

Transient acute hydrocephalus after aneurysmal subarachnoid hemorrhage and aneurysm embolization: a single-center experience

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ABSTRACT

Title

Transient acute hydrocephalus after aneurysmal subarachnoid hemorrhage and aneurysm embolization: a single center experience

Purpose

Acute hydrocephalus is a common complication after aneurysmal subarachnoid hemorrhage (aSAH). It can be self-limiting or require cerebrospinal fluid diversion. We aimed to determine the transient acute hydrocephalus (TAH) rate in patients with aSAH treated endovascularly and evaluate its predictive factors.

Methods

A retrospective review of 357 patients with aSAH who underwent endovascular treatment from March 2013 to December 2019 was performed. Clinical and radiographic data were analyzed and risk factors with potential significance for acute hydrocephalus were identified. We constructed a new risk score, the Drainage Or Transiency of Acute Hydrocephalus after Aneurysmal SAH (DOTAHAS) score, that may differentiate patients who would experience TAH from those needing surgical interventions.

Results

Acute hydrocephalus occurred in 129 patients (36%), out of whom in 66 patients (51%) it was self-limiting while 63 patients (49%) required external ventricular drainage placement. As independent risk factors for acute hydrocephalus, we identified older age, poor initial clinical condition, aSAH from posterior circulation, and the extent of cisternal and intraventricular hemorrhage. The following three factors were shown to predict acute hydrocephalus transiency and therefore included in the DOTAHAS score, ranging from 0 to 7 points: Hunt and Hess grade ≥ 3 (1 point), modified Fisher grade 4 (2 points), and Ventricular Hijdra Sum Score (vHSS) ≥ 6 (4 points). Patients scoring ≥ 3 points had significantly higher risk for EVD ($P < 0.0001$) than other patients.

Conclusion

The newly developed DOTAHAS score can be useful in identifying patients with transient acute hydrocephalus. Further score evaluation is needed.

Keywords

Acute hydrocephalus; Aneurysmal subarachnoid hemorrhage; EVD; Risk score; TAH

Transient acute hydrocephalus after aneurysmal subarachnoid hemorrhage and aneurysm embolization: a single center experience

INTRODUCTION

Hydrocephalus (HCP) is a common complication of aneurysmal subarachnoid hemorrhage (aSAH), with the incidence varying between 6.5% and 67% [1]. Generally complicates 20%–35% of aSAH patients [1, 2].

The acute phase can be self-limiting[3], while some patients require a cerebrospinal fluid (CSF) diversion [4]. External ventricular drain (EVD) placement is the usual treatment for patients with acute hydrocephalus (aHCP) after aSAH [5]. A temporary EVD is needed in 15%–87% of aSAH patients [6].

Since the 1980s, investigators reported risk factors related to aHCP. The amount of intraventricular blood was first identified as a risk factor [7]. In patients without intraventricular blood, the risk of aHCP was found to be significantly higher in cases with a higher amount of subarachnoid blood [8]. Higher risk for aHCP has been reported in patients with aSAH from posterior circulation aneurysms [9, 10]. In up to 50% of patients, spontaneous resolution of aHCP was found to occur within 24 hours [11].

We wondered if there might be a possibility to predict who would experience transient acute hydrocephalus (TAH). We decided to identify the factors related to aHCP development in our series of patients treated exclusively endovascularly and compare them with previous reports. Only a few studies were conducted, and risk scores constructed focused on the development of shunt-dependent hydrocephalus (SDHC) [6, 12]. These studies inspired us to develop a likewise simple score from easily obtainable clinical parameters that may differentiate patients who would experience TAH from those who need CSF diversion. This score may help to decide make the decision whether to treat aHCP immediately surgically.

METHODS

Patients

Medical records and radiological findings of 452 consecutive patients with aSAH admitted and treated endovascularly in our institution from March 2013 to December 2019 were analyzed retrospectively after the Institutional Ethics Committee approved the study. Written informed consent was obtained from all patients. The study's exclusion criteria were previous significant cerebral infarction, in-hospital mortality, CSF diversion due to causes other than HCP, and any missing data during the follow-up.

We finally recruited 357 patients to construct a risk score that may differentiate patients who would experience TAH from those who need surgical interventions.

Diagnosis of SAH

Patients were diagnosed with aSAH by the presence of blood on a CT scan or xanthochromic CSF in combination with an aneurysm confirmed by CT or digital subtraction angiography (DSA).

