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CLINICAL ARTICLE - VASCULAR

Impact of intraventricular hemorrhage measured by Graeb and LeRoux score on case fatality risk and chronic hydrocephalus in aneurysmal subarachnoid hemorrhage

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Abstract

Background Reliable prognostic tools to estimate the case fatality rate (CFR) and the development of chronic hydrocephalus (CHC) in aneurysmal subarachnoid hemorrhage (SAH) are not well defined. This study aims to investigate the practicability and reliability of Fisher, Graeb, and LeRoux scores for SAH patient prognosis.

Methods A total of 206 patients with aneurysmal SAH were retrospectively analyzed in prediction of CFR and CHC. Clinical data was evaluated and grading was performed using Fisher, Graeb, and LeRoux scores. Univariate and multivariate analyses were performed to identify relevant predictive parameters.

Results CFR was 17.0 % and was associated with higher age, higher Hunt & Hess (H&H) grade, lower Glasgow Coma Scale (GCS) at admission, as well as a higher Fisher, Graeb, and LeRoux score ($p<0.001$). There were 19.9 % that developed CHC requiring permanent cerebrospinal fluid diversion. Low initial GCS ($p=0.003$), high H&H ($p<0.001$), intracerebral hematoma ($p=0.003$), high Fisher ($p=0.047$), Graeb and LeRoux scores ($p<0.001$) were associated with a higher rate of ventricular-peritoneal shunting (VPS) in surviving patients. In multivariate analyses, Graeb score (odds ratio (OR) 1.183 [1.027, 1.363], $p=0.020$), LeRoux score (OR 1.120 [1.013–1.239, $p=0.027$), and H&H (OR 2.715 [1.496, 4.927], $p=0.001$) remained independent prognostic factors for VPS.

Conclusions Graeb or LeRoux scores improve the prediction of shunt dependency and in parts of CFR in aneurysmal SAH patients therefore confirming the relevance of the extent and distribution of intraventricular blood for the clinical course in SAH.

Keywords Subarachnoid hemorrhage · Aneurysm · Case fatality risk · Chronic hydrocephalus · Fisher score · Graeb score · LeRoux score

Introduction

Aneurysmal subarachnoid hemorrhage (SAH) occurs in seven per 100.000 individuals per year [9, 15, 30]. The outcome for patients with SAH remains poor, with approximately one-third to one-fourth of patients dying within 30 days [14, 28]. There is significant morbidity among survivors, which still poses substantial challenges during the early phase of patient management.

Twenty-six to 75 % of all SAH patients develop acute hydrocephalus that needs to be treated by the placement of an external ventricular drainage (EVD) [18, 32, 33]. Out of these patients, 6–40 % will require permanent CSF diversion during follow-up [2, 25, 29]. While it is well established that subarachnoid bleeding is inversely correlated with the patient's outcome [2, 6, 16, 20, 27], the prognostic importance of intraventricular hemorrhage (IVH) is still a matter of debate. IVH after SAH occurs in more than 50 % of patients

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[22]. There are studies indicating that the distribution of IVH is associated with a poorer prognosis [16, 35], while others postulate the opposite [1, 17]. However, it is well accepted that intraventricular blood volume is related to a higher case fatality rate [4, 38] and the development of acute hydrocephalus (AHC) [24]. Treatment of SAH-associated AHC is crucial and routinely done by the placement of an external ventricular drainage (EVD) [8, 10, 36, 37]. Various mechanisms have been proposed for the development of hydrocephalus among patients with SAH [11]. Some suggest that due to alterations in cerebrospinal fluid (CSF) dynamics hydrocephalus occur [2, 3], while others believe in obstructive mechanisms [15, 19] and absorptive problems at the arachnoid granulations [7, 12]. However, AHC may not resolve and therefore a significant fraction of patients develop a CHC (6–40 %) with the necessity for a permanent VPS [2, 25, 29].

In assessing the relationship between IVH and patient outcome or CHC, most studies simply categorize IVH as being absent or present. However, the distribution of intraventricular blood may vary from minor blood sedimentation to massive accumulation in all four ventricles. Various scoring systems to classify intraventricular blood distribution are present, namely Fisher [13], Graeb [16], and LeRoux [23]. The Fisher score was initially used to correlate the amount of ventricular blood to vasospasms in SAH patients [13], whereas the Graeb score determined the neurological outcome in IVH due to SAH, trauma, and hypertensive hemorrhage [16], and the LeRoux score tested blunt head trauma patients [23].

