levene ventricular index >4 mm above the 97th percentile) managed with an Ommaya reservoir at our institution between 2002 and 2017 was used to train a *k*-nearest neighbor algorithm. Validation of results was done with cross-validation technique. Three scenarios were calculated: 1) considering all features regardless whether or not they are correlated with the output variable; 2) considering the features as predictors if they have a correlation >30% with the output variable; 3) considering the output of the previous analysis.**

■ RESULTS: **When considering the outputs of a previous multivariate analysis, the algorithm reached 86% of cross-validation accuracy.**

■ CONCLUSIONS: **The use of machine learning–based algorithms can help in early identification of patients with permanent need of a shunt. We present a predictive algorithm for a permanent shunt with an accuracy of 86%; accuracy of the algorithm can be improved with larger volume of data and previous analysis.**

INTRODUCTION

Intraventricular hemorrhage (IVH) is a serious and common pathology in premature infants. Bleeding begins in the fragile subependymal capillary network of the germinal matrix, a richly vascularized collection of neuronal-glial precursor cells in the developing brain.[1] IVH is the most frequent cause of acquired hydrocephalus.[2] This condition can lead to delays in motor, language, and cognition development.[3]

A permanent shunt can cause severe complications in patients weighing ≤1500 g.[4-6] Therefore, different options have been described to treat posthemorrhagic hydrocephalus until an acceptable weight is reached. Repeated lumbar taps, ventricular taps, and placement of an external ventricular drain are associated with high rates of shunt infection and have been shown to be less effective in reducing the need for permanent shunts than ventricular reservoirs (Ommaya) and ventriculosubgaleal shunting.[7-9] There is no evidence of superiority between the 2

Key words
- Algorithm
- Cerebrospinal fluid shunt
- Intraventricular hemorrhage
- Machine learning
- Neurosurgery
- Ommaya
- Preterm hydrocephalus

Abbreviations and Acronyms
CSF: Cerebrospinal fluid
IVH: Intraventricular hemorrhage
***k*NN**: *k*-Nearest neighbor
ML: Machine learning
TRIPOD: Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis

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techniques, with shunt conversion rates of 65%–95%.[10-12] Permanent shunting can lead to a greater degree of neurological abnormalities and a smaller cranial circumference, not to mention a significant rate of shunt revision.[4,8,11,13] Selection of patients requiring permanent shunting can lead to earlier shunt implantation and avoid unnecessary taps that result in complications.[14,15]

Algorithms based on machine learning (ML) are anticipated to occupy an important place in medicine, changing certain jobs for the better.[16] This is a reality in many companies that use algorithms for their business strategies. In medicine, the sensitivity of the data, the exquisite precision that algorithms must have, and the mistrust or lack of knowledge of health care professionals have slowed down their implementation.[17,18] The objective of this study was to develop a predictive algorithm for the conversion of an Ommaya reservoir to a permanent shunt using the power of artificial intelligence through ML. In a second phase, an external center was contacted to provide more data for the external validation of the algorithm.