All of the patients received brain CT scans in the emergency room. In 6 patients with sudden headache and normal head CT, lumbar puncture confirmed SAH. All the patients had a physical examination upon arrival at our institution. Their Hunt and Hess grades before aneurysm repair were scored by a neurologist from the Neurointensive Care Unit.

CT scans were acquired on the 128-detector row CT (SOMATOM Definition AS+, Siemens, Forchheim, Germany).

The CT images were analyzed separately by two interventional neuroradiologists. The amount and distribution of the hemorrhage in subarachnoid spaces and the ventricles were determined using Fisher scale [13], modified Fisher scale [14], Barrow Neurological Institute (BNI) grading scale [15], and grading scale proposed by Hijdra [16].

The BNI score was evaluated as reported by Wilson et al.[15], measuring the maximal subarachnoid blood clot perpendicular to the direction of the cistern or fissure on the axial scan. The calculation of the Hijdra score was performed by evaluating the amount of subarachnoid and intraventricular blood as described by Hijdra [16, 17].

DSA and Intervention

We performed CT angiography in all SAH patients in order to confirm the ruptured aneurysm. The decision for endovascular treatment was made based on the patient's clinical status, location, and the angioarchitecture of the aneurysm. We categorized aneurysms by location and size (<5 mm, 5 to 10 mm, and >10 mm).[18]

Diagnosis of Hydrocephalus

HCP may be present immediately after the hemorrhage or develop later in the course of aSAH. All of the patients received brain CT scans in the emergency room. The first post-embolization follow-up brain CT scan was performed in all patients at 24 hours. Sequential CT scans were performed depending on the patient's clinical status. Emergency brain CT scans were done in case of clinical deterioration, new-onset focal neurologic deficits, seizures, or progressive loss of consciousness.

Hydrocephalus was assessed retrospectively based on the description given by Jartti and colleagues[19]; based on a visual impression by observing ventricular size, significantly dilated temporal horn of the lateral ventricles in the absence of evident brain atrophy, rounded frontal horns, and diminished cerebral sulci. The effect of the amount and distribution of blood on the CT scan was taken into consideration.

For linear measures of ventricular size, we determined the Evan's and bicaudate index (BCI) [20, 21]. Age-adjusted relative sizes were calculated by dividing the BCI's by the corresponding upper limit (95th percentile) per age group [7, 22].

Acute hydrocephalus was defined as the development of ventricle enlargement within 72 hours of the aneurysmal rupture [1]. The diagnosis of hydrocephalus was made only in case of consensus and if fulfilling the required criteria.

Immediate EVD was performed if the consciousness deterioration was thought to be related to HCP. In patients with lower Hunt and Hess grades (≤ 3) and ventricle enlargement but unimpaired or mildly impaired consciousness, we advocated close monitoring and repeated CT scans to evaluate ventricular changes instead of deciding for immediate EVD placement. If consciousness impaired and no other reason for this impairment was found, EVD was carried out. Cases of resolution of aHCP and clinical improvement were regarded as TAH. Transiency

of aHCP was confirmed on a 3-month follow-up MR examination, which is our standard follow-up protocol.

Statistical Analysis and Score Design

Continuous data distribution was assessed using the Kolmogorov-Smirnov test, and depending on the results, appropriate non-parametric tests were used in the analyses that followed. A chi-square test was used to determine differences in categorical clinical variables except in cases when there were less than 10 participants per cell when Fisher's exact test was used. The mann-Whitney U test was used to analyze differences in continuous variables. All scores that were significant in bivariate analysis were used in multivariate analysis and construction of DOTAHAS prediction score. Cut-off values of continuous variables were made based on the optimal ratio of sensitivity and specificity (Youden index J). Binary logistic regression was used as a multivariate method in the prediction of EVD. Confidence intervals for sensitivity and specificity were "exact" Clopper-Pearson confidence intervals. *P* values below 0.05 were considered significant. MedCalc® Statistical Software version 19.6.1 (MedCalc Software Ltd, Ostend, Belgium; <https://www.medcalc.org>; 2020) was used in all statistical procedures.