The aim of this retrospective single-centered study was to evaluate the possible impact of IVH distribution for CFR and CHC in SAH patients. We tested easily applicable scoring systems such as Fisher, Graeb, and LeRoux scores for their reliability and their correlation. The identification of predictive factors for CHC in patients with SAH is essential for an improved management of SAH patients.

Materials and methods

Over a 40-month period (January 1, 2011 to April 30, 2014), all patients admitted or transferred to our department with aneurysmal subarachnoid hemorrhage (SAH) who were 18 years of age or older and with a cranial computer tomography (cCT) within 72 h after postulated onset of SAH prior to any intervention, such as external ventricular drainage (EVD), were enrolled in this study. Cranial CT and/or lumbar puncture proved the diagnosis of subarachnoid hemorrhage. Either four-vessel cerebral digital subtraction angiography, cCT angiography, or magnetic resonance imaging (MRI) angiography-classified aneurysmal subarachnoid hemorrhage. All patients with no evidence of aneurysm were classified as perimesencephalic subarachnoid hemorrhage and were excluded from further analysis. In total, 206 patients fulfilled the inclusion criteria for retrospective analyses of the data. Six potential patients had to be excluded because diagnosis of SAH was obtained by MRI and not by cCT. In all patients, data on gender, age, GCS at admission, Hunt & Hess (H&H) score, localization, and treatment of aneurysm either by coil embolization or neurosurgical clipping, development of delayed cerebral ischemia (DCI) according to Vergouwen [34], intracerebral hemorrhage (ICH) as well as the amount of intraventricular blood volume according to the scoring systems by Fisher [13], Graeb [16], and LeRoux [23] (Table 1) were analyzed to evaluate prognostic factors of CFR and development of CHC. Localization of aneurysms was distributed into two groups. The anterior circulation group contained aneurysms of the anterior cerebral, anterior communicating, internal carotid, and middle cerebral artery. Posterior aneurysms included aneurysms of the basilar artery, posterior communicating artery, vertebral artery, and its branches. We excluded one patient in which identification of rupture site was not possible. Data of surviving patients were used for analyses of CHC. Initial GCS was not available in two patients, while Fisher, Graeb, and LeRoux scores were not available in one single patient. The classification of the intraventricular blood volume in all cCT according to these scoring systems was performed by a single investigator (PC) blinded for case fatality rate and VPS. Acute hydrocephalus was defined as the need to place an EVD (VENTRIGUARD, NEUROMEDEX, Hombrechtikon, Switzerland) within in the first 72 h after admission. Treatment of aneurysm was performed in 131 patients by endovascular coil embolization and in 63 patients by intraoperative clipping after interdisciplinary discussion. In 13 patients, no treatment of aneurysm was performed because of their poor neurological and medical condition. All patients requiring a permanent cerebro-spinal fluid drainage before discharge eventually got a VPS. The indication for ventricular-peritoneal shunting within the first 3 months after SAH was defined as CHC. Different devices depending on the neurological state of the patient were used by either Codman (Codman and Shurtleff, Johnson & Johnson, Raynham, MA, USA) or Miethke (Christoph Miethke GmbH & Co. KG, B. Braun Melsungen AG, Melsungen, Germany). Any patient enrolled in this study that died within the first 30 days after SAH was included in the case fatality rate. In accordance with local and institutional laws and data protection regulations, no approval by the local ethic committee was necessary. The study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Statistical analysis

Student's t test, Chi-square test, and trend test (Mantel-Haenszel Chi-square), depending on the scale of the

Table 1 Scoring system for the blood amount according to Fisher [13], Graeb [16], and LeRoux [23]

Score	Fisher	Graeb		LeRoux
		Score for each lateral ventricle	Score for 3rd and 4th ventricles	Score for each ventricle
0		No blood	No blood	No blood
1	None evident	Trace of blood	Blood present, size normal	Trace of blood
2	Less than 1 mm thick	<50 % filled	Filled with blood and expanded	<50 % filled
3	More than 1 mm thick	>50 % filled		>50 % filled
4	Diffuse or none with intraventricular hemorrhage or parenchymal extension	Completely filled and expanded		Completely filled and expanded

Scores of each ventricle were aggregated to a total score, the maximum score in Graeb score is 12, in LeRoux score it is 16

measurements (continuous, nominal, ordinal), were used to perform statistical analysis of data and to examine the correlation between the parameters using IBM SPSS Statistics 19 (IBM Corporation, Armonk, NY, USA) an R version 3.0 (R Foundation, Vienna, Austria). Pearson's product–moment correlation was calculated to describe the correlation between the Graeb and LeRoux scores. Receiver operating characteristics (ROC) analyses was used to calculate sensitivity and specificity for Fisher, Graeb, and LeRoux scores followed by DeLong's test for differences between areas under the ROC curves to identify the best fitting IVH scoring system for the following multivariate analyses. The level of statistical significance was set at $p<0.05$.

