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ORIGINAL WORK

Predictors of Ventriculoperitoneal shunting following Subarachnoid Hemorrhage treated with External Ventricular Drainage

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Abstract

Background/Objectives: Aneurysmal subarachnoid hemorrhage (aSAH) is commonly associated with hydrocephalus due to subarachnoid hemorrhage blood products obstructing cerebrospinal fluid outflow. Hydrocephalus after aSAH is routinely managed with temporary external ventricular drainage (EVD) followed by standard EVD weaning protocols, which determine the need for ventriculoperitoneal shunting (VPS). We sought to investigate aSAH patients who initially passed EVD weaning trials and had EVD removal, but later presented with recurrent, delayed, symptomatic hydrocephalus requiring a VPS.

Methods: We conducted a retrospective review of all patients at our tertiary care medical center who presented with aSAH, requiring an EVD. We analyzed variables associated with ultimate VPS dependency during hospitalization.

Results: We reviewed 489 patients with aSAH over a 6-year period (2008–2014). One hundred and thirty-eight (28.2%) developed hydrocephalus requiring a temporary EVD. Forty-four (31.9%) of these patients died or had withdrawal of care during admission, and were excluded from final analysis. Of the remaining 94 patients, 29 (30.9%) failed their clamp trial and required VPS. Sixty-five (69.1%) patients passed their clamp trial and were discharged without a VPS. However, 10 (15.4%) of these patients developed delayed hydrocephalus after discharge and ultimately required VPS [mean (range) days after discharge, 97.2 (35–188)]. Compared to early VPS, the delayed VPS group had a higher incidence of symptomatic vasospasm (90.0% vs 51.7%; $P = 0.03$). When comparing patients discharged from the hospital without VPS, delayed VPS patients also had higher 6- and 12-month mortality ($P = 0.02$) and longer EVD clamp trials ($P < 0.01$) than patients who never required VPS but had an EVD during hospitalization. Delayed hydrocephalus occurred in only 7.8% of patients who passed the initial EVD clamp trial, compared to 14.3% who failed the initial trial and 80.0% who failed 2 or more trials.

Conclusion: Patients who failed their initial or subsequent EVD clamp trials had a small, but increased risk of developing delayed hydrocephalus ultimately requiring VPS. Additionally, the majority of patients who presented with delayed hydrocephalus also suffered symptomatic vasospasm. These associations should be further explored and validated in a larger prospective study.

Keywords: Aneurysm, Subarachnoid hemorrhage, Arachnoid granulations, Chronic hydrocephalus, Vasospasm

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Introduction

Aneurysmal subarachnoid hemorrhage (aSAH) occurs when an intracranial aneurysm ruptures and spills blood in the subarachnoid space, which can extend into the cerebrospinal fluid (CSF) cavities and ventricles. Hydrocephalus after aSAH is reported to occur in 6–67% of patients and requires temporary CSF diversion via external ventricular drainage (EVD) or lumbar drainage [1–5]. While hydrocephalus after aSAH may be transient, many patients will require permanent CSF diversion with ventriculoperitoneal shunting (VPS). Before EVD removal, most neurosurgeons perform a weaning trial by clamping the EVD system and monitoring intracranial pressure (ICP) for 24–48 h. The EVD system is typically not reopened unless the ICP is sustained at 20 mmHg or greater for 5 min or massive spikes in ICP are noted.

A small subpopulation of patients will develop hydrocephalus in a delayed fashion after successful weaning and removal of EVD, thus requiring VPS. The incidence of delayed VPS (dVPS) after aSAH and initial EVD removal remains poorly understood and is the basis of our study. The etiology and risk factors of delayed hydrocephalus after hospitalization are rarely investigated [6–8], even within the established consortium [1]. While recent studies suggest that high modified Fisher score, presence of ventricular blood, and poor clinical grade (e.g., high World Federation of Neurological Surgeons scale or Hunt and Hess score) are predictive of ultimate VPS dependence, there is minimal literature on why some patients who initially pass their clamp trial subsequently develop hydrocephalus [7–11].

Therefore, we sought to investigate risk factors associated with delayed hydrocephalus after aSAH, since this entity may impair or cause delay in neurologic improvement, preventing optimal outcomes. In reviewing the literature on hydrocephalus and VPS in aSAH, we could only find one article that highlighted subsequent VPS after hospital discharge [7].

