applied sciences

MDPI

Article

Analysis of the Risk Factors for De Novo Subdural Hygroma in Patients with Traumatic Brain Injury Using Predictive Modeling and Association Rule Mining

Kwang Hyeon Kim, Byung-Jou Lee and Hae-Won Koo *

Department of Neurosurgery, Inje University Ilsan Paik Hospital, College of Medicine, Goyang 10380, Republic of Korea
* Correspondence: hwkoo@paik.ac.kr

Abstract: The relationship between risk factors for de novo hygroma in patients with traumatic brain injury (TBI) was investigated. We collected data on 222 patients with TBI to determine the risk factors for de novo hygroma, including sex, age, centrum semiovale perivascular space (CSO-PVS) grade, trauma cause, hypertension, and diabetes. The importance of the risk factors was analyzed, and the feature contribution of the risk factors to all patients and each patient was analyzed using predictive modeling. Additionally, association rule mining was performed to determine the relationship between all factors, and the performance metrics of the predictive model were calculated. The overall feature importance was analyzed in the order of age, CSO-PVS, hypertension, and trauma cause. However, trauma cause, underlying disease, age, and sex as risk factors were different for a specific patient through the individual feature analysis. The mean area under the curve for the predictive model was 0.80 ± 0.04 using K-fold cross validation. We analyzed the risk factors for de novo hygroma in TBI and identified detailed relationships. Age and CSO-PVS severity were strongly correlated with de novo hygroma. Furthermore, according to the results of feature importance analysis and association rule mining, the significance of the risk factors may vary in each individual patient.

Keywords: CSO-PVS; hygroma; risk factor analysis; explainable predictive modeling; association rule mining

Citation: Kim, K.H.; Lee, B.-J.; Koo, H.-W. Analysis of the Risk Factors for De Novo Subdural Hygroma in Patients with Traumatic Brain Injury Using Predictive Modeling and Association Rule Mining. *Appl. Sci.* **2023**, *13*, 1243. https://doi.org/10.3390/app13031243

Academic Editors: Keun Ho Ryu and Nipon Theera-Umpon

Received: 20 December 2022
Revised: 11 January 2023
Accepted: 16 January 2023
Published: 17 January 2023

1. Introduction

Traumatic brain injury (TBI) entails the potential for severe damage to the brain parenchyma following head trauma [1]. Using the Glasgow coma scale (GCS), TBI is classified as severe (GCS $\leq$ 8), moderate (GCS 9–13), and mild (GCS 14–15) [2]. Among patients who visit the emergency department for clinical examination and evaluation, the most common degree of head injury is mild TBI [1]. However, various situations in daily life can cause the trauma, such as traffic accidents, falls, and sports events [3–6]. In TBI, an external impact applied to the skull by an accelerated object causes brain cell damage. This is followed by secondary responses that include changes in the cerebral blood flow, local and systemic inflammation, changes in oxygen transport and metabolism, ischemia, and apoptosis of neuronal cells [7]. Intravascular thrombosis is common in severe TBI and contributes to focal ischemia. Generally, TBI can be classified as either focal or diffuse [8]. Focal damage tends to occur at the site of impact, and focal neurological deficits may refer to the site of damage. Care should be taken in patient observation to identify delayed local contusion and hematomas, which may occur several days after trauma. In contrast, diffuse shearing of axons due to rapid deceleration or rotational force occurs in the brain white matter, gray synapse, corpus callosum, and brainstem, causing non-lateral neurological defects, such as encephalopathy, or local defects, such as skull fractures [9].

The most widely known hypothesis about the mechanism of the occurrence of subdural hygroma after TBI in a patient is that the arachnoid is ruptured and cerebrospinal

fluid flows into the subdural space through the arachnoid rupture and is then formed in isolation [10,11].

In contrast, perivascular spaces (PVS) are fluid structures that surround small blood vessels in the brain [12]. PVS is an important factor in the mechanism of brain injuries [13–15]. As a result of analyzing risk factors in patients with mild TBI, it was reported that newly developed hygroma and enlarged centrum semiovale (CSO)-PVS are associated [3].

Chong et al. (2015) reported predictive modeling results for the risk factors for TBI in children using machine learning [16]. In cases of 39 and 156 age-matched controls, the road traffic accident, a history of loss of consciousness, vomiting, and signs of base of skull fracture were found to be the four important risk factors (AUC = 0.98). Raj et al. (2019) developed a simple and scalable machine learning-based algorithm that can predict mortality in real time during intensive care after traumatic brain injury [17]. Using a dataset of 472 patients, machine learning-based logistic regression modeling was developed, and 30-day mortality was predicted using variables based on intracranial pressure (ICP), mean arterial pressure (MAP), cerebral perfusion pressure (CPP), and Glasgow Coma Scale (GCS). As a results, the study distinguished survivors from non-survivors with up to 81% and 84% accuracy based on key variables. The receiver operating characteristic curve (AUC) increased from 0.67 on day 1 to 0.81 on day 5.

In addition, a study that predicted the mortality of TBI patients was reported by Hsu et al. (2021) [18]. Although patient prognostic factors (GCS) were used in machine learning for mortality prediction, there is a limitation to identifying causal relationships between risk factors. However, machine learning studies on the de novo of subdural hygroma and related risk factors in TBI patients have not been reported. Since subdural hygroma is a cause of serious complications in patients with TBI, a substantial approach to the association of risk factors related to patient outcome prediction is required. Moreover, a predictive model study is required for a patient-specific prediction for each patient. In this study, we analyzed the importance of risk factors for de novo hygroma, including age, CSO-PVS, and underlying disease, in patients with mild TBI and the risk factors for individual patients using artificial intelligence techniques. Additionally, we attempted to identify the relationship between trauma episodes, underlying diseases, and de novo hygroma factors in patients with mild TBI.

2. Materials and Methods

2.1. Patient Dataset Preparation

To evaluate the risk factors for de novo hygroma, including age, CSO-PVS severity, and underlying diseases, among patients with TBI who visited our institution from January 2013 to November 2016, (1) brain magnetic resonance imaging (MRI), including T2-weighted imaging, was performed; and (2) patients without a history of trauma or diseases, such as stroke, tumor, or degenerative disease (e.g., dementia or Parkinson's disease) were selected as the inclusion criteria. Here, a patient with mild TBI is defined as (1) a loss of consciousness (LOC) < approximately 30 min; or (2) an initial GCS score of 13–15; and (3) a posttraumatic amnesia (PTA) < 24 h. Among these patients with mild TBI, a dataset of 222 patients was collected, and the patients classified the severity of CSO-PVS.