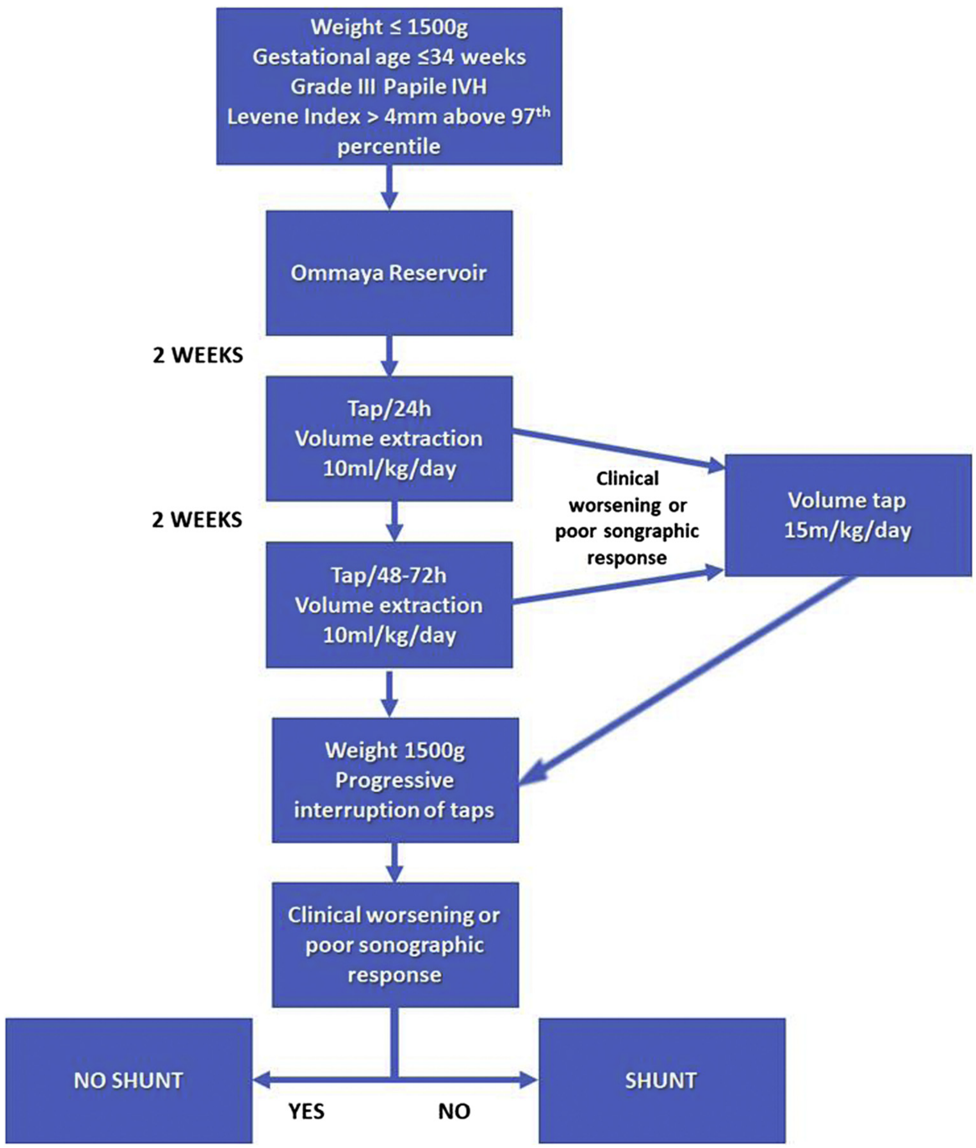

Figure 1. Treatment algorithm. Clinical worsening was defined as a bulging fontanelle, bradycardia, or arterial hypertension. Poor sonographic response was defined as a ventricular index greater than the preoperative value. IVH, intraventricular hemorrhage

MATERIALS AND METHODS

This study was carried out following the Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) guidelines. Informed consent was obtained for each patient. Ethical committee approval from our institution was obtained. There are currently no standardized guidelines for the development of an artificial intelligence algorithm; the most relevant guidelines are TRIPOD. The process of developing an algorithm can be complicated, but it is described below because it is necessary to begin to introduce this terminology into clinical practice to promote the dissemination of these algorithms and standardization in their production.

Data were obtained from a database of our hospital records (tertiary hospital) of 43 preterm neonatal patients (gestational age $\leq$34 weeks), with low birth weight ($\leq$1500 g), presence of IVH classified as Papile grade III or IV, and progressive hydrocephalus with frontal Levene ventricular index >4 mm above the 97th percentile who required placement of an Ommaya reservoir between 2002 and 2017. Patients with infections associated with the Ommaya reservoir were excluded. The treatment algorithm is summarized in **Figure 1**.

Demographic and clinical variables and the rate of permanent shunt placement were collected. Clinical worsening was defined as a bulging fontanelle, bradycardia, or arterial hypertension. Poor sonographic response was defined as a ventricular index greater than the preoperative value. In some cases, a lumbar tap was performed as a temporizing measure before placement of an Ommaya reservoir. Availability of labeled patient data made it especially interesting to consider supervised ML techniques. Patients were classified as 0 when they did not need a permanent shunt and 1 when they did.

The *k*-nearest neighbor (*k*NN) algorithm was used. The output of the algorithm is the class that is the most frequent among the selected neighbors (shunt vs. no shunt):

- *k* was initialized; this refers to selecting the number of neighbors that will be considered.
- For each example in the data:
  - Distance between this point and the other points from the dataset was calculated. Storing these distances would result in a vector of size (1,*n*), with *n* being the number of examples in the dataset.
  - Vector was sorted in ascending order.
  - First *k* positions were selected.
  - Mode was taken from the label assigned to the selected examples.