Results

A total of 206 patients, 143 female (69.4 %) and 63 male (30.6 %), with an age of 54.6±13.4 years (median, 53 years, range, 23–88 years) were enrolled in this study. Acute hydrocephalus requiring EVD existed in 131 of the 206 patients (63.6 %).

Case fatality rate

Case fatality rate in this cohort was 17.0 % (35 patients), which was statistically significantly associated with higher age ($p=0.002$), higher H&H grade ($p<0.001$), lower GCS score at admission ($p<0.001$), higher Fisher score ($p<0.001$), higher Graeb score ($p<0.001$), and higher LeRoux score ($p<0.001$). The presence of AHC, ICH, localization, and treatment of aneurysm as well as development of DCI or gender had no statistically significant influence on CFR. Details of these results are presented in Table 2.

Table 2 Distribution and results of the univariate analysis for case fatality rate

Characteristic		Dead 35 (17.0) *n* (%)	Alive 171 (83.0) *n* (%)	*p* value
Gender	Female	28 (80.0)	115 (67.3)	0.123
	Male	7 (20.0)	56 (32.7)	
Age (years) mean±SD		60.9±13.8	53.3±12.9	0.002
Median		59	52	
Range		36–88	23–87	
AHC	No	9 (25.7)	66 (38.6)	0.179
	Yes	26 (74.3)	105 (61.4)	
GCS	<=7	23 (67.6)	33 (19.4)	<0.001
	8–14	6 (17.6)	38 (22.4)	
	15	5 (14.7)	99 (58.2)	
H&H	I–III	8 (22.9)	129 (75.4)	<0.001
	IV–V	27 (77.1)	42 (24.6)	
Aneurysm localization	ant.	23 (67.6)	125 (73.1)	0.522
	post.	11 (32.4)	46 (26.9)	
Aneurysm treatment	Coil	17 (77.3)	113 (66.1)	0.279
	Clip	5 (22.7)	58 (33.9)	
DCI	No	27 (77.1)	121 (70.8)	0.437
	Yes	8 (22.9)	50 (29.2)	
ICH	No	21 (60.0)	118 (69.0)	0.307
	Yes	14 (40.0)	53 (31.0)	
Fisher	1	0 (0.0)	6 (3.5)	<0.001
	2	1 (2.9)	17 (9.9)	
	3	1 (2.9)	41 (24.0)	
	4	33 (94.3)	107 (62.6)	
Graeb	0	4 (11.4)	75 (43.9)	<0.001
	1–8	20 (57.1)	81 (47.4)	
	>8	11 (31.4)	15 (8.8)	
LeRoux	0	4 (11.4)	75 (43.9)	<0.001
	1–11	18 (51.4)	79 (46.2)	
	>11	13 (37.1)	17 (9.9)	

AHC acute hydrocephalus, *GCS* Glasgow coma scale, *H&H* Hunt & Hess, *Ant.* anterior circulation, *Post.* posterior circulation, *DCI* delayed cerebral ischemia, *ICH* intracerebral hematoma

Hydrocephalus

Chronic hydrocephalus requiring VPS was necessary in 19.8 % (34 patients) out of 171 patients surviving the first 30 days. Gender, age, proof of DCI, aneurysm localization, and treatment were not associated with CHC. Similar to the analyses of the CFR, a low initial GCS (p=0.003), higher H&H (p<0.001), presence of ICH (p=0.003) as well as higher Fisher (p=0.047), Graeb (p<0.001) and LeRoux (p<0.001) scores were significantly associated with a higher rate of VPS in univariate analyses. In contrast to the analysis of CFR, acute hydrocephalus was also significantly associated with a higher rate of VPS. AHC had a positive predictive value for VPS of 30.5 % and a negative predictive value of 97.0 %. For details see Table 3.