Several basic demographic characteristics and risk factors were evaluated in patients with mild TBI. We collected data on the incidence of highly CSO-PVS with age, sex, hypertension, and diabetes at the time of admission. The Institutional Review Committee of Inje University Ilsan Paik Hospital approved this study, including the review and publication of information obtained from patient records (IRB No. 2017-04-029). As all patient data were anonymized and de-identified before analysis, the requirement of informed consent for the use of patient medical data was waived.

2.2. Predictive Modeling and Statistical Analysis

To analyze the risk factors affecting de novo hygroma, the analysis was performed according to the architecture shown in Figure 1. First, an analysis of variance was performed

to analyze the statistical significance of risk factors (p-value < 0.05). Second, a XGBoost classifier model was established for predictive modeling. The training and test sets were split into 80:20. Third, Shapley additive explanation (SHAP) influence scoring was analyzed to quantify the contribution between risk factors. Additionally, partial dependence analysis was performed to analyze the relationship between factors. Furthermore, association rule mining was used to investigate the association rule between de novo hygroma and highly affected factors, such as CSO-PVS severity and underlying diseases, throughout extracting electronic medical record data for the patients. Performance indicators of predictive modeling were calculated by the area under the curve (AUC).

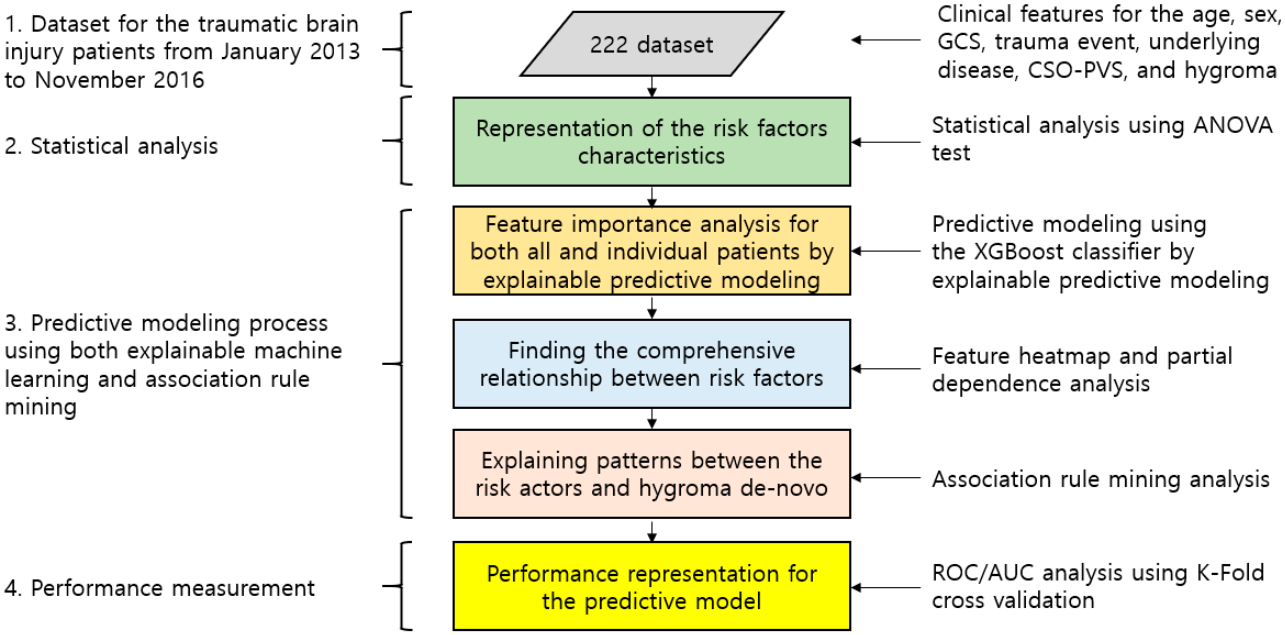

Figure 1. Research diagram for the composite analysis of the risk factors for de novo hygroma in patients with traumatic brain injury using predictive modeling and association rule-mining.

2.3. SHAP and Association Rule Mining

In this study, SHAP and association rule mining were used to analyze the characteristics and relationships of the risk factors related to the results.

First, SHAP was derived from game theory, which calculates the importance of players who influence the game outcome [19,20]. This method emerged to overcome the black-box limitation of an unknown model structure in machine learning modeling and can be applied to enable white-box modeling. It is called an explainable artificial intelligence (XAI) technique because it can infer the correlation of the output to the input value. We detected the explanatory outcome for the risk factors of the model using a tree explainer in the XGBoost classifier model [21,22].

Second, association rule mining is a technique that identifies relationships between different items in a case [23]. Association rules are built by retrieving data for if–then patterns for two or more entities and defining which relationships are the most important using specific criteria for support and confidence [24]. In this study, an a priori algorithm was used, and the metrics of the algorithm were as follows: (1) Support is how often an item appears in a given case; (2) Confidence is defined as the number of times an if–then statement is found to be true in a case; (3) Lift can be used to compare the expected confidence with the actual confidence. Thus, lift shows the number of times an if–then statement is expected to be true; (4) Conviction represents the degree to which the consequence depends on the preceding items; and (5) Leverage calculates the difference between the observed frequency in which items appear together and the expected frequency in case they are independent.

For programming development, Scikit-learn 1.2.0, SHAP 0.41.0, Mlxtend 0.20.0, and Statsmodels 0.13.2 modules were used in Python 3.9.12 environment.

3. Results

3.1. Patient Demographic

Table 1 shows the demographic analysis and statistical significance verification results for a dataset of 222 patients. Risk factors, including sex, age, hygroma, trauma causes, and underlying diseases, were selected and analyzed. Among these factors, the severity of trauma caused was slip down, in-car TA, bicycle TA, and hitting accident in this particular order. All factors showed statistical significance for the hygroma except for the hypertension and cause of trauma ($p < 0.05$) using ANOVA method.

Table 1. Analysis of demographics for the development of de novo subdural fluid collection in patients with mild traumatic brain injury.

Group	Category	Mean ± STD or *n* (%)	*p*-Value †
Age	years	50.55 ± 18.82	<0.001
Sex	Male	142 (63.96%)	0.015
	Female	80 (36.04%)	
Trauma cause	Slip down	66 (29.73%)	0.815
	In-car TA	41 (18.47%)	
	Bicycle TA	34 (15.32%)	
	Hitting	24 (10.81%)	
	Out-car TA	22 (9.91%)	
	Fall down	21 (9.46%)	
	Syncope	14 (6.30%)	
Hypertension, *n* (%)	Yes	56 (25.23%)	0.116
	No	166 (74.77%)	
Diabetes, *n* (%)	Yes	35 (15.77%)	0.001
	No	187 (84.23%)	
CSO-PVS, *n* (%)	High-degree	91 (40.99%)	<0.001
	Low-degree	131 (59.01%)	
Hygroma *	Development	54 (24.32%)	-
	Non-development	168 (75.68%)	

Abbreviations: STD, standard deviation; TA, traffic accident; CSO-PVS, centrum semiovale perivascular space. Note: Symbol, * is the target variable and † was performed using an analysis of variance (ANOVA).