A series of steps were followed. First, the dataset was loaded, and the distribution of the variables was analyzed. Variables that were not of interest as predictors were discarded, missing values were imputed, and outliers were detected. For variables with a higher percentage of outliers in their data, a logarithmic transformation was applied to smooth these variables. Variables were standardized, as having variables with such different magnitudes can handicap the performance of ML algorithms. A standard scaler was used for this purpose. Correlation between the features and the output variable was calculated to find those that were candidates to be predictors for the model by having a closer relationship with the output.

After selection of the variables, the dataset was split into a training set and a test set. The training set was used to fit the parameters of the model. The amount of data chosen for this should be greater than testing data to contemplate as many cases as possible. This is key in ML because in a classification problem the training set should contain data from all the groups that may exist because if a group is not seen, it will never be predicted correctly. The test dataset is independent of the training dataset but follows the same probability distribution as the training dataset, as they belong to the same population.

The same data used to build the model cannot be used to evaluate it because the model could simply memorize the data instead of learning, so any data of the training set would be perfectly predicted or classified, but it would not have any generalization. For this reason, a part of the data was saved, and the training set never saw this data. Once the data were trained, the test was to predict the target variable.

Accuracy can be used to evaluate the performance of the model. To evaluate accuracy, the target variable with the prediction is compared. Accuracy is defined as follows:

$$accuracy = \frac{true\ positives + true\ negatives}{sample\ size}$$

Obtaining good accuracy does not mean that the algorithm has understood the problem, as it could be that the distribution of training and test sets was favorable to obtain a better accuracy.

To validate the model in a more robust way, the cross-validation technique was used. The dataset was divided into *k*-folds, and each of them was the test set at some point. An example is shown in **Table 1** for 4 folds, D1, D2, D3, and D4, applied to a *k*NN algorithm. The accuracy assigned for each number of neighbors considered (*k* parameter) is the average of the 4 accuracies of the different datasets resulting from cross-validation.

Number of neighbors to be considered and number of folds for cross-validation achieved the best accuracy using a grid search algorithm. Grid search computes the calculations for all the values specified in the grid. If *k*-fold grid is [3,4,5] and *k*-neighbor is [3,4,5,6,7,8,9,10], the *k*NN algorithm will be calculated first using 3 folds (2 for training and 1 for validation) for all the specified *k*-neighbor values, then with 4 folds, and so on. All possible combinations of these parameters were tested, and a given accuracy was obtained. The values with the highest accuracy were selected.

Regarding sample size, no other previous research was available for the analysis. To impute the empty values of the dataset for categorical variables, distribution of variables was analyzed with respect to the output variable, and the value that was most frequent for that output value was assigned. For continuous variables, empty data were filled with the mean of the distribution. The correlation between variables and the output class was calculated to obtain those that could be most closely related. When selecting the predictors for the model, whether having more or fewer predictors affected the performance of the model was analyzed, and the correlation values obtained previously would be those on which the selection would be based.

Table 1. Cross-Validation Example

k (*k*NN)	Training	Test	Accuracy
1	D1, D2, D3	D4	A4_1
1	D1, D2, D4	D3	A3_1
1	D1, D3, D4	D2	A2_1
1	D2, D3, D4	D1	A1_1
2	D1, D2, D3	D4	A4_2
2	D1, D2, D4	D3	A3_2
2	D1, D3, D4	D2	A2_2
2	D2, D3, D4	D1	A1_2

*k*NN, *k*-nearest neighbor; D1, fold 1; D2, fold 2; D3, fold 3; D4, fold 4.