Table 3 Univariate analysis of the ventricular peritoneal shunting (VPS) in surviving patients

Characteristic		VPS 34 (19.9 %) *n* (%)	No VPS 137 (80.1 %) *n* (%)	*p* value
Gender	Female	26 (76.5)	90 (65.2)	0.200
	Male	8 (23.5)	48 (34.8)	
Age (years) mean±SD		56.2±14.6	52.6±12.4	0.143
Median		54	51.5	
Range		28–86	23–87	
ACH	No	2 (5.9)	64 (46.7)	<0.001
	Yes	32 (94.1)	73 (53.3)	
GCS	<=7	23 (67.6)	22 (16.0)	0.003
	8–14	6 (17.6)	26 (19.0)	
	15	5 (14.7)	89 (65.0)	
H&H	I–III	17 (50.0)	113 (81.9)	<0.001
	IV–V	17 (50.0)	25 (18.1)	
Aneurysm localization	Ant.	24 (70.6)	101 (73.1)	0.714
	Post.	10 (29.4)	36 (26.3)	
Aneurysm treatment	Coil	23 (67.6)	90 (65.7)	0.829
	Clip	11 (32.4)	47 (34.3)	
DCI	No	20 (58.8)	101 (73.7)	0.095
	Yes	14 (41.2)	36 (26.3)	
ICH	No	16 (47.1)	102 (74.5)	0.003
	Yes	18 (52.9)	35 (25.5)	
Fisher	1	0 (0.0)	6 (4.4)	0.047
	2	1 (2.9)	16 (11.7)	
	3	6 (17.6)	35 (25.5)	
	4	27 (79.4)	80 (58.4)	
Graeb	0	8 (23.5)	67 (48.9)	<0.001
	1–8	15 (44.1)	66 (48.2)	
	>8	11 (32.4)	4 (2.9)	
LeRoux	0	8 (23.5)	67 (48.9)	<0.001
	1–11	15 (44.1)	64 (46.7)	
	>11	11 (32.4)	6 (4.4)	

ACH acute hydrocephalus, *GCS* Glasgow coma scale, *H&H* Hunt & Hess, *Ant.* anterior circulation, *Post.* posterior circulation, *DCI* delayed cerebral ischemia, *ICH* intracerebral hematoma

Multivariate analysis

To analyze the correlation between Graeb and LeRoux scores, Pearson's product–moment correlation was used resulting in a highly significant correlation (r=0.9799, p<0.001) (Fig. 1). ROC-AUC analyses for sensitivity and specificity of Fisher, Graeb, and LeRoux scores are presented in Fig. 2, demonstrating values for Graeb score with an AUC of 0.691 and 0.685 for LeRoux score exceeding Fisher score for sensitivity and specificity in the prognostic value for shunt dependency. DeLong's test for two correlated ROC-AUC curves in Fisher and Graeb scores was statistically significant with p=0.03. The same test using the Fisher and LeRoux scores was just statistically significant with p=0.047. Between Graeb and LeRoux scores, no statistical significance was found (p= 0.57). Validation of correlation between Graeb and LeRoux scores and ROC-AUC analyses were performed to clarify if both scores can be analyzed in the same multivariate logistic regression. We chose Graeb and LeRoux to be tested separately in multivariate logistic regression because simultaneous testing would induce estimating problems due to multicollinearity since Graeb and LeRoux scores are highly correlated. For the same reason, ACH was excluded from multivariate analyses.

Multivariate logistic regression analysis demonstrated no statistically significant independent factor for CFR. For details see Table 4.

In contrast to CFR, Graeb score (OR=1.183 [1.027, 1.363], p=0.020) and LeRoux score (OR=1.120 [1.013, 1.239], p=0.027) were independent prognostic factors for VPS as well as Hunt & Hess grade (OR=2.715 [1.496, 4.927], p=0.001). The results of the multivariate logistic regression for Graeb score analysis for VPS are demonstrated in