3.2. Feature Importance Analysis for the Entire Dataset and Individual Case

Feature importance analysis was performed for the entire dataset and individual cases, as shown in Figure 2. The overall feature importance indicated that age, CSO-PVS, hypertension, and trauma cause were significant risk factors for de novo hygroma (Figure 2A). Individual feature importance analysis for a 66-year-old man with underlying hypertension and CSO-PVS due to a slipping-down accident (Figure 2B) showed that age, CSO-PVS, and underlying disease positively impacted the de novo hygroma status. Cohort feature importance analysis of sex is shown in Figure 2C. The tendency is the same all groups, except for sex. Figure 2D shows another cohort feature importance analysis for CSO-PVS. Age and CSO-PVS severity were shown to be strongly important risk factors.

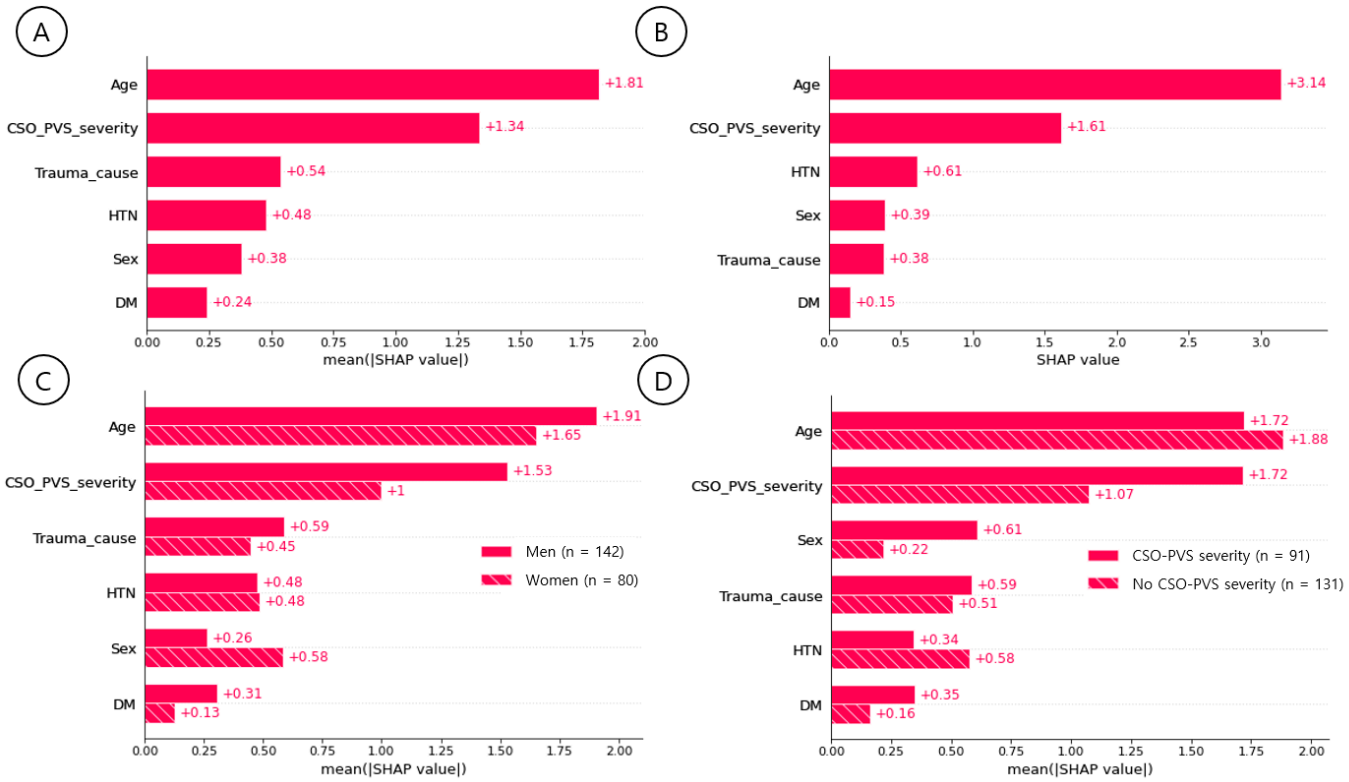

Figure 2. Feature importance analysis for the entire dataset and for each case: (**A**) overall feature importance indicates that age, CSO-PVS, trauma cause, and hypertension were important risk factors for de novo hygroma; (**B**) individual feature importance analysis for a 66-year-old man with hypertension, diabetes, and CSO-PVS due to a slipping-down accident indicates that age and CSO-PVS positively impacted the de novo hygroma status, and underlying disease and sex also positively impacted the de novo hygroma; (**C**) cohort feature importance for sex—the tendency is the same in all groups, except for sex; and (**D**) another cohort feature importance analysis for CSO-PVS. Age and CSO-PVS severity were strongly important risk factors. (HTN, hypertension; DM, diabetes).

3.3. Dependency between CSO-PVS Severity and Age

The feature importance was analyzed for the risk factors using a heatmap and individual feature analysis using partial dependence analysis (Figure 3). Among the risk factors, age and CSO-PVS severity highly impacted the de novo hygroma status (Figure 3A). The dependence analysis results show the relationship between CSO-PVS severity and age, as shown in Figure 3B. Most patients aged more than 86 years had a high correlation (62%) with CSO-PVS severity for the development of hygroma. Also, patients who had no or mild CSO-PVS severity showed lower dependency (mean 18.03%) over the entire age, but patients who had high CSO-PVS severity showed higher dependency across age groups (mean 37.97%).

3.4. Association Rule between De Novo Hygroma and CSO-PVS Severity

Figure 4 shows the hierarchical relationship between CSO-PVS severity and other risk factors. The red lines show cases that have de novo hygroma with high-grade CSO-PVS. However, blue lines show those that did not have de novo hygroma with high-grade CSO-PVS.