Table 2. Variables of Dataset

Variable	Type	Empty Examples (%)
Sex	Qualitative dichotomous	0
Birth weight	Quantitative continuous	0
Birth weight percentile	Discrete quantitative	20.9
Gestational age	Quantitative continuous	0
Papile hemorrhage grade	Discrete quantitative, 4 categories	0
Levene ventricular index	Quantitative continuous	6.9
Levene ventricular index percentile	Discrete quantitative	27.9
Lumbar punctures	Qualitative dichotomous	0
Patent ductus arteriosus	Qualitative dichotomous	4.6
Necrotizing enterocolitis	Qualitative dichotomous	4.6
Sepsis	Qualitative dichotomous	4.6
Time to Ommaya reservoir	Quantitative continuous	0
Extraction rate	Qualitative dichotomous	2.3
Time with Ommaya reservoir	Quantitative continuous	0
Poor sonographic response during taps	Qualitative dichotomous	0
Poor clinical response during taps	Qualitative dichotomous	20.9
Preoperative glycorrhachia	Quantitative continuous	2.3
Glycorrhachia during Ommaya taps	Quantitative continuous	0
Preoperative proteinorrhachia	Quantitative continuous	2.3
Proteinorrhachia during Ommaya taps	Quantitative continuous	0
Preoperative lactatorrhachia	Quantitative continuous	37.2
Lactatorrhachia during Ommaya taps	Quantitative continuous	32.5
Preoperative red blood cells in CSF	Discrete quantitative	4.6
Red blood cells in CSF during Ommaya taps	Discrete quantitative	2.3
Preoperative white blood cells in CSF	Discrete quantitative	4.6
White blood cells in CSF during Ommaya taps	Discrete quantitative	2.3

CSF, cerebrospinal fluid.

Three different scenarios were compared: 1) considering all features regardless of whether they are correlated or not with the output variable; 2) considering the features as predictors if they have a correlation >30% with the output variable; 3) considering the output of previous analyses associated with higher likelihood of permanent cerebrospinal fluid (CSF) shunting[19]: high CSF lactate levels, absence of symptomatic patent ductus arteriosus, and higher CSF extraction requirement. Cross-validation accuracy was evaluated for the 3 scenarios, and the features involved in the scenario with highest accuracy were considered the selected predictors.

RESULTS

The inclusion criteria were met by 43 patients. Of patients, 32 underwent permanent shunting. The remaining 11 patients did not show a poor sonographic response or clinical worsening, and therefore the Ommaya reservoir was removed.

The dataset contained 27 variables (Table 2). Some variables had to be eliminated. Poor clinical response during the taps was eliminated because of a very high percentage of empty data and no significant correlation with the output variable. Birth weight percentile and Levene ventricular index percentile were discarded because of higher empty values than the variables without percentile. Subsequently, the dataset was reduced to (43, 23). Pearson correlation of the variables with respect to the output was calculated to consider them as predictors as explained in Materials and Methods (Table 3).

Of the kNN algorithm, only the hyperparameter k, the number of neighbors considered to establish the output of the algorithm, was tuned. For this purpose, a grid search between different values of parameter k was established. Considering that the dataset has 43 possible neighbors, the grid was established in all those values of k between 3 and 20. The differences between cross-validation with 3 folds and 4 folds were also tested.

Algorithm prediction is simple to interpret: 1 means that a patient is considered to need permanent shunting and zero means that a patient is not considered to need permanent shunting. Accuracy of this prediction was calculated for each scenario and number of folds (Tables 4–6). Best results were always associated with 4 folds. A configuration of 14 neighbors for the third scenario was the best case, achieving 86% of cross-validation accuracy as shown in Table 6. Therefore, by knowing the variables that have the greatest influence on the possibility or not of ending up with a shunt with previous analysis[19] and applying a cross-validation method in which data are divided for training and validation, higher accuracy is obtained. This means that physicians would simply enter the required patient data in Table 7, and the algorithm, adjusted by these parameters, would predict with an accuracy of 86% whether a patient will need a shunt or not. For simplification of this process for practicing neurosurgeons, 2 examples are presented.

Table 3. Pearson Correlation

Variable	Value
Preoperative lactatorrhachia	0.476325
Extraction rate	0.386793
Patent ductus arteriosus	0.371575
Lactatorrhachia during Ommaya taps	0.321158
Sepsis	0.320407
Poor sonographic response during punctures	0.305517
Glycorrhachia during Ommaya taps	0.300215
Preoperative white blood cells in CSF	0.281767
Papile hemorrhage grade	0.210015
White blood cells in CSF during Ommaya taps	0.189426
Lumbar punctures	0.121162
Time to Ommaya	0.120452
Red blood cells in CSF during Ommaya taps	0.097777
Proteinorrhachia during Ommaya taps	0.087865
Time with Ommaya reservoir	0.079582
Preoperative glycorrhachia	0.075219
Birth weight	0.044192
Sex	0.040291
Preoperative red blood cells in CSF	0.024695
Levene ventricular index	0.020125
Necrotizing enterocolitis	0.013575
Gestational age	0.012370
Preoperative proteinorrhachia	0.011811

CSF, cerebrospinal fluid.