Methods

Patient Population

After institutional board review approval, we retrospectively reviewed all aSAH patients' electronic health records at our tertiary care medical center from October 1, 2008, to October 1, 2014. We adhered to Strengthening the Reporting of Observational Studies in Epidemiology guidelines for reporting cohort studies [12]. We collected patient data, including age and sex, admission Hunt and Hess score, modified Fisher, Glasgow Coma Scale (GCS) scores, ICP before and during EVD clamp trial, days from EVD placement to clamp trial, duration of clamp trial, and modified Rankin scale (mRS) score at discharge and 1 year, when available. We also recorded aneurysm location and size, occurrence of vasospasm, and timing of VPS. We excluded patients with angiogram-negative, or *pretruncal*, SAH, those without hydrocephalus who did not require EVD placement, and those who died or had withdrawal of care during hospitalization. The study population included only aSAH patients who had EVD placed as standard of care for hydrocephalus and were discharged from the hospital with a mRS of 1–5. Patients were divided into two groups: the early VPS (eVPS) group, consisting of patients who underwent VPS during their initial hospitalization, and the dVPS, made up of patients who passed their EVD clamp trial and still developed delayed hydrocephalus requiring VPS. Patients were followed up postoperatively with clinic visits at 2 weeks, and then at 3-month intervals, or as needed by clinical condition. To limit the risk of ascertainment bias, four authors reviewed the patients eligible for inclusion, and causes of death were documented to be sure patients with mortality were not misclassified.

Initial EVD Management

Patients who presented with aSAH and radiographic evidence of ventriculomegaly on head computed tomography (CT) with symptomatic hydrocephalus (e.g., drowsy or deteriorating/declining on GCS) received an EVD in accordance with American Heart Association aSAH guidelines [13]. EVD placement is performed either at the bedside using established sterile, anatomic landmark techniques in emergencies, or prior to aneurysm treatment in the surgical operating room or neuroangiography suite. After initial EVD placement, the drainage pressure was typically maintained at 20 mmHg until the aneurysm was secured to prevent risk of over drainage, possibly leading to inadvertent aneurysm re-rupture. Once the aneurysm was secured, the drainage pressure setting was typically decreased to 5 mmHg to allow sufficient bloody aSAH drainage. In some cases, EVD was placed after aneurysm treatment if there was progression of hydrocephalus or neurologic deterioration noted after aneurysm coiling or clipping treatment.

Patients with aSAH are admitted to the neurocritical care unit and are managed under the care of a multidisciplinary neurocritical care team including a neurosurgeon, a neurointensivist, residents, fellows, medical students, and advanced practice providers.

EVD Weaning Protocol

EVD weaning was defined as sufficient challenging of the EVD system from 5 up to 20 mmHg, or about 5 mmHg each day, until finally clamping the drain and monitoring ICP. The treating neurosurgeon requested clamping of the EVD if the CSF output values were minimal for a given drainage setting (e.g., <5 mL/h output if set at

15 mmHg or 20 mmHg), typically no sooner than 7 days after aSAH, assuming there was no active symptomatic or severe radiographic vasospasm (noted on transcranial Doppler or CT angiogram). After EVD clamping, ICP was monitored continuously by neurocritical care nursing, and the treating neurocritical care team was paged if the patient developed signs of hydrocephalus, such as increased nausea, vomiting, worsening headache, or poor upgaze; and decline in GCS not attributable to medications.

A successful EVD clamp trial was defined as no neurologic deterioration during clamp trial and stable CT after 24 h. The EVD was subsequently removed after CT showed no enlargement of the ventricular size in patients who had a successful EVD clamp trial. An unsuccessful EVD clamp trial occurred when the patient had neurologic decline during the EVD clamping trial, ICP of 20 mmHg or greater for 5 min, or a rapid unstable spike in ICP (i.e., 40–60 mm Hg or higher). In these patients, the nurse would reopen the EVD system to its last setting to drain CSF. A subsequent EVD clamp trial could be ordered the next day if the ICP was borderline or hydrocephalus signs were equivocal (e.g., headache without decline in mental status), before committing a patient to a permanent VPS. Unsuccessful successive EVD clamp trial attempts during hospitalization led to VPS. Once the treating team is aware that a patient may be trending toward VPS placement, CSF is sent for culture, and VPS is placed only in patients with sterile CSF. Most patients (6/10) who returned with delayed hydrocephalus had CSF sent during VPS placement, and none returned with positive cultures. All patients with signs of hydrocephalus during follow-up were shunted.