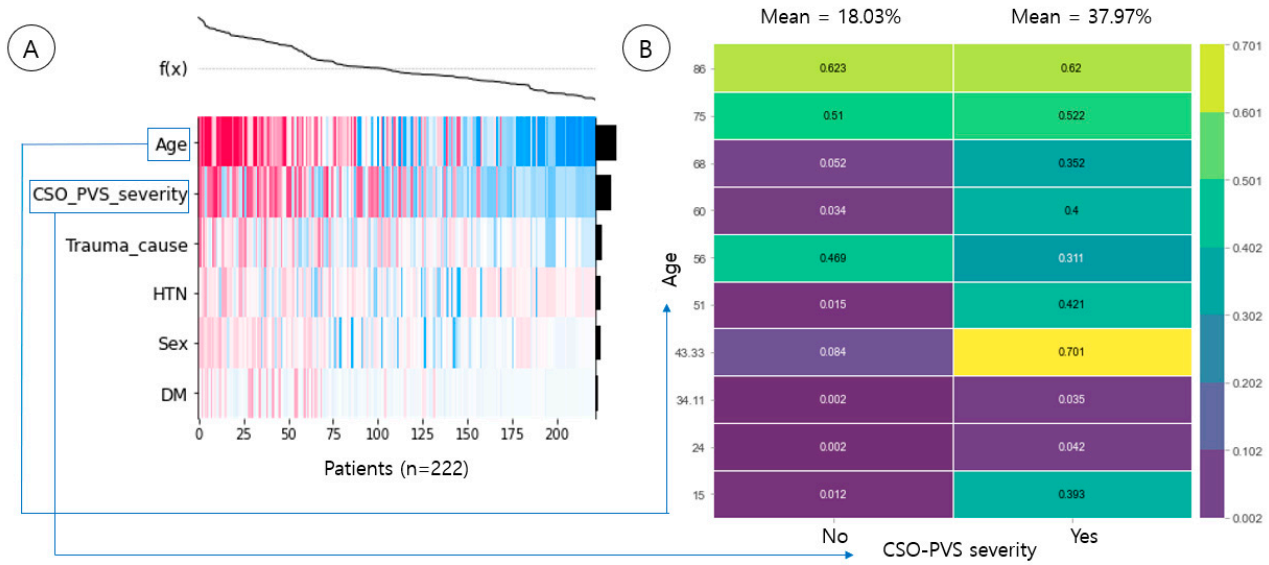

Figure 3. Feature importance heatmap and individual feature analysis using partial dependence analysis: (**A**) among the risk factors, age and CSO-PVS severity highly impacted the de novo hygroma status. Red and blue are positive and negative impact, respectively, and the color fading is the difference in intensity of impact change.; and (**B**) dependence analysis result between CSO-PVS severity and age. Most patients aged more than 86 years had a high correlation (62%) with CSO-PVS severity for the development of hygroma. Patients who had no or mild CSO-PVS severity showed lower dependency (mean 18.03%) over the entire age, but patients with high CSO-PVS severity showed higher dependency across age group (mean 37.97%). Note: trauma cause indices: 1, slip down; 2, out-car traffic accident; 3, syncope; 4, hitting; 5, bicycle traffic accident; 6, in-car traffic accident; 7, slip down; f(x), model function (y) of contribution for x; HTN, hypertension; DM, diabetes.

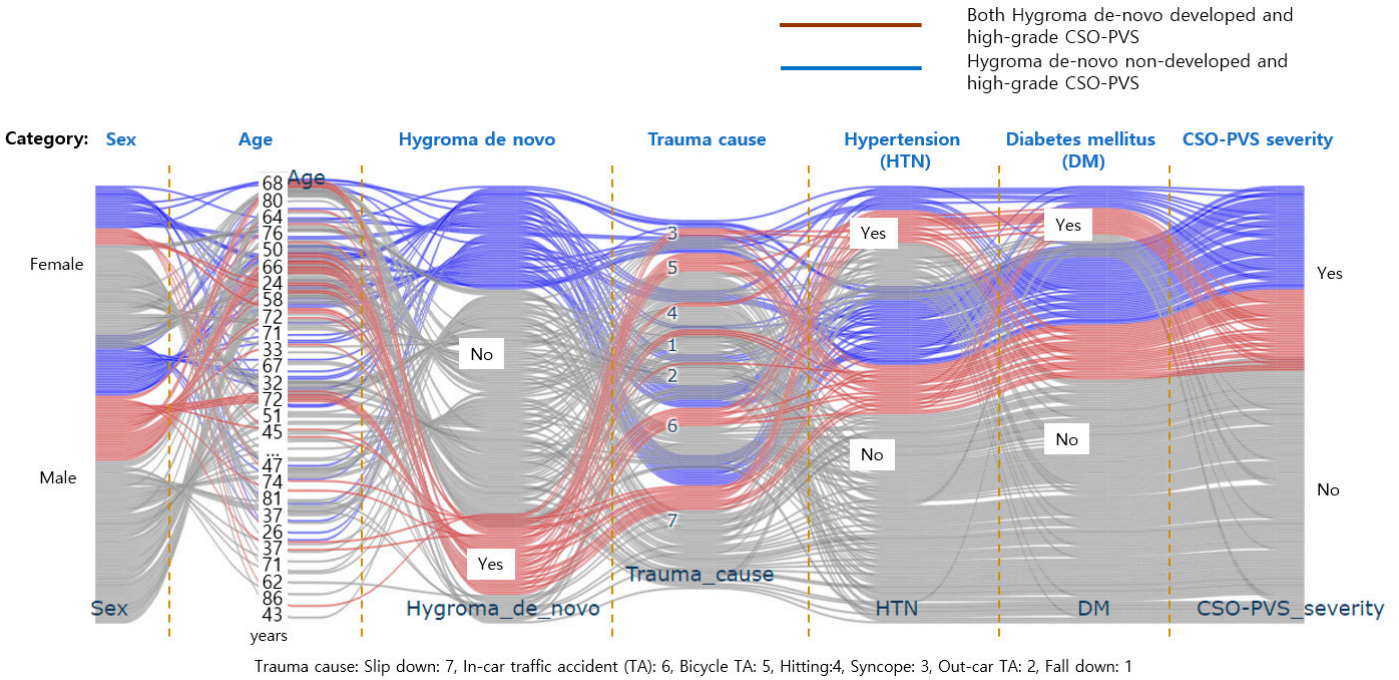

Figure 4. Hierarchical analysis of the relationship between CSO-PVS severity and the risk factors. The red lines show cases with de novo hygroma with high-grade CSO-PVS. However, blue lines show cases without de novo hygroma with high-grade CSO-PVS.

Table 2 shows the results of the correlation analysis on the red and blue lines shown in Figure 4. De novo hygroma was found to increase CSO-PVS severity (lift = 1.81). The reliability of the dependency relationship for the two variables was 0.74. Additionally, it was analyzed to be useful for predicting whether this relationship occurs (conviction = 2.28). In contrast, in the relationship between the underlying disease (hypertension and diabetes) and CSO-PVS severity, conviction < 2, which decreased the predictability of occurrence. However, the reliability of the dependency relationship also decreased.