Case Examples

Case 1: Shunt. Figure 2 shows transfontanellar ultrasound of a patient who was born at 29 weeks of gestation weighing 1200 g and had grade III IVH. The patient needed placement of an Ommaya reservoir after developing posthemorrhagic hydrocephalus. During the Ommaya taps, the patient's mean CSF lactate level was 3.4 mmol/L, and a high CSF extraction rate, defined as extraction of >10 mL/kg/day of CSF, was required. The patient did not have a symptomatic patent ductus arteriosus. These data were introduced into the algorithm, and the result was "shunt." Despite this result, the usual management in our center was followed. After discontinuation of the taps, the patient demonstrated poor tolerance with clinical worsening and ventricle enlargement and required permanent shunting with a ventriculoperitoneal shunt valve.

Case 2: No Shunt. Figure 3 shows transfontanellar ultrasound of a patient who was born at 26 weeks of gestation weighing 996 g and had grade IV IVH. The patient needed placement of an Ommaya reservoir after developing posthemorrhagic hydrocephalus. During the Ommaya taps, the patient's mean CSF lactate level was 2.9 mmol/L, and a low CSF extraction rate, defined as extraction of ≤10 mL/kg/day of CSF. The patient had a symptomatic patent ductus arteriosus, which was treated accordingly. These data were introduced into the algorithm, and

Table 4. Scenario 1 Accuracy

k	Score	Fold	*k*	Score	Fold
3	0.786364	4	3	0.831502	3
4	0.806313	4	4	0.776557	3
5	0.856818	4	5	0.85348	3
6	0.856818	4	6	0.778388	3
7	0.786364	4	7	0.807692	3
8	0.786364	4	8	0.661172	3
9	0.763636	4	9	0.734432	3
10	0.713131	4	10	0.663004	3
11	0.760859	4	11	0.708791	3
12	0.715404	4	12	0.708791	3
13	0.733081	4	13	0.732601	3
14	0.733081	4	14	0.75641	3
15	0.733081	4	15	0.732601	3
16	0.733081	4	16	0.732601	3
17	0.733081	4	17	0.732601	3
18	0.733081	4	18	0.732601	3
19	0.733081	4	19	0.732601	3
20	0.733081	4	20	0.732601	3

Table 5. Scenario 2 Accuracy

k	Score	Fold	*k*	Score	Fold
3	0.836364	4	3	0.804029	3
4	0.785859	4	4	0.758242	3
5	0.763131	4	5	0.734432	3
6	0.793182	4	6	0.734432	3
7	0.790404	4	7	0.734432	3
8	0.717677	4	8	0.760073	3
9	0.738131	4	9	0.710623	3
10	0.695455	4	10	0.712454	3
11	0.720455	4	11	0.708791	3
12	0.718182	4	12	0.734432	3
13	0.755808	4	13	0.732601	3
14	0.730808	4	14	0.758242	3
15	0.755808	4	15	0.732601	3
16	0.778535	4	16	0.732601	3
17	0.733081	4	17	0.732601	3
18	0.733081	4	18	0.732601	3
19	0.733081	4	19	0.732601	3
20	0.733081	4	20	0.732601	3

Table 6. Scenario 3 Accuracy

k	Score	Fold	*k*	Score	Fold
5	0.687626	4	5	0.734432	3
6	0.763131	4	6	0.758242	3
7	0.662626	4	7	0.708791	3
8	0.763131	4	8	0.734432	3
9	0.710354	4	9	0.734432	3
10	0.763131	4	10	0.782051	3
11	0.735354	4	11	0.758242	3
12	0.763131	4	12	0.782051	3
13	0.830808	4	13	0.758242	3
14	0.863636	4	14	0.758242	3
15	0.758081	4	15	0.758242	3
16	0.758081	4	16	0.758242	3
17	0.733081	4	17	0.732601	3
18	0.733081	4	18	0.732601	3
19	0.733081	4	19	0.732601	3
20	0.733081	4	20	0.732601	3

the result was "no shunt." Again, despite this result, the usual management in our center was followed. After discontinuation of the taps, the patient demonstrated stable ventricular size with no symptoms and was discharged home. After a year of follow-up, the patient is doing well with no signs or symptoms of hydrocephalus.