RESULTS

Patient Characteristics

452 consecutive patients with aSAH were treated in our institution endovascularly between March 2013 and December 2019. Of them, 357 patients survived the initial phase had neither significant cerebral infarction nor CSF diversion due to other causes than HCP (Figure 1). There were 242 female patients (67,8%) and 115 male patients (32,2%), and their mean age was 56,59±12,79 years. The demographic and clinical characteristics and factors with potential significance for aHCP development are listed in Table 1.

Acute Hydrocephalus

In 95 (27%) of the 357 patients, HCP was present on the initial CT scan. Furthermore, additional 34 patients developed HCP within 72 hours. Altogether 129 patients were diagnosed with aHCP, among whom 66 patients experienced TAH, while 63 patients needed EVD placement. Patients with aHCP on initial CT scan were significantly older ($P = 0.030$).

Poorer initial clinical condition, amount of cisternal hemorrhage using BNI, modified Fisher and Hijdra scales, intraventricular hemorrhage (IVH), the amount of IVH using Hijdra scale, and SAH from posterior circulation were identified as significant risk factors for aHCP. Gender, intracerebral hemorrhage (ICH), and aneurysm size were without predictive significance (Table 1).

Risk Factors for EVD

Factors related to the transiency of acute hydrocephalus are shown in Table 2. In the EVD group, there were significantly higher values of Hunt and Hess grade ($P < 0.001$), modified Fisher grade ($P = 0.035$), ventricular Hijdra score ($P < 0.001$), and rBCI ($P = 0.001$) and Evans' index ($P = 0.001$) on the initial CT scans.

In the EVD group HCP on initial CT was also significantly more prevalent: 53 (84.1%) vs. 42 (63.6%), $P = 0.008$, as well as intracerebral haemorrhage (ICH) at the initial CT: 21 (33.3%)

vs. 5 (7.6%), $P < 0.001$. There was no significant difference in gender, age, BNI score, subarachnoid Hijdra score, IVH at the initial CT, aneurysm size, and localization.

Construction of DOTAHAS Prediction Score

Previously significant categorical variables (aHCP and ICH at the initial CT) were interpreted on a binary basis (pathological vs non-pathological findings). ROC curve analysis and optimal cut-off values for significant continuous clinical variables in the prediction of EVD are shown in Table 3.

All categorized values were used in the multivariate regression model to predict the chance of belonging to the EVD group (Table 4). A binary logistic regression model was significant ($P < 0.001$) with 53.1% of the explained variance of the dependent variable (EVD). Only three variables in the multivariate model were significant: Ventricular Hijdra score (>5) with OR: 14.46 (95% CI: 3.86-54.19), modified Fisher grade (>3) with OR: 7.85 (95% CI: 1.67-36.80) and Hunt and Hess grade (>2) with OR: 3.47 (95% CI: 1.33-9.08), controlled for the influence of all other predictor variables in the regression model. We calculated proposed weighting scores with those significant OR: ventricular Hijdra score (>5) with 4 points, modified Fisher grade (>3) with 2 points (2 times less than the previous score), and Hunt and Hess grade (>2) with 1 point (2 times less than the previous score).

The scoring sensitivity and specificity of our new score in EVD detection are shown in Table 5.

Optimal criterion of DOTAHAS score was >2 , with corresponding area under the ROC curve (AUC) 0.832; 95% CI: 0.756 to 0.892 and significance level $P < 0.001$. The DOTAHAS score distribution is shown in Figure 2. Among EVD patients, pathological score values (>2) were present in 53 (84.1%) while in TAH patients only in 22 (33.3%) cases, resulting in significant OR of predicting EVD 10.6 times (95% CI 4.56-24.74) $P < 0.001$.

ROC curve comparisons of DOTAHAS score with other significant continuous scores is shown in Figure 3. AUC for EVD score was significantly better ($P < 0.05$) than all other scores except Hunt and Hess grade with a p-value of borderline significance ($P = 0.066$).

DISCUSSION

EVD is the standard of care in managing aHCP following aSAH.[4] The decision to perform EVD may be doubted because of its most frequent complications, e.g., severe cerebrospinal liquor infection, hemorrhage along the catheter tract, and catheter malposition [23].

According to *AHA/ASA Guidelines for the Management of Aneurysmal Subarachnoid Hemorrhage* symptomatic aHCP should be managed by cerebrospinal fluid diversion (EVD or lumbar drainage, depending on the clinical scenario; Class I, Level B) [4].