Table 2. Association rule mining analysis of the relationship between CSO-PVS severity and other risk factors.

	Consequents	Support	Confidence	Lift	Leverage	Conviction
Hygroma de novo	CSO-PVS severity	0.18	0.74	1.81	0.08	2.28
Hypertension	CSO-PVS severity	0.13	0.50	1.22	0.02	1.18
Diabetes	CSO-PVS severity	0.11	0.69	1.67	0.04	1.88

3.5. Performance Measurement for the Predictive Model

A performance metric was analyzed for AUCs for both the predictive model and conventional logistic regression model (Figure 5). The predictive model was cross-validated using K-fold (K = 5). As a result, the mean AUC was calculated as 0.80 ± 0.04. Performance of the conventional logistic regression model showed an AUC of 0.80 for the logistic regression model shown in Figure 5A,B, respectively.

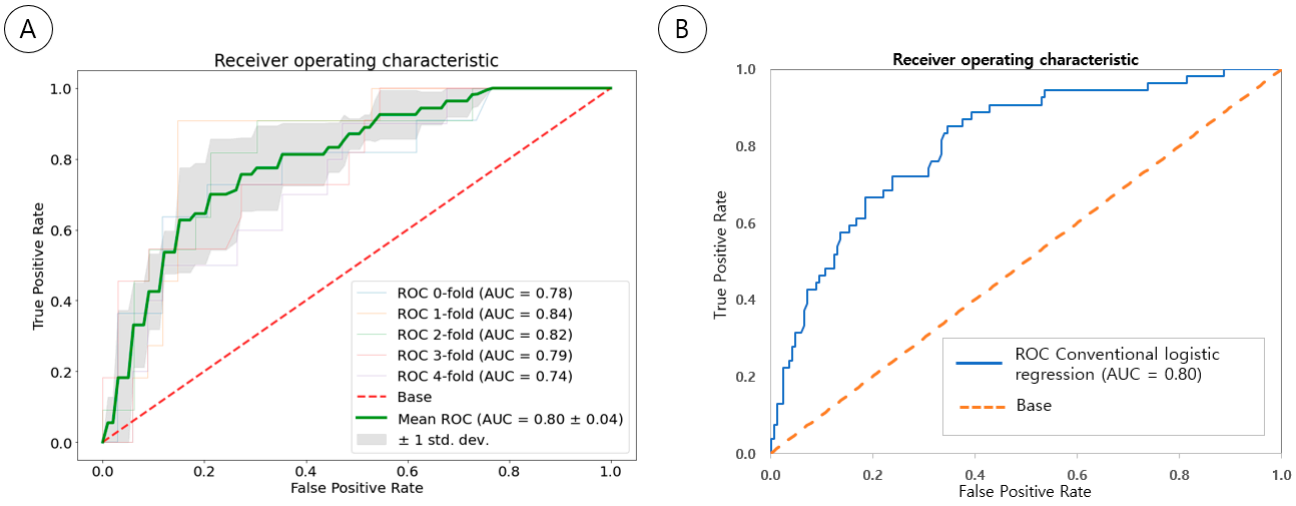

Figure 5. AUCs of the predictive model and classical logistic regression model: (**A**) K-fold cross validation (K = 5) of the XGBoost classifier (mean AUC 0.80 ± 0.04); and (**B**) AUC of the classical logistic regression model (AUC = 0.80).

4. Discussion

4.1. De Novo Hygroma with Mild TBI Using a Machine Learning Technique

In the field of neuroscience, studies are also being published that can expand the interface by adding new specific factors and defining the relationship between symptoms and diseases using machine learning technology [25–28]. Advances in this field are rapidly accelerating as improvements in neurological diagnosis and surgical treatment for the diagnosis and management of patients with TBI reduce mortality and improve patient care [8]. The cause of trauma in patients with TBI is epidemiologically diverse, including

battlefield injuries, traffic accidents, sports-related injuries, work-related accidents, head injuries in a criminal situation, and life injuries [8,9]. Studies have reported that an enlarged PVS is a radiological marker for patients with mild TBI [3,15,29–31]. Regarding PVS research using machine learning, studies using medical images are the main focus. Most studies have used a neural network for labeled images of enlarged PVS to detect and quantify the enlarged perivascular space on an MRI [32]. Particularly, in a study on risk factors using machine learning, Huang et al. performed PVS dilation using a convolutional neural network using T2 MR images of PVS in healthy elderly patients. In conclusion, it was reported that intracranial volume was associated with deep white matter PVS volume ($p < 0.001$) and that intracranial arterial diameter was related to cardiac matter PVS volume ($p = 0.032$) [33]. In contrast, our study was characterized by analyzing patient-specific risk factors contributing to enlarged PVS using explainable artificial intelligence techniques. In this study, the SHAP explainer was used to change the structure of a model that was difficult to interpret from a black-box model to a white-box one by applying explainable artificial intelligence techniques [34]. In this study, the overall feature importance was presented (Figure 2A). At this time, factors, such as age, CSO-PVS, and hypertension, were analyzed as major factors influencing the development of de novo hygroma, followed by trauma cause, sex, and diabetes. However, in the individual feature importance analysis, the severity of the CSO-PVS factor had a negative impact on the development of hygroma, and simultaneously, the contribution was the third smallest, and hypertension, trauma cause, and sex also showed the same impact (Figure 2A,B). Therefore, Figure 2B not only shows the priority of the risk factors contributing to the development of de novo hygroma but also indicates that the contribution to a specific patient is different, which provides a hint to the medical team for individual treatment of patients (e.g., consideration of the underlying diseases) (Figure 2B). In contrast, an analysis of a patient cohort was also possible, and it was found that the order of hypertension was different for factors contributing to the development of de novo hygroma (Figure 2D). Moreover, most patients aged more than 73.44 years had a high correlation (79.6% to 80.2%) with CSO-PVS severity for the development of hygroma. However, patients who had no or mild CSO-PVS had lower dependency (1.2%–55.5%) over the entire age, as shown in Figure 3B.

