Clinical Neurology and Neurosurgery 170 (2018) 67–72

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

# Intraventricular extension of an aneurysmal subarachnoid hemorrhage is an independent predictor of a worse functional outcome

Mario Zanaty[a], Daichi Nakagawa[a], Robert M. Starke[b], Enrique C. Leira[c], Edgar A Samaniego[d], Waldo G. Guerrero[d], James Torner[e], Yasunori Nagahama[a], Olatilewa Awe[a], Jeremy Greenlee[a], Joseph S. Hudson[a], Lauren Allan[f], Reem Elwy[g], Nohra Chalouhi[h], Pascal Jabbour[h], Royce Woodroffe[a], Anthony Piscopo[a], David Hasan[a,*]

[a] Department of Neurosurgery, University of Iowa Hospitals and Clinics, Iowa City, IA, United States
[b] Department of Neurosurgery and Radiology, University of Miami, Miami, Fl, United States
[c] Department of Neurology, University of Iowa Hospitals and Clinics, Iowa City, IA, United States
[d] Department of Neurology and Neurointerventional Radiology, University of Iowa Hospitals and Clinics, Iowa City, IA, United States
[e] Department of Epidemiology, University of Iowa College of Public Health, United States
[f] Department of General Surgery, University of Iowa Hospitals and Clinics, Iowa City, IA, United States
[g] Department of Neurosurgery, Doki, Giza, Egypt
[h] Department of Neurosurgery, Thomas Jefferson University, Philadelphia, PA, United States

ARTICLE INFO

*Keywords:*
IVH
Functional outcome
SAH
Memory deficit
Cognition

ABSTRACT

*Objective:* The objective of this study is to determine the impact of intraventricular hemorrhage (IVH) on the cognitive prognosis of subarachnoid hemorrhage (SAH) due to ruptured cerebral aneurysm, independent of the presence of intraparenchymal hemorrhage, hydrocephalus or vasospasm.

*Patient and Methods:* A Retrospective review of a prospectively collected database of patients with aneurysmal SAH from July 2009 to November 2016 was performed. Patients were included if they had a saccular aneurysm with a Hunt-Hess grade (HHG) 1–3. Those who underwent craniectomy/clipping and those with vasospasm were excluded. Patients with IVH were grouped into 5 groups depending on the blood distribution in the ventricles. Functional outcomes studied were modified Rankin score (mRS) 0–2, cognitive impairment and memory impairment, and the presence of amnesia to the event. A univariate followed by a multivariate analysis ware performed.

*Results:* A total of 443 patients were identified and 124 patients met the criterion. There were no significant differences in the proportion of patients with mRS of 0–2 between patients with IVH and those without IVH but with EVD (external ventricular drain). There was a higher proportion of cognitive deficits in patients with IVH (71.95%), compared to those without (31.58%; $p = 0.01$). Patients with IVH had a higher rate of anterograde amnesia (100% *vs.* 4.3% $p < 0.0001$), lower rate of mRS 0–2 (78% vs 100% $p < 0.001$), and higher rate of cognitive impairment (71.9% *vs.* 13% $p < 0.0001$) compared with those who did not require an EVD. Grade 3 and grade 4 were shown to have lower rate of patients with mRS 0–2 and a higher rate of cognitive impairment.

In multivariate analysis, independent predictors of cognitive and memory impairment were increasing HHG (OR = 155.33; $P < 0.01$), ACOM/A1/ACA/anterior choroidal aneurysms, (OR = 5.24; $P = 0.04$), increasing Fischer scale (OR = 6.93; $P = 0.01$), and increasing IVH grade (OR = 6.9; $P = 0.01$). Only worse HHG (OR = 2704.22; $P = 0.01$) and IVH grade 2–4 were associated (perfect predictor, OR cannot be extracted) with anterograde amnesia.

*Conclusion:* IVH is an independent prognosticator of SAH cognitive outcomes. The effect of IVH drainage and other intraventricular therapies on SAH course is an attractive topic for further investigation.

## 1. Introduction

In North America, the incidence of aneurysm rupture is approximately 8–11 per 100,000 persons per year [12]. It accounts for 27% of all stroke-related years of life lost before age 65, and it has a predilection for a relatively younger age [12]. Many of the survivors are

* Corresponding author: University of Iowa Hospitals and Clinics, 200 Hawkins Drive, Iowa City, IA, United States.
*E-mail address:* david-hasan@uiowa.edu (D. Hasan).

https://doi.org/10.1016/j.clineuro.2018.04.032
Received 23 March 2018; Received in revised form 26 April 2018; Accepted 28 April 2018
Available online 30 April 2018

left with long term cognitive deficits and memory impairment in their productive years with major responsibilities with respect to work and family [1,2]. Cognitive impairment including memory, executive function, and language impairment are most frequently observed within the first 3 months after the ictus [14]. These deficits can persist as long as 75 months and sometimes longer [3]. It has been reported that the presence of a hematoma in an eloquent brain area can affect language and that the Fisher score and the presence of acute hydrocephalus are associated with cognitive deficits [11]. In this study, we investigated the relevance of intraventricular hemorrhage (IVH) as an independent predictor of cognitive function, regardless of the presence of intraparenchymal hemorrhage (IPH), hydrocephalus, or vasospasm.