Outcomes

We compared the need for early shunt versus delayed shunt versus no shunt based on admission variables, including vasospasm, Hunt and Hess score, modified Fisher score, intraventricular hemorrhage, aneurysm size, number of failed clamp trials, duration of clamp trial, and outcome (mRS at discharge and 1 year).

Statistical Analysis

Categorical variables were analyzed using the χ^2 test for independence. Continuous variables were compared between groups using the 2-sample t test. Overall survival and mortality were estimated using the Kaplan–Meier method. Mortality was compared between the groups using log-rank tests. A P value less than 0.05 was considered statistically significant. All analyses were completed using SAS, version 9.4 (SAS Institute Inc.).

Results

Patient Characteristics

During the study period, 489 aSAH patients were seen at our institution. One hundred and thirty-eight (28.2%) of these patients had signs of hydrocephalus requiring EVD placement (Fig. 1) [14–16], 44 (31%) of whom died or had withdrawal of care prior to discharge, leaving 94 patients included in our final analyses. Data are outlined in Tables 1 and 2. Twenty-nine (30.9%) patients failed their clamp trial and required eVPS prior to discharge. Sixty-five (69.1%) patients passed their clamp trial and were discharged without VPS, but 10 (15.4%) of those developed hydrocephalus after discharge and required dVPS at a mean (range) of 97.2 (35–188) days after discharge. For all included patients, the mean (standard deviation, SD) age of all included patients was 55.5 (12.7), time for EVD weaning was 13.3 (5.7) days following placement, and mRS at discharge and 1 year after discharge were 3.2 (1.3) and 2.8 (1.8), respectively. Complete patient demographic and characteristics are available in Tables 1 and 2. All patients in the dVPS group had ventricular dilation on head CT at the time of their delayed presentation, with symptoms including short-term memory loss, nausea, vomiting, gait instability, confusion, and urinary incontinence. All patients had resolution of their symptoms after shunt placement.

Follow-Up

Among the eVPS group ($n=29$), 23 (79.3%) patients were available at 12-month follow-up and 15 (51.7%) were available at 24-month follow-up; mean (range) follow-up time was 32.7 (4–72) months. In the dVPS group ($n=10$), 7 (70.0%) patients were available at 12-month follow-up and 6 (60.0%) were available at 24-month follow-up; mean (range) follow-up time was 39.6 (2–80) months. For the group without VPS ($n=55$), 40 (72.7%) patients were available at 12-month follow-up and 26 (47.3%) were available at 24-month follow-up; mean (range) follow-up time was 29.6 (1–88) months. Mean (SD) follow-up time for all included patients was 31.6 (22.7) months.

Comparison of dVPS and No VPS

Our first analyses compared the dVPS group with the patients who never required a VPS (Table 1). All patients in the no VPS group had an EVD during their hospitalization, which was successfully weaned and discontinued. Mean age at admission trended toward statistical significance ($P=0.07$), with the dVPS patients being younger (47.6 vs 55.5 years). More patients in the dVPS group had symptomatic vasospasm requiring interventions with intra-arterial verapamil or balloon angioplasty (90.0% vs