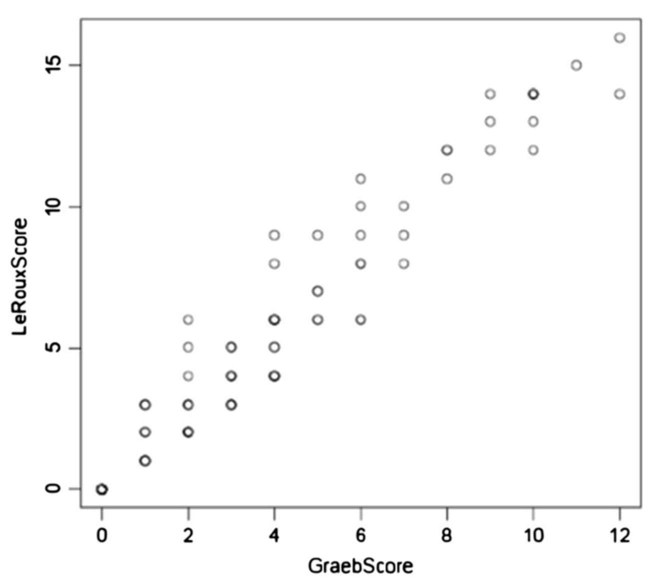

Fig. 1 Correlation of Graeb and LeRoux score using Pearson's product–moment correlation; correlation (r=0.9799, p<0.001)

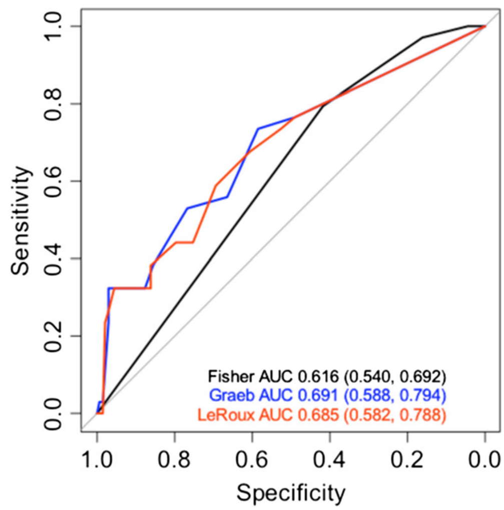

Fig. 2 ROC-AUC analyses for Fisher, Graeb, and LeRoux score

Table 5 (results for multivariate logistic regression of LeRoux score are not presented in detail).

Discussion

Aneurysmal subarachnoid hemorrhage is a devastating disease with a high rate of mortality and permanent morbidity. Predictive tools are needed to improve the clinical management. Here, we report a clinical retrospective analysis of 206 patients with aneurysmal SAH analyzing the reliability of Fisher, Graeb, and LeRoux scores to predict the CFR and CHC. The CFR in our cohort was 17 % of patients within 30 days. Univariate analyses revealed higher age, H&H grade, Fisher, Graeb, and LeRoux scores as negative predictors for death within 30 days, as well as lower GCS score. However, the presence of ICH, the localization of the aneurysm, and whether it was treated by endovascular coiling or microsurgical clipping had no predictive influence on the CFR. Acute hydrocephalus was diagnosed in 63.6 % of all enrolled patients and in 61.4 % of patients surviving the first 30 days. Of the surviving patients, 19.8 % needed continuous CSF drainage by VPS. Higher H&H grade, ICH, Fisher, Graeb, and LeRoux scores were positive predictors for the requirement of VPS, whereas GCS was inversely correlated. However,

Table 4 Multivariate logistic regression analysis for case fatality rate

Variable	*p* value	OR	95 % CI
Glasgow Coma Scale	0.248	0.911	0.78–1.067
Hunt & Hess grade	0.167	1.597	0.822–3.103
Fisher score	0.610	1.359	0.418–4.417
Graeb score	0.100	1.113	0.980–1.264

OR odds ratio, 95 % CI 95 % confidence interval of OR

Table 5 Multivariate analysis for ventricular peritoneal shunting

Variable	*p* value	OR	95 % CI
Glasgow Coma Scale	0.067	1.151	0.990–1.337
Hunt & Hess grade	0.001	2.715	1.496–4.927
Fisher score	0.577	0.795	0.354–1.782
Intracerebral hemorrhage	0.452	1.447	0.553–3.790
Graeb score	0.020	1.183	1.027–1.363

OR odds ratio, *95 % CI* 95 % confidence interval of OR

gender, age, aneurysm localization, and treatment modality (endovascular coiling or microsurgical clipping) did not demonstrate any correlation. In conclusion, with greater IVH blood distribution, the outcome deteriorated and shunt dependency increased. Noteworthy, ACH had a significant influence on the VPS rate but not on CFR.

We focused on quick and easy applicable scoring systems for the prognosis of CFR and CHC. Fisher, Graeb, and LeRoux scores categorize mainly due to ventricle affiliation and blood content being less or more than 50 % (Table 1). Therefore they lack precise IVH volume measurements. However, their weakness is also their strength, as they may be applied within a couple of seconds and are easily taught.