4.2. Data Mining Approach for Investigating the Causal Relationship

The concept of association rules became known to several researchers through the work of Agrawal et al. [23]. In other words, priorities are created to develop related rules by scoring and quantifying the rules for factors that exist in a specific dataset or database. This approach, applying association rules, based on a patient's past clinical history and current condition indicators, can be useful for doctors to treat patients [24,35,36]. A doctor's diagnosis and treatment must go through a very complex decision-making process, and errors that may occur in the final result of treatment may be included. Association rule mining is used to identify the causal relationship between symptoms for various external factors medically and to refer to the information of the combination of quantified causal relationships in the decision-making process that helps treatment [37,38]. Ho et al. used an association rule data mining method to analyze coexisting complications after TBI [37]. At this time, the mortality risk among post-TBI patients was evaluated based on variables, such as age, sex, clinical characteristics, length of stay, length of intensive care unit stay, length of noninvasive ventilation, and the Charlson comorbidity index score. Consequently, we identified that the most common post-TBI complication association analysis included acute respiratory failure and pneumonia due to upper respiratory tract infection. However, according to Ho et al., a shortcoming of the study was that the severity assessment based on the GCS and LOC used in our study was not considered. Therefore, our study is meaningful because it examined risk factors, including the cause of failure and severity, in patients with mild TBI in the field of neuroscience.

4.3. Cause of Trauma Analysis from the Perspective of TBI

Research on the head injury for subdural hygroma in the 1970s focused on the occurrence and treatment of hygroma rather than focusing on the diversity of causes of brain injury [39]. Oka et al. judged head injury based on LOC and classified symptoms including headache and vomiting. Additionally, the generation of subdural fluid was observed, and a review for appropriate image acquisition or surgical treatment was performed [39]. In the 2000s, studies considering more complex TBI-related factors were published. For example, based on MRI findings, Orrison et al. found a statistical relationship between the number of bouts and lateral ventricle size in 100 boxers and martial arts fighters. Relationships were identified, and a study was conducted to determine whether hitting through years of fighting was related to creating an enlarged PVS (p = 0.0388) by inducing pathological changes in players [31]. In the 2020s, research is being conducted to identify risk factors, treatment, and clinical results for posttraumatic hydrocephalus, and as part of this study, patients with mild TBI (mean GCS score = 14.84) were targeted, and the causes of the trauma were analyzed. Hitting is the fourth most severe among trauma causes (Table 1). Although the severity of damage among various causes of TBI is different, understanding the dependence of hygroma and trauma events can be attempted by analyzing the risk factors using explainable predictive modeling.

However, our future research can include more precise risk factors through examining the pathophysiology of TBI, including biochemical, genetic, genomic, and proteomic markers of inflammation, through which individual predictive diagnosis studies can be conducted.

4.4. XAI for Clinical Applications

Transparency and trust in artificial intelligence models are key factors in providing convincing results for researchers and users in an application called a clinical decision support system (CDSS) [40–42].

In the fields of neurosurgery and neuroscience, explainable artificial intelligence techniques are being actively studied [43,44]. In other words, XAI helps to overcome the limitations of simple numerical result analysis using existing statistical techniques by providing reasoning grounds for decisions necessary for the diagnosis and treatment of patients [27,28,45–47]. Therefore, healthcare professionals note the CDSS, which can utilize the clinical usefulness of XAI. The improvement of the patient's quality of life is provided by minimizing the possibility of human error that may occur in the patient's diagnosis and treatment process and is guaranteed by providing the best treatment prognosis when the cause of the disease is diversified.

4.5. Limitation of This Study

A machine learning approach is more flexible when applied to samples using a large size or big data, but this study used patient follow-up data collected at a single institution in a certain period. Hence, the nature of the relatively small sample size (n = 222) and the homogeneous patient population (patients of a single nationality with no racial diversity) should be considered entire analysis results. However, recognizing these limitations, cross-validation was applied for the performance validation. In the case of assessment for CSO-PVS severity, it was measured and rated on an axial T2-weighted MRI [48]. Enlarged PVSs were defined as the sharp structure of cerebrospinal fluid (CSF) signal intensity that followed the orientation of perforating arteries. Thus, after assessment of all relevant MRI slices, the unilateral section of the slice with the highest number of PVSs was recorded. To validate the authors' hypothesis, PVS severity in the centrum semiovale was categorized and PVS severity was interpreted by two board-certified neurosurgeons. At this step, Cohen's kappa value (0.78) was calculated to test reliability for the evaluation of CSO-PVS. Thus, this process for data curation should be addressed. As a result of comparison with the performance of conventional statistical techniques, mean AUC and AUC using machine learning were 0.80 + 0.04 and 0.80, respectively (Figure 5). In other words, numerical

comparisons between performance metrics in machine learning and conventional statistical models are within almost the same range of each performance metric. It is judged that a more meaningful comparison will be possible if a larger size of data is used in a further study. More specifically, the importance of this study was, first, to identify various risk factors (age, gender, CSO-PVS severity, underlying disease, and cause of trauma) associated with de novo hygroma in individual TBI patients for patient-specific customized treatment as a feasibility study using explainable predictive modeling. Second, the study aimed to address the probability of prediction results by deriving the correlation of each prognostic factor as the clinical decision support system (CDSS).

5. Conclusions

We analyzed patient risk factors for de novo hygroma in patients with TBI and identified detailed relationships for patient-specific customized treatment as a feasibility study using an explainable predictive model. Although this study has limitations in using a small sample size, potential bias, and single institutional population, it was confirmed that age and CSO-PVS severity showed a strong correlation with the development of de novo hygroma. Furthermore, the importance of the risk factors may vary in each patient according to the results of the feature importance analysis and association rule mining. In our future research, more diverse types of risk factors can be included for the development of more precise patient-specific customized treatments through pathophysiology analysis, including biochemical, genetic, genomic, and proteomic markers of inflammation.

Author Contributions: K.H.K. developed the analysis software and performed the analysis; B.-J.L. and H.-W.K. contributed to the interpretation of the results of the statistical analysis performed by K.H.K.; H.-W.K. conceived the presented idea and supervised the project; K.H.K. wrote the manuscript; B.-J.L. and H.-W.K. contributed to the interpretation of the results and to the writing of the final version of the manuscript. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: This study was approved by the Institutional Review Board of Inje University Ilsan Paik Hospital (IRB No. 2017-04-029). All ethical rules were followed during the study, and written informed consent was obtained from the participants.

Informed Consent Statement: Not applicable.