Nonetheless, indications for EVD after aSAH remains still non-standardized and subject to discussion [24].

aHCP may not be the sole cause of clinical deterioration, and besides, may resolve spontaneously within 24 hours in half of the patients with acute hydrocephalus and unimpaired consciousness on admission [11], which additionally opens the question about the pathophysiology of that form of hydrocephalus [25].

Guided by the idea of potential aHCP transiency, we identified single risk factors to create a new predictive risk score in our retrospective single center study.

We identified intraventricular and cisternal hemorrhage as the most crucial determinants for aHCP development. Our data are in partial accordance with van Gijn et al. [7], who reported aHCP associated with the extent of IVH but not with cisternal hemorrhage and site of the

ruptured aneurysm. Hasan et al.[8] found the same, and besides, showed a higher amount of cisternal blood, especially in ambient cisterns, to be a risk factor for aHCP in the absence of IVH. We analyzed only the total extent of cisternal blood regardless of the thickness of blood in different cisterns.

Higher IVH prevalence than in the previous series (97% compared to 47% found by Hasan et al.) arises from the various grading scales used (Fisher vs. Hijdra scale) and variances in determining the presence of IVH.

The rate of aHCP is higher than in the previous series, where it occurred in 20% on the initial CT scan [7, 8], and up to 24% within the first week [8].

Our results are in accordance with Mehta et al., who found the incidence of aHCP to be 31%, and the grade of SAH, IVH, and posterior circulation aneurysms to be significantly related to aHCP development.[9]

The rate of acute hydrocephalus transiency is in keeping with the results presented by Hasan et al [11]. Identification of single risk factors does not assess the chance of transiency of HCP after aSAH.

Inspired by studies that constructed risk scores for SDHC development [6, 12], we correlated single risk factors with aHCP transiency. The new risk score, named DOTAHAS (the Drainage or Transiency of Acute Hydrocephalus after Aneurysmal SAH) score, was constructed based on parameters that showed significance in our multivariate analysis.

According to this statistical model, we have assigned each parameter's weight in developing aHCP. The following factors proved to predict who would experience TAH and were included in the score, ranging from 0 to 7 points: Hunt and Hess grade ≥ 3 (1 point), modified Fisher grade 4 (2 points), and ventricular Hijdra Sum Score (vHSS) ≥ 6 (4 points).

To the best of our knowledge, our retrospective single center study is the first one focused on predictors for transiency of aHCP, with the risk score developed to differentiate patients who need EVD placement from those who may experience transient acute posthemorrhagic hydrocephalus.

Such a risk score may help avoid unnecessary EVD and EVD-associated complications in patients who may suffer from self-limiting acute hydrocephalus.

Although we aimed to develop a simple risk score that may improve the ability to recognize patients who will not need surgical intervention, each patient's individualized treatment strategy should be of concern when assessing the need for CSF diversion.

The proposed DOTAHAS score may serve as a supporting diagnostic tool for the early prediction of hydrocephalus transiency. In the future, it may be a reasonable argument for EVD placement delay, which might reduce the number of EVD-related complications, decrease the length of hospital stay, and lower hospitalization expense.

Study Limitations

Our study's main limitations are its retrospective nature, restriction to single center and exclusively endovascularly treated patients and lack of further validation of the newly constructed score. A relatively large cohort reduced lower completeness of recorded data. All the patients with any missing data were excluded from the study. Bias due to adherence to the single center protocol was overcome in the data analysis. First, the CT images were analyzed separately by two experienced neuroradiologists. Second, the diagnosis of hydrocephalus for this study was made only in case of consensus and if fulfilling the required criteria; development of ventricle enlargement based on defined linear indices and the definition given by Jarri and al. We also excluded patients who did not meet the criteria mentioned above, although they were initially treated as having hydrocephalus and have received EVD. Since the ventricular drainage strategies differ among centers, further validation on other SAH cohorts is needed.

CONCLUSION

Our data show that the proposed DOTAHAS score, consisting of 3 easily obtainable and straightforward clinical and radiological parameters, can predict who would experience transient acute hydrocephalus early in the course of aSAH. A prospective score evaluation is required to see if the DOTAHAS score can reach future clinical recognition.

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FIGURE LEGENDS

Figure 1. Flow chart demonstrating sample selection and distribution of patients.