At first, Fisher score tried to correlate the amount of ventricular blood to vasospasms in SAH patients [13]. A high Fisher score has been associated with 14-day mortality but was insignificant for the need of CSF shunt implantation [24]. This might be due to the fact that Mayfrank et al. excluded Fisher score IV and created a subgroup including all patients that showed IVH [24]. This subgroup was furthermore divided into three groups (0 points; 1–6 points; 7–16 points) [24], according to the LeRoux scoring system, which was initially developed for blunt head trauma patients [23]. Univariate analysis showed a significant relationship between high LeRoux scores and VPS dependency as well as 14-day mortality [24]. The true predictive value of a high LeRoux score is still conflicting, as Zacharia et al. showed no predictive value for VPS [39] in patients with IVH and high LeRoux scores. The Graeb score was initially used to determine the neurological outcome in IVH due to SAH, trauma and hypertensive hemorrhage [16]. Tested on patients with significant IVH, defined as a Graeb score above 6, these patients were 24 times more likely to develop ACH compared to patients with minimal or no IVH [35], while being an insignificant prognostic factor for shunt dependency in IVH patients [39].

Our findings demonstrate high age, high H&H grade, low GCS score, and high Fisher/Graeb/LeRoux scores to be associated with an increased CFR, being 17.0 %, which is below the CFR of recent published studies [4, 5]. In conclusion, cumulative spread of blood in divers ventricles deteriorates the prognosis of SAH patients. These results are in agreement with previous studies which demonstrated an inverse correlation to bleeding extension and outcome [5, 21, 24, 26]. So far, subarachnoid blood [20] and parenchymal hematomas [5] have been clearly linked to a poor outcome, whereas IVH per se seems to only rarely affect the neurological outcome [16]. Nevertheless, the pathogenic mechanisms by which increasing blood extension worsens the prognosis of SAH patients are still poorly understood. The most prominent belief is that due to obstructing blood clots CSF outflow is hindered, resulting in ACH and ventriculomegaly [26]. Both have been suggested to relate to the extent of brain damage [24, 26, 31] hence downgrading the neurological outcome. In our group, 61.7 % of patients with an aneurysmal associated SAH displayed intraventricular hemorrhage which is in line with previously published series [4, 35].

There is a clear relationship between ACH and IVH, as postulated by numerous studies [17, 19, 24]. However, only a portion of patients develops CHC, as ACH may resolve on its own [24]. Within our group, we identified ICH, high Fisher, Graeb, and LeRoux scores, as well as ACH to be predictors of VPS. Chronic hydrocephalus requiring VPS was necessary in 19.8 % of our patients surviving the first 30 days. The rate of VPS in our study is in accordance with previously published studies [24, 26]. Zacharia et al. previously described that IVH volume has no effect on VPS shunting [39]. However, according to the scores used in this study, we did not measure the exact IVH volume but rather anatomical distribution patterns. Given the anatomical relationship of the CSF compartment, it is intuitive that an increased intraventricular spread will result in an impaired CSF circulation and outflow, which also means that the patient will most likely need an artificial CSF drainage. Supporting our hypothesis that the distribution of intraventricular blood plays an important role as it may vary from minor blood sedimentation to massive accumulation of all four ventricles was that a high Graeb and LeRoux score was significantly associated with a greater rate of CHC, while correlating extremely well ($p<0.001$). Graeb and LeRoux scores showed to exceed the Fisher score for sensitivity and specificity in the prognostic value for shunt dependency as seen in ROC analyses.

It remains unclear exactly how subarachnoid blood and its distribution into the CSF department contributes to the development of CHC. Despite the hypothesis of obstructed arachnoid villi by blood, known for ACH [7, 12], and the anatomical flow diversion [2, 3]. Future studies need to investigate whether SAH patients gain from interventions aiming to accelerate the clearance of ventricular blood.

Conclusions

This is the first study demonstrating that either Graeb or LeRoux score improve the prediction of shunt dependency and in parts of CFR in SAH patients therefore confirming the relevance of the extent and distribution of intraventricular blood for the clinical course in SAH. Both scores correlate exceedingly well and display an increased sensitivity and specificity in comparison to Fisher scores for the prediction of VPS dependency. Both scores can be applied shortly after the initial cCT has been done in SAH patients, giving physicians a tool to predict the clinical course of SAH patients.

Conflict of interest None.

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