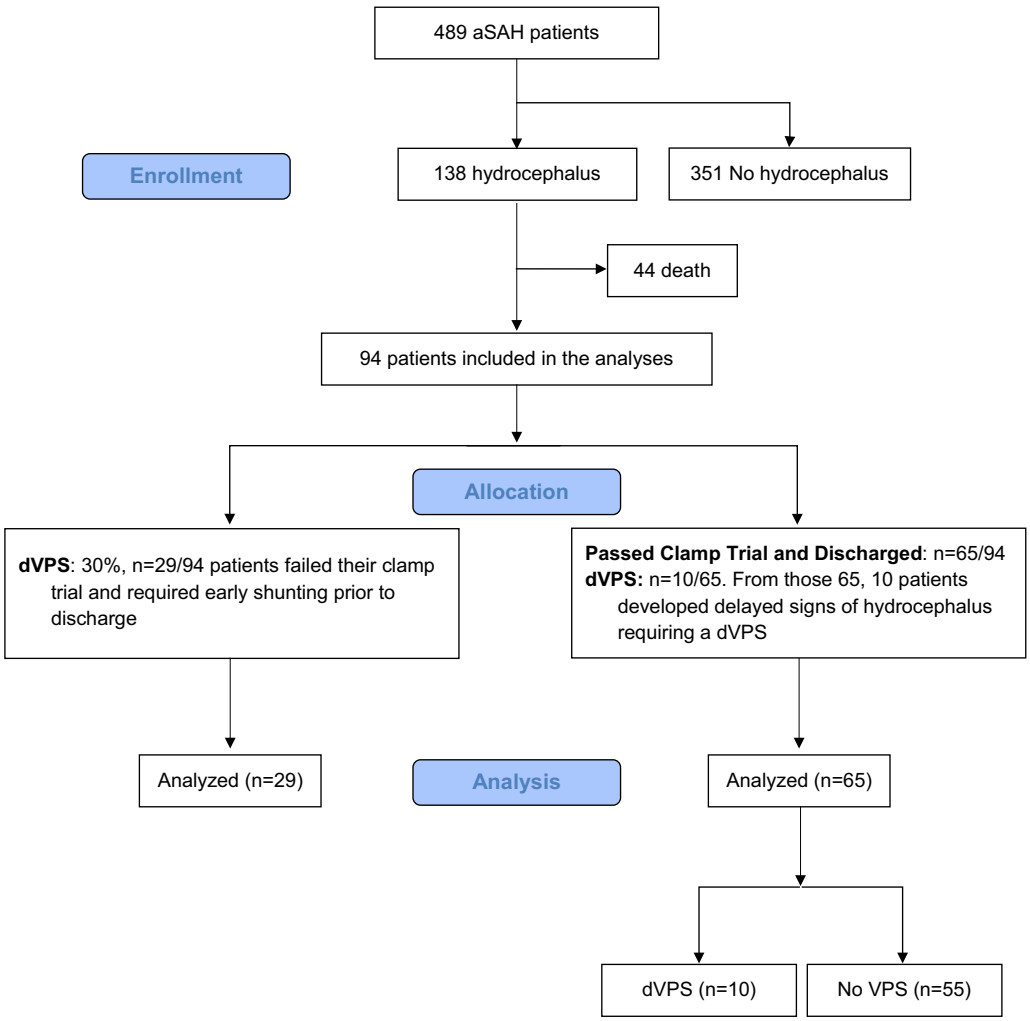

Fig. 1 Flow diagram for all patients with aneurysmal subarachnoid hemorrhage (aSAH) [14–16]. *dVPS* delayed ventriculoperitoneal shunt, *eVPS* early ventriculoperitoneal shunt, *VPS* ventriculoperitoneal shunt

52.7%; $P=0.03$). Figure 2a shows a trend toward greater survival in patients who passed their clamp trial and never required a VPS than those with dVPS.

Initial outcomes were worse in the dVPS group, with significantly worse mRS at discharge ($P=0.02$). However, outcomes were similar by 1-year post-discharge ($P=0.10$). Thirty-five (63.6%) of the 55 patients in the no VPS group had a successful first EVD clamp trial, 18 (33.3%) passed their second trial, and only 1 (1.9%) required more than 2 trials. Among the 10 patients in the dVPS group, 3 (30.0%) had a successful first clamp trial, 3 (30.0%) passed a second trial, and 4 (40.0%) required more than 2 trials. Also, patients with dVPS had significantly decreased survival at 6 months ($P=0.02$) and 1 year ($P=0.02$), but at 2 years, there was no significant difference ($P=0.14$). The patients who died had poor neurological function and died secondary to complications of immobility such as sepsis from decubitus ulcers and pulmonary embolism.

Comparison of dVPS and eVPS

In our comparison of the eVPS and dVPS groups, we found no significant difference in sex ($P=0.94$); admission Hunt and Hess score ($P>0.99$), modified Fisher ($P=0.48$), and GCS ($P=0.51$) scores; presence of intraventricular hemorrhage ($P=0.98$); ICP levels during EVD clamp trial ($P=0.39$); days from EVD placement to EVD clamp trial ($P=0.58$); aneurysm size ($P=0.59$); or mRS by discharge ($P=0.24$) and at 1 year ($P=0.71$) (Table 2). Patients with dVPS were more likely than those with eVPS to have suffered symptomatic vasospasm requiring intervention (90.0% vs 51.7%; $P=0.03$). The amount of patients with aneurysms of the posterior circulation