## 2. Patient and methods

### 2.1. Patient cohort

After obtaining institutional review board approval from our institution, we searched our prospectively maintained database for all patients with aneurysmal SAH from July 2009 to November 2016. A total of 443 patients were identified in the registry. These patients were treated by a single dual trained neurovascular surgeon and a strict patient management protocol was applied. Medical charts, angiographic studies, MRI, and computed tomographic (CT) scans were carefully reviewed. Patient's age, sex, aneurysm size, and location were recorded. Patients were included if they had an aneurysmal SAH from a saccular aneurysm with a Hunt-Hess grade (HHG) 1–3, documented after treating the hydrocephalus and correcting electrolyte abnormalities (see discussion). Patients with other forms of aneurysm (mycotic or fusiform), higher HHG, and those who underwent craniectomy or craniotomy with clipping were excluded. We excluded surgical clipping because it has been previously shown that cognitive deficits of the patients after aneurysmal SAH treated surgically were significantly worse compared to the endovascular group [11]. Patients with IVH from a clot expansion were exclude since they were likely to undergo craniotomy and clipping or craniectomy and had a HHG > 3. Patients who had early ischemic deficit or clinical vasospasm were also excluded. A total of 124 patients met the criterion and were included. (Fig. 1).

### 2.2. Patient outcomes

Patients were initially divided initially to 2 groups, those who required a ventriculostomy due to hydrocephalus or other concerns, and those who did not. Those who required a ventriculostomy were further subdivided to 5 groups depending on the distribution of the blood in the ventricles:

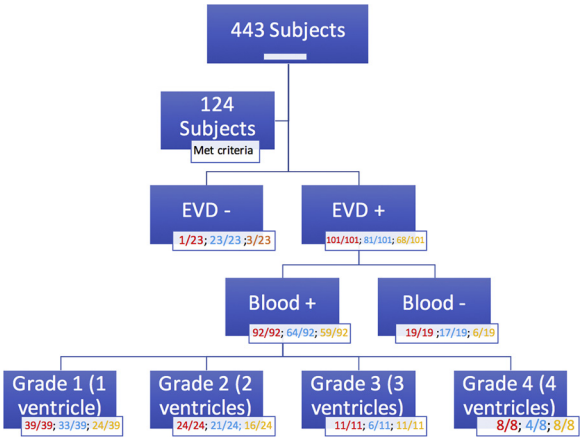


**Fig. 1.** Patient selection and stratification.

- Grade 0: No blood in the ventricles
- Grade I: Presence of blood in 1 ventricle only (regardless of which ventricle)
- Grade II: Presence of blood in 2 ventricles
- Grade III: Presence of blood in 3 ventricles
- Grade IV: Presence of blood in 4 ventricles

Modified Rankin scale (mRS), cognitive impairment and memory impairment, and assessment of anterograde amnesia were performed at 6–8 weeks follow-up and at 6 months. The cognitive and memory status was assessed by patient interrogation evaluating their ability to name, perform complicated tasks, perform on a word recall short term memory assessment, and perform complex executive functions and complex calculation. Patients and their families were asked how close the patient is to his/her baseline and whether the patient has impairment in activities of daily living (ADLs) such as feeding, grooming, personal hygiene, bathing, toileting and dressing. Aneurysm location, age, gender, HHG, Fischer scale, and IVH grade were included in the analysis to assess whether they have an effect on mRS, amnesia and cognitive outcome.

### 2.3. Statistical analysis

Data are presented as mean and range for continuous variables, and as frequency for categorical variables. Patients treated with EVD were compared to those who haven't. Patients with IVH were compared to those without. In the EVD group, patients were compared in term of mRS, cognitive and memory impairment. The analysis was carried out using Student's t-test, Wilcoxon rank sum, Mann-Whitney test, $\chi 2$ test, or Fisher's exact test as appropriate. Univariate analysis of predictors (aneurysm location, HHG, Fischer scale, IVH grade, age and gender) was carried out using logistic regression analysis. Interaction and confounding was assessed through stratification and relevant expansion covariates. Factors predictive in univariable analysis ($p < 0.20$) were entered in a multivariable logistic regression analysis with stepwise selection. P-values of $\leq 0.05$ were considered statistically significant. Statistical analysis was carried out with Stata 14.0 (College Station, TX).

## 3. Results

Four hundred forty-three patients were identified, of which, 124 subjects met the inclusion criteria. Patient's mean age was 57.8 ± 13. The proportion of female was 68.54% (85/124). One hundred one [M1] patients required a ventriculostomy (101/124 = 81.46%) while 23 (23/124; 18.54%) did not, due to minimal presence of SAH and no hydrocephalus and IVH (Fig. 1). Of the patients who underwent EVD placement, 82 had IVH (82/101; 81.19%), while 19 (19/101; 18.81%) did not (Grade 0, labeled as blood -). The following were the proportions of each grade: grade 1 (39/82; 47.56%), grade 2 (24/82; 29.27%), grade 3 (11/82; 13.41%) and grade 4 (8/32; 25%).

Only one (1/23; 4.34%) patient who did not require an EVD had an anterograde amnesia, compared to all patients 101/101 (100.00%) who had an EVD placed ($P < 0.0001$). All patients (23/23; 100.00%) who did not require an EVD had an mRS 0–2 on follow-up, compared to 81/101 (80.20%) in the EVD group ($P = 0.002$). In the EVD group, 68/101 (67.33%) had cognitive deficits at follow-up compared to 3/23 (13.04% $P = 0.002$) of those who did not require an EVD (Fig. 2A).

There was no significant difference in the proportion of patients with an mRS of (0–2) between patients with IVH (64/82; 78.05%) and those without IVH but with EVD, labeled as grade 0 (17/19; 89.47%, Fig. 2B). There was no significant difference in terms of anterograde amnesia between grade 0 (19/19; 100.00%) and patients with IVH (82/82; 100.00%). There was, however, a statistically significant difference in the proportion of patients with cognitive deficits, with a higher proportion in patients with IVH (59/82; 71.95%) compared to those without (6/19; 31.58%; $P = 0.01$).