Data Availability Statement: Clinical data used in this study are approved by the IRB. Thus, data may not be used for any other purpose.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Heegaard, W.; Biros, M. Traumatic brain injury. *Emerg. Med. Clin. N. Am.* **2007**, *25*, 655–678. [CrossRef] [PubMed]
2. Bruns Jr, J.; Hauser, W.A. The epidemiology of traumatic brain injury: A review. *Epilepsia* **2003**, *44*, 2–10. [CrossRef]
3. Koo, H.-W.; Oh, M.; Kang, H.K.; Park, Y.K.; Lee, B.-J.; Han, S.R.; Yoon, S.W.; Choi, C.Y.; Sohn, M.-J.; Lee, C.H. High-degree centrum semiovale-perivascular spaces are associated with development of subdural fluid in mild traumatic brain injury. *PLoS ONE* **2019**, *14*, e0221788. [CrossRef]
4. Lange, R.T.; Brickell, T.A.; Ivins, B.; Vanderploeg, R.D.; French, L.M. Variable, not always persistent, postconcussion symptoms after mild TBI in US military service members: A five-year cross-sectional outcome study. *J. Neurotrauma* **2013**, *30*, 958–969. [CrossRef] [PubMed]
5. Dunne, J.; Quiñones-Ossa, G.A.; Still, E.G.; Suarez, M.N.; González-Soto, J.A.; Vera, D.S.; Rubiano, A.M. The epidemiology of traumatic brain injury due to traffic accidents in Latin America: A narrative review. *J. Neurosci. Rural. Pract.* **2020**, *11*, 287–290. [CrossRef] [PubMed]
6. Echemendia, R.J.; Julian, L.J. Mild traumatic brain injury in sports: Neuropsychology's contribution to a developing field. *Neuropsychol. Rev.* **2001**, *11*, 69–88. [CrossRef]
7. Mayer, A.R.; Quinn, D.K.; Master, C.L. The spectrum of mild traumatic brain injury: A review. *Neurology* **2017**, *89*, 623–632. [CrossRef]

8. Pervez, M.; Kitagawa, R.S.; Chang, T.R. Definition of traumatic brain injury, neurosurgery, trauma orthopedics, neuroimaging, psychology, and psychiatry in mild traumatic brain injury. *Neuroimaging Clin.* **2018**, *28*, 1–13. [CrossRef] [PubMed]
9. Esselman, P.C.; Uomoto, J. Classification of the spectrum of mild traumatic brain injury. *Brain Inj.* **1995**, *9*, 417–424. [CrossRef]
10. St John, J.; Dila, C. Traumatic subdural hygroma in adults. *Neurosurgery* **1981**, *9*, 621–626. [CrossRef]
11. Schachenmayr, W.; Friede, R. The origin of subdural neomembranes. I. Fine structure of the dura-arachnoid interface in man. *Am. J. Pathol.* **1978**, *92*, 53.
12. Kwee, R.M.; Kwee, T.C. Virchow-Robin spaces at MR imaging. *Radiographics* **2007**, *27*, 1071–1086. [CrossRef] [PubMed]
13. Smeijer, D.; Ikram, M.K.; Hilal, S. Enlarged perivascular spaces and dementia: A systematic review. *J. Alzheimer's Dis.* **2019**, *72*, 247–256. [CrossRef] [PubMed]
14. Opel, R.A.; Christy, A.; Boespflug, E.L.; Weymann, K.B.; Case, B.; Pollock, J.M.; Silbert, L.C.; Lim, M.M. Effects of traumatic brain injury on sleep and enlarged perivascular spaces. *J. Cereb. Blood Flow Metab.* **2019**, *39*, 2258–2267. [CrossRef] [PubMed]
15. Inglese, M.; Bomsztyk, E.; Gonen, O.; Mannon, L.J.; Grossman, R.I.; Rusinek, H. Dilated perivascular spaces: Hallmarks of mild traumatic brain injury. *Am. J. Neuroradiol.* **2005**, *26*, 719–724. [PubMed]
16. Chong, S.-L.; Liu, N.; Barbier, S.; Ong, M.E.H. Predictive modeling in pediatric traumatic brain injury using machine learning. *BMC Med. Res. Methodol.* **2015**, *15*, 1–9. [CrossRef]
17. Raj, R.; Luostarinen, T.; Pursiainen, E.; Posti, J.P.; Takala, R.S.; Bendel, S.; Konttila, T.; Korja, M. Machine learning-based dynamic mortality prediction after traumatic brain injury. *Sci. Rep.* **2019**, *9*, 17672. [CrossRef]
18. Hsu, S.-D.; Chao, E.; Chen, S.-J.; Hueng, D.-Y.; Lan, H.-Y.; Chiang, H.-H. Machine learning algorithms to predict in-hospital mortality in patients with traumatic brain injury. *J. Pers. Med.* **2021**, *11*, 1144. [CrossRef]
19. Cohen, S.; Ruppin, E.; Dror, G. Feature selection based on the shapley value. *Other Words* **2005**, *1*, 98Eqr.
20. Lundberg, S.M.; Erion, G.; Chen, H.; DeGrave, A.; Prutkin, J.M.; Nair, B.; Katz, R.; Himmelfarb, J.; Bansal, N.; Lee, S.-I. From local explanations to global understanding with explainable AI for trees. *Nat. Mach. Intell.* **2020**, *2*, 56–67. [CrossRef]
21. Gunning, D.; Stefik, M.; Choi, J.; Miller, T.; Stumpf, S.; Yang, G.-Z. XAI—Explainable artificial intelligence. *Sci. Robot.* **2019**, *4*, eaay7120. [CrossRef]
22. Ji, X.; Tong, W.; Liu, Z.; Shi, T. Five-feature model for developing the classifier for synergistic vs. antagonistic drug combinations built by XGBoost. *Front. Genet.* **2019**, *10*, 600. [CrossRef] [PubMed]
23. Agrawal, R.; Imieliński, T.; Swami, A. Mining association rules between sets of items in large databases. In Proceedings of the 1993 ACM SIGMOD international conference on Management of Data, Washington, DC, USA, May 1993; pp. 207–216.
24. Pazhanikumar, K.; Arumugaperumal, S. Association rule mining and medical application: A detailed survey. *Int. J. Comput. Appl.* **2013**, *80*. [CrossRef]
25. Kim, K.H.; Koo, H.-W.; Lee, B.-J.; Sohn, M.-J. Analysis of risk factors correlated with angiographic vasospasm in patients with aneurysmal subarachnoid hemorrhage using explainable predictive modeling. *J. Clin. Neurosci.* **2021**, *91*, 334–342. [CrossRef]
26. Kim, K.H.; Koo, H.-W.; Lee, B.-J.; Yoon, S.-W.; Sohn, M.-J. Cerebral hemorrhage detection and localization with medical imaging for cerebrovascular disease diagnosis and treatment using explainable deep learning. *J. Korean Phys. Soc.* **2021**, *79*, 321–327. [CrossRef]
27. Staartjes, V.E.; Stumpo, V.; Kernbach, J.M.; Klukowska, A.M.; Gadjradj, P.S.; Schröder, M.L.; Veeravagu, A.; Stienen, M.N.; van Niftrik, C.H.; Serra, C. Machine learning in neurosurgery: A global survey. *Acta Neurochir.* **2020**, *162*, 3081–3091. [CrossRef] [PubMed]
28. Raju, B.; Jumah, F.; Ashraf, O.; Narayan, V.; Gupta, G.; Sun, H.; Hilden, P.; Nanda, A. Big data, machine learning, and artificial intelligence: A field guide for neurosurgeons. *J. Neurosurg.* **2020**, *1*, 1–11. [CrossRef] [PubMed]
29. Inglese, M.; Grossman, R.I.; Diller, L.; Babb, J.S.; Gonen, O.; Silver, J.M.; Rusinek, H. Clinical significance of dilated Virchow-Robin spaces in mild traumatic brain injury. *Brain Inj.* **2006**, *20*, 15–21. [CrossRef]
30. Wu, Y.; Wu, H.; Zeng, J.; Pluimer, B.; Dong, S.; Xie, X.; Guo, X.; Ge, T.; Liang, X.; Feng, S. Mild traumatic brain injury induces microvascular injury and accelerates Alzheimer-like pathogenesis in mice. *Acta Neuropathol. Commun.* **2021**, *9*, 1–14. [CrossRef]
31. Orrison Jr, W.W.; Hanson, E.H.; Alamo, T.; Watson, D.; Sharma, M.; Perkins, T.G.; Tandy, R.D. Traumatic brain injury: A review and high-field MRI findings in 100 unarmed combatants using a literature-based checklist approach. *J. Neurotrauma* **2009**, *26*, 689–701. [CrossRef]
32. Moses, J.; Sinclair, B.; Law, M.; O'Brien, T.J.; Vivash, L. Automated Methods for Detecting and Quantitation of Enlarged Perivascular spaces on MRI. *J. Magn. Reson. Imaging* **2022**, *57*, 11–24. [CrossRef] [PubMed]
33. Huang, P.; Zhu, Z.; Zhang, R.; Wu, X.; Jiaerken, Y.; Wang, S.; Yu, W.; Hong, H.; Lian, C.; Li, K. Factors associated with the dilation of perivascular space in healthy elderly subjects. *Front. Aging Neurosci.* **2021**, *13*, 624732. [CrossRef] [PubMed]
34. Barda, A.J.; Horvat, C.M.; Hochheiser, H. A qualitative research framework for the design of user-centered displays of explanations for machine learning model predictions in healthcare. *BMC Med. Inform. Decis. Mak.* **2020**, *20*, 257. [CrossRef]
35. Klann, J.G.; Szolovits, P.; Downs, S.M.; Schadow, G. Decision support from local data: Creating adaptive order menus from past clinician behavior. *J. Biomed. Inform.* **2014**, *48*, 84–93. [CrossRef] [PubMed]
36. Perçın, İ.; Yağin, F.H.; Güldoğan, E.; Yoloğlu, S. ARM: An interactive web software for association rules mining and an application in medicine. In Proceedings of the 2019 International Artificial Intelligence and Data Processing Symposium (IDAP), Malatya, Turkey, 21–22 September 2019; pp. 1–5.