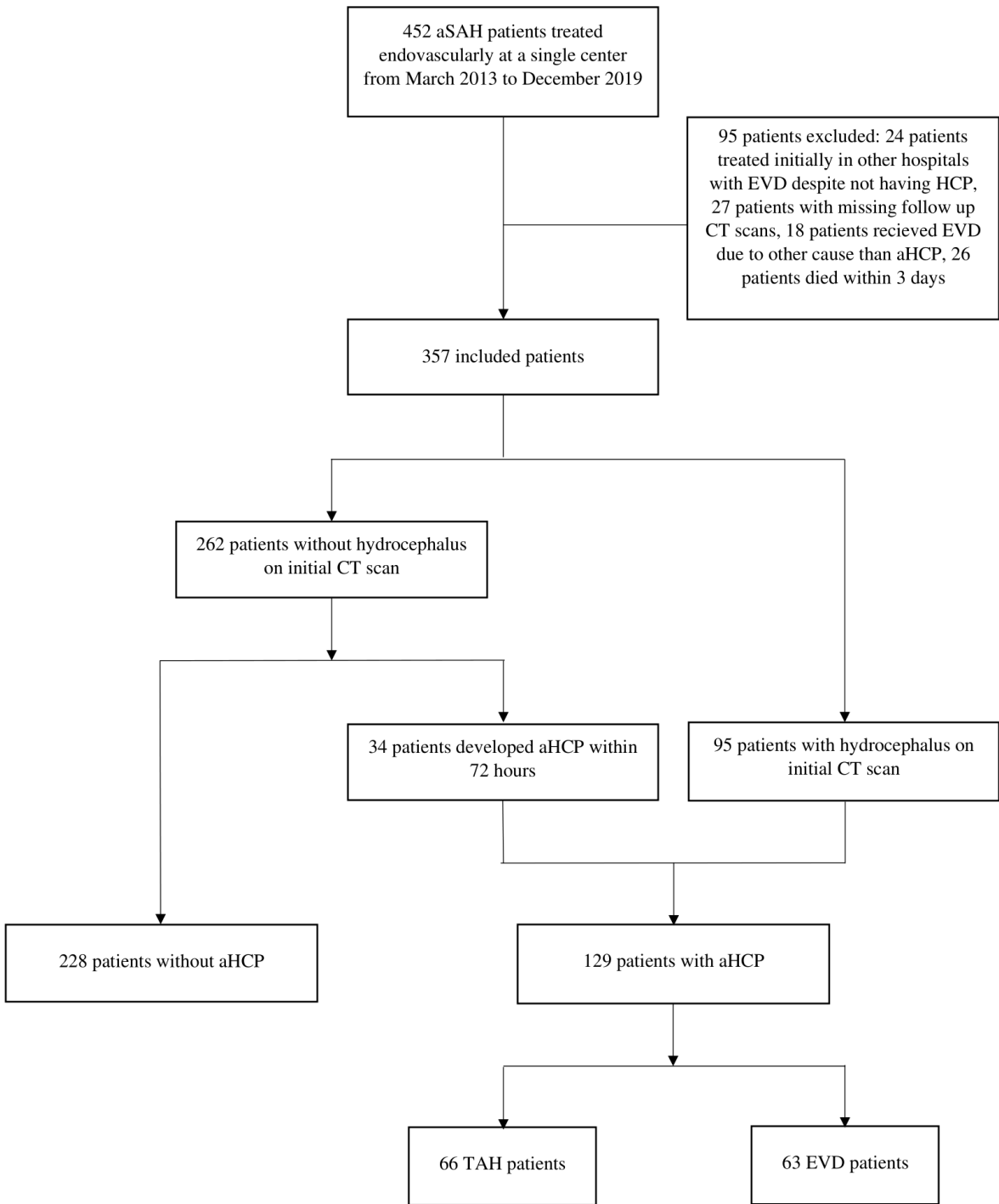
aSAH = after aneurysmal subarachnoid hemorrhage; EVD = external ventricular drain; HCP = hydrocephalus; aHCP = acute hydrocephalus; CT = computed tomography; TAH = transient acute hydrocephalus.