DISCUSSION

Artificial intelligence techniques such as ML and its algorithms are being developed in multiple fields of medicine. An example in neurosurgery is the development of a convolutional neural network with an area under the curve of 0.846 for the diagnosis of intracranial hemorrhage.[20]

Table 7. Final Algorithm Parameters

Inclusion criteria	
	Birth weight (<1500 g)
	Gestational age (≤34 weeks)
	Hemorrhage grade (Papile III–IV)
	Levene ventricular index (>4 mm above 97th percentile)
Variables for prediction	
	Persistent patent ductus arteriosus (yes/no)
	Extraction rate (≤10 mg/kg/day/>10 mg/kg/day)
	Mean CSF lactate during Ommaya taps (mmol/L)

CSF, cerebrospinal fluid.

The first limitation of this study is that we have a relatively small dataset with missing values; this is a problem in medicine where it is difficult to obtain a large volume of reliable data. Big data refers to datasets or combinations of datasets whose size (volume), complexity (variability), and speed of growth (velocity) make it difficult to capture, manage, process, or analyze using conventional technologies and tools. In these situations of large data volume, ML can be of great help. However, ML is not exclusively used for big data and can also be used with smaller datasets. Another limitation is that in this article we have only just developed the algorithm, and therefore it is reliable only in patients from our dataset, and its accuracy should be validated with external data. This generates a problem of generalizability. An accuracy of 86% suggests there is not much overfitting; however, external validation would again be necessary.[21] We have a second study phase pending with another center for external validation with another dataset.

There are different types of bridging treatments until the shunt can be placed,[7-9] with conversion rates of 65%–95%.[10-12] High variability in the management of these patients increases heterogeneity and limits the applicability of the study. Variables with the greatest weight in the Pearson correlation analysis were preoperative lactatorrhachia, extraction rate, and patent ductus arteriosus. This is consistent with the findings previously reported by Palpán Flores et al.[19]

Despite the aforementioned limitations, we present an algorithm with an accuracy of 86%. The Ommaya reservoir is a widely used device for the management of hydrocephalus.[22] Also, the rest

Figure 2. Coronal slices of transfontanellar ultrasound from case 1. (**A**) Image obtained at the moment of placement of the Ommaya reservoir. (**B**) Image obtained when the taps were discontinued. (**C**) Control image obtained 2 weeks later. Note the ventricular enlargement from (**B**) to (**C**).

of the variables used for the calculation of this algorithm are variables that are easily obtainable and available. The kNN algorithm is arguably the simplest ML algorithm after linear regression. These facts improve implementation of the algorithm.

IVH has a strong social[23] and economic impact.[24] The rate of Ommaya reservoir infection can be associated with tap frequency. Identifying patients at increased risk of developing hydrocephalus can help prevent these complications, improving patient function and reducing impact on families and health care systems.[19]

Finally, this is the first study of these characteristics in IVH of prematurity and the first algorithm developed by neurosurgeons in the field of pediatric neurosurgery. We strongly believe this is a field for future research and that expanding these algorithms helps to improve and refine them. The main strength of this study is not its accuracy, but that it serves as a starting point for the development of future algorithms and research. Classical statistical tests cannot be forgotten; our algorithm shows the highest accuracy rate in scenario 3, when the outputs of previous analyses are known in advance. This suggests that both techniques are complementary and should be used to enhance each other, rather than compete with each other.

CONCLUSIONS

The use of ML-based algorithms can help in the early identification of patients with permanent need of a shunt. We present a predictive algorithm for a permanent shunt with an accuracy of 86%. The accuracy of this algorithm can be improved with a larger volume of data and previous analysis. A validation study is needed to validate the accuracy of the algorithm.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Miguel Sáez-Alegre: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Validation, Visualization, Writing – original draft, Writing – review & editing. **Rocío Martín:** Data curation, Formal analysis, Visualization, Writing – original draft, Writing – review

Figure 3. Coronal slices of transfontanellar ultrasound from case 2. (**A**) Image obtained at the moment of placement of the Ommaya reservoir. (**B**) Image obtained when the taps were discontinued. (**C**) Control image obtained 2 weeks later. Note that ventricular size remains unchanged after discontinuation of the taps.

& editing. **Alexis Palpán:** Investigation. **Fernando Carceller:** Investigation. **Jesús Sáez-Alegre:** Data curation. **Guillermo Servera:** Methodology, Software. **Rudolf Bauer:** Software. **Pablo García Feijoo:** Supervision. **Javier Saceda:** Supervision, Validation.

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