37. Ho, C.-H.; Liang, F.-W.; Wang, J.-J.; Chio, C.-C.; Kuo, J.-R. Impact of grouping complications on mortality in traumatic brain injury: A nationwide population-based study. *PLoS ONE* **2018**, *13*, e0190683. [CrossRef]
38. Tandan, M.; Acharya, Y.; Pokharel, S.; Timilsina, M. Discovering symptom patterns of COVID-19 patients using association rule mining. *Comput. Biol. Med.* **2021**, *131*, 104249. [CrossRef]
39. Oka, H.; Motomochi, M.; Suzuki, Y.; Ando, K. Subdural hygroma after head injury. *Acta Neurochir.* **1972**, *26*, 265–273. [CrossRef]
40. Holzinger, A.; Langs, G.; Denk, H.; Zatloukal, K.; Müller, H. Causability and explainability of artificial intelligence in medicine. *Wiley Interdiscip. Rev. Data Min. Knowl. Discov.* **2019**, *9*, e1312. [CrossRef]
41. Handelman, G.S.; Kok, H.K.; Chandra, R.V.; Razavi, A.H.; Huang, S.; Brooks, M.; Lee, M.J.; Asadi, H. Peering into the black box of artificial intelligence: Evaluation metrics of machine learning methods. *Am. J. Roentgenol.* **2019**, *212*, 38–43. [CrossRef]
42. Markus, A.F.; Kors, J.A.; Rijnbeek, P.R. The role of explainability in creating trustworthy artificial intelligence for health care: A comprehensive survey of the terminology, design choices, and evaluation strategies. *J. Biomed. Inform.* **2021**, *113*, 103655. [CrossRef]
43. Mirchi, N.; Bissonnette, V.; Yilmaz, R.; Ledwos, N.; Winkler-Schwartz, A.; Del Maestro, R.F. The Virtual Operative Assistant: An explainable artificial intelligence tool for simulation-based training in surgery and medicine. *PloS ONE* **2020**, *15*, e0229596. [CrossRef]
44. Choi, K.S.; Choi, S.H.; Jeong, B. Prediction of IDH genotype in gliomas with dynamic susceptibility contrast perfusion MR imaging using an explainable recurrent neural network. *Neuro-Oncol.* **2019**, *21*, 1197–1209. [CrossRef] [PubMed]
45. Yoo, T.K.; Ryu, I.H.; Choi, H.; Kim, J.K.; Lee, I.S.; Kim, J.S.; Lee, G.; Rim, T.H. Explainable machine learning approach as a tool to understand factors used to select the refractive surgery technique on the expert level. *Transl. Vis. Sci. Technol.* **2020**, *9*, 8. [CrossRef] [PubMed]
46. Celtikci, E. A systematic review on machine learning in neurosurgery: The future of decision-making in patient care. *Turk Neurosurg* **2018**, *28*, 167–173. [CrossRef] [PubMed]
47. Buchlak, Q.D.; Esmaili, N.; Leveque, J.-C.; Farrokhi, F.; Bennett, C.; Piccardi, M.; Sethi, R.K. Machine learning applications to clinical decision support in neurosurgery: An artificial intelligence augmented systematic review. *Neurosurg. Rev.* **2020**, *43*, 1235–1253. [CrossRef]
48. Richens, D.; Kotidis, K.; Neale, M.; Oakley, C.; Fails, A. Rupture of the aorta following road traffic accidents in the United Kingdom 1992–1999. The results of the co-operative crash injury study. *Eur. J. Cardio-Thorac. Surg.* **2003**, *23*, 143–148. [CrossRef] [PubMed]