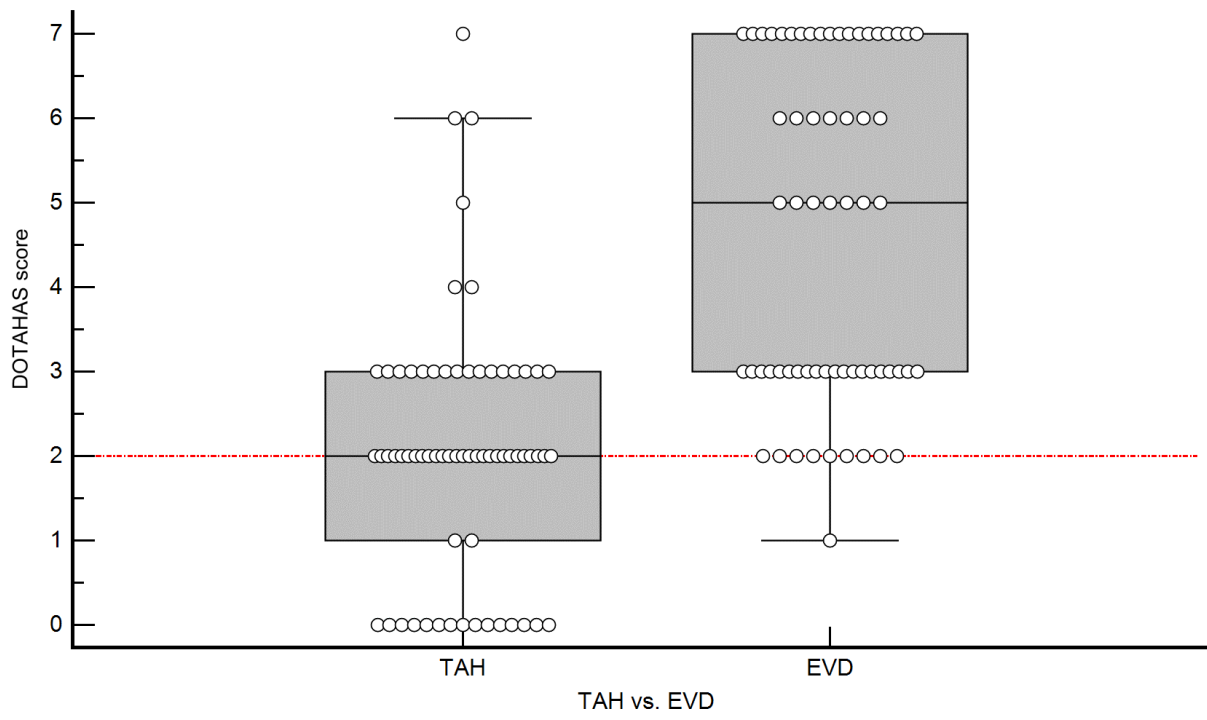
Figure 2. Differences in the distribution of DOTAHAS scores between patients with transient acute hydrocephalus and external ventricular drain.

DOTAHAS = the Drainage or Transiency of Acute Hydrocephalus after Aneurysmal SAH score; TAH = transient acute hydrocephalus; EVD = external ventricular drain.

Figure 3. ROC curve comparison of DOTAHAS score with other significant continuous scores.

ROC = receiver operating characteristic curve; DOTAHAS = the Drainage or Transiency of Acute Hydrocephalus after Aneurysmal SAH score.





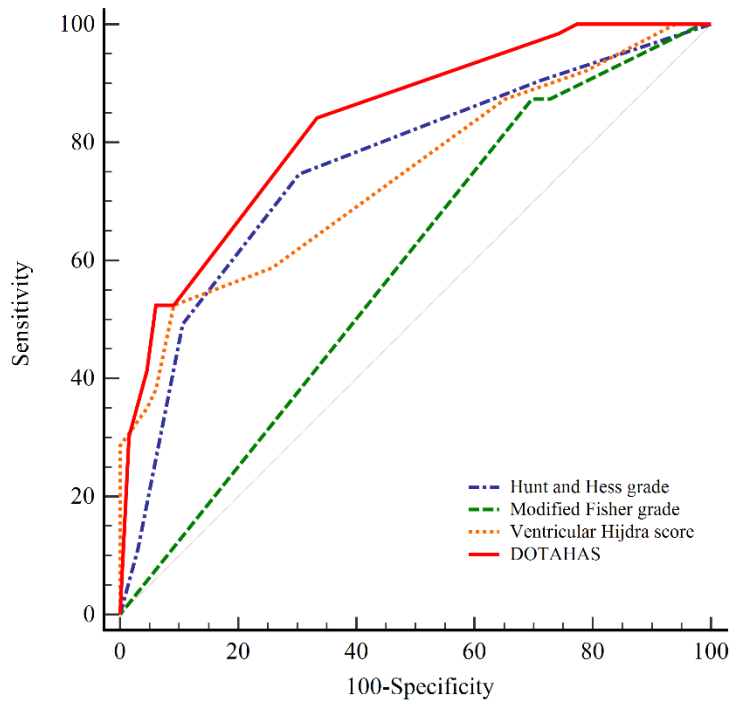


Table 1. Comparison of baseline characteristics between patients with and without acute hydrocephalus.

	Without acute hydrocephalus n=228	With acute hydrocephalus n=129	P value
Women gender: n (%)	151 (66.2)	91 (70.5)	0.402
Age in years: median (IQR)	57.0 (48.0-63.0)	59.0 (52.0-67.0)	0.030
Hunt and Hess grade: n (%)			< 0.001
	1 126 (55.3)	25 (19.4)	
	2 50 (21.9)	37 (28.7)	
	3 42 (18.4)	29 (22.5)	
	4 8 (3.5)	29 (22.5)	
	5 2 (0.9)	9 (7.0)	
Modified Fisher grade: n (%)			< 0.001
	0 7 (3.1)	0 (0.0)	
	1 56 (24.6)	1 (0.8)	
	2 28 (12.3)	25 (19.4)	
	3 39 (17.9)	2 (1.6)	
	4 98 (43.0)	101 (78.3)	
BNI Score: n (%)			< 0.001
	1 7 (3.1)	0 (0.0)	
	2 85 (37.3)	28 (21.7)	
	3 80 (35.1)	40 (31.0)	
	4 52 (22.8)	60 (46.5)	
	5 4 (1.8)	1 (0.8)	
Hijdra score: median (IQR)	12.0 (6.0-20.0)	22.0 (15.0-26.0)	< 0.001
Subarachnoid Hijdra score: median (IQR)	11.0 (5.0-18.0)	17.0 (11.0-22.0)	< 0.001
Ventricular Hijdra score: median (IQR)	1.0 (0.0-3.0)	4.0 (4.0-6.0)	< 0.001
IVH at the initial CT: n (%)	124 (54.4)	125 (96.9)	< 0.001
ICH at the initial CT: n (%)	39 (17.1)	26 (20.2)	0.473
Posterior circulation: n (%)	29 (12.7)	43 (33.3)	< 0.001
Aneurysm size (mm): median (IQR)	6.0 (4.0-8.0)	6.0 (4.0-8.0)	0.450

CT = computed tomography; n = number; IQR=interquartile range; EVD = external ventricular drain; TAH = transient acute hydrocephalus; BNI = Barrow Neurological Institute; rBCI = relative bicaudate index; IVH = intraventricular hemorrhage; ICH = intracerebral hemorrhage. Bold numbers indicate significant associations.

Table 2. Comparison of characteristics between patients with transient acute hydrocephalus and external ventricular drain.

	TAH N=66	EVD N=63	P value
Women gender: n (%)	51 (77.3)	40 (63.5)	0.122
Age in years: median (IQR)	57.0 (45.5-65.3)	61.0 (53.0-70.0)	0.062
Hunt and Hess grade: n (%)			< 0.001
	1 19 (28.8)	6 (9.5)	
	2 27 (40.9)	10 (15.9)	
	3 13 (19.7)	16 (25.4)	
	4 5 (7.6)	24 (38.1)	
	5 2 (3.0)	7 (11.1)	
Modified Fisher grade: n (%)			0.035
	1 1 (1.5)	0 (0.0)	
	2 17 (25.8)	8 (12.7)	
	3 2 (3.0)	0 (0.0)	
	4 46 (69.7)	55 (87.3)	
BNI Score: n (%)			0.128
	1 0 (0.0)	0 (0.0)	
	2 19 (28.8)	9 (14.3)	
	3 20 (30.3)	20 (31.7)	
	4 27 (40.9)	33 (52.4)	
	5 0 (0.0)	1 (1.6)	
Hijdra score: median (IQR)	20.0 (12.0-26.0)	23.0 (17.0-28.0)	0.022
Subarachnoid Hijdra score: median (IQR)	16.0 (9.8-22.0)	18.0 (12.0-22.0)	0.439
Ventricular Hijdra score: median (IQR)	4.0 (3.0-5.0)	6.0 (4.0-9.0)	< 0.001
Acute hydrocephalus: n (%)	42 (63.6)	53 (84.1)	0.008
rBCI index: median (IQR)	1.05 (0.94-1.15)	1.15 (1.00-1.24)	0.001
Evans' index: median (IQR)	0.29 (0.27-0.32)	0.32 (0.30-0.34)	0.001
IVH at the initial CT: n (%)	62 (93.9)	63 (100.0)	0.120
ICH at the initial CT: n (%)	5 (7.6)	21 (33.3)	< 0.001
Posterior circulation: n (%)	22 (33.3)	21 (33.3)	1.000
Aneurysm size (mm): median (IQR)	5.3 (4.0-8.0)	6.0 (4.0-8.0)	0.497

TAH = transient acute hydrocephalus; EVD = external ventricular drain; n = number; IQR=interquartile range; BNI = Barrow Neurological Institute; rBCI = relative bicaudate index; CT = computed tomography; IVH = intraventricular hemorrhage; ICH = intracerebral hemorrhage. Bold numbers indicate significant associations.

Table 3. Receiver operating characteristic curve analysis and optimal cut-off values for significant continuous clinical variables in prediction of external ventricular drain.

	Area under the ROC curve (AUC)	95% CI	Youden index <i>J</i>	Associated criterion	Sensitivity (%)	Specificity (%)	<i>P</i> value
Hunt and Hess grade	0.758	0.675 to 0.829	0.44	> 2	74.60	69.70	< 0.001
Modified Fisher grade	0.587	0.497 to 0.673	0.18	> 3	87.30	30.30	0.014
Evans' index	0.674	0.586 to 0.754	0.32	> 0.29	77.78	54.55	< 0.001
Ventricular Hijdra score	0.742	0.658 to 0.815	0.43	> 5	52.38	90.91	< 0.001
rBCI index	0.675	0.587 to 0.755	0.31	> 1.1	58.73	72.73	< 0.001

ROC = receiver operating characteristic curve; AUC = area under the ROC curve; CI = confidence interval; rBCI = relative bicaudate index. Bold numbers indicate significant associations. Bold numbers indicate significant associations.

Table 4. Construction of the DOTAHAS score based on the significant variables from the multivariate regression model in prediction of external ventricular drainage and proposed weighting score.

<i>P</i> value <0.001; R ² =53.1%	OR	95% CI		<i>P</i> value	Proposed weighting score
		Lower	Upper		
Hunt and Hess grade (>2)	3.47	1.33	9.08	0.011	1
Modified Fisher grade (>3)	7.85	1.67	36.80	0.009	2
Evans' index (>0.29)	2.38	0.63	9.06	0.203	0
Positive ICH at the initial CT	3.33	0.90	12.33	0.072	0
Ventricular Hijdra score (>5)	14.46	3.86	54.19	<0.001	4
rBCI index (>1.1)	2.55	0.78	8.37	0.123	0
Acute hydrocephalus at the initial CT	0.30	0.06	1.35	0.115	0

R² = coefficient of determination; OR = odds ratio; CI = confidence interval; ICH = intracerebral hemorrhage; CT = computed tomography; rBCI = relative bicaudate index. Bold numbers indicate significant associations.

Table 5. Sensitivity and specificity of DOTAHAS score values according to the need of external ventricular drain placement.

Criterion	Sensitivity (%)	95% CI	Specificity (%)	95% CI
≥0	100	94.3 - 100.0	0	0.0 - 5.4
>0	100	94.3 - 100.0	22.73	13.3 - 34.7
>1	98.41	91.5 - 100.0	25.76	15.8 - 38.0
>2*	84.13	72.7 - 92.1	66.67	54.0 - 77.8
>3	52.38	39.4 - 65.1	90.91	81.3 - 96.6
>4	52.38	39.4 - 65.1	93.94	85.2 - 98.3
>5	41.27	29.0 - 54.4	95.45	87.3 - 99.1
>6	30.16	19.2 - 43.0	98.48	91.8 - 100.0
>7	0	0.0 - 5.7	100	94.6 - 100.0

***Optimal criterion: AUC=0.832; 95% CI: 0.756 to 0.892; P value<0.001**

CI = confidence interval; AUC = area under the ROC curve.