Table 1 Overall comparisons between patients with dVPS and patients with no VPS

Patient characteristics	No VPS ($n=55$)	dVPS ($n=10$)	Total ($N=65$)	P value
Sex, no. (%)				0.28
Female	42 (76.4)	6 (60.0)	48 (73.8)	
Male	13 (23.6)	4 (40.0)	17 (26.2)	
Age on visit				0.07
Median (Q1, Q3)	57.0 (48.0, 64.0)	45.0 (40.0, 56.0)	55.0 (46.0, 62.0)	
Aneurysm location, no. (%)				0.27
Anterior circulation	28 (50.9)	7 (70.0)	35 (53.8)	
Posterior circulation	27 (49.1)	3 (30.0)	30 (46.2)	
Aneurysm diameter (mm)[a]				0.26
Median (Q1, Q3)	5.0 (4.0, 6.0)	6.2 (4.6, 7.5)	5.0 (4.1, 6.3)	
Modified Fisher score				0.72
Median (Q1, Q3)	4.0 (3.0, 4.0)	4.0 (4.0, 4.0)	4.0 (4.0, 4.0)	
Glasgow Coma Scale[a]				0.11
Median (Q1, Q3)	13.0 (7.0, 15.0)	7.5 (4.0, 13.0)	13.0 (7.0, 15.0)	
IVH, no. (%)				0.53
Absent	10 (18.2)	1 (10.0)	11 (16.9)	
Present	45 (81.8)	9 (90.0)	54 (83.1)	
Vasospasm, no. (%)				0.03
Absent	26 (47.3)	1 (10.0)	27 (41.5)	
Present	29 (52.7)	9 (90.0)	38 (58.5)	
ICP during clamp[a]				0.20
Median (Q1, Q3)	8.5 (5.5, 12.0)	10.7 (7.3, 14.7)	8.8 (5.8, 12.6)	
Days to clamp trial[a]				0.30
Median (Q1, Q3)	13.0 (9.0, 15.0)	15.0 (8.0, 20.0)	13.0 (9.0, 16.0)	
mRS at discharge				0.02
Median (Q1, Q3)	3.0 (2.0, 4.0)	4.0 (3.0, 5.0)	3.0 (2.0, 4.0)	
mRS at 1 year[a]				0.09
Median (Q1, Q3)	2.0 (1.0, 4.0)	3.5 (2.0, 5.0)	2.0 (1.0, 4.0)	

dVPS delayed ventriculoperitoneal shunt, *ICP* intracranial pressure, *IVH* intraventricular hemorrhage, *mRS* modified Rankin scale, *Q1* first quartile, *Q3* third quartile, *VPS* ventriculoperitoneal shunt

[a] Refers to the loss of some patient data during follow-up for the following variables: total number available for aneurysm diameter (mm) No VPS ($n=54$), dVPS ($n=8$), total ($n=62$); Glasgow coma scale No VPS ($n=54$), total ($n=64$); ICP during clamp No VPS: ($n=53$), total ($n=63$); days to clamp trial No VPS ($n=53$), total ($n=63$); mRS at 1 year No VPS ($n=42$), total ($n=52$)

showed a trend toward statistical significance (70.0% vs 35.7%; $P=0.06$), with dVPS patients being more likely to have aneurysms of the posterior circulation than those with eVPS. Survival estimates at 2 years were similar for both groups (Fig. 2b).

Discussion

This study suggests that after initial aSAH with EVD placement and successful removal, a subset of patients may be at risk for delayed hydrocephalus after EVD removal. This phenomenon of delayed hydrocephalus after aSAH occurred in about 15% of patients after discharge and appeared slowly up to 6 months later, with a clinical picture similar to normal pressure hydrocephalus (NPH). We feel this is an important finding, since most patients with aSAH develop acute hydrocephalus from elevated ICP related to CSF outflow obstruction through the ventricular system from blood and either obstructive or non-communicating hydrocephalus, requiring CSF diversion. Communicating hydrocephalus is thought to occur from microscopic obstruction of the arachnoid granulations and decreased CSF absorption from subarachnoid blood or protein [17–19]. To our knowledge, only one other study by Lewis et al. [7] has described this delayed hydrocephalus and VPS after aSAH patients. In their study, hydrocephalus and VPS occurred at a median of 54 days after EVD removal. They also hypothesized that elevated CSF drainage in the first week predicted dVPS. Although their study was limited by its retrospective design, it is one of the larger studies to date

Table 2 Overall comparisons between patients with eVPS and patients with dVPS

Patient characteristics	eVPS ($n=29$)	dVPS ($n=10$)	Total ($N=39$)	*P* value
Sex, no. (%)				0.94
Female	17 (58.6)	6 (60.0)	23 (59.0)	
Male	12 (41.4)	4 (40.0)	16 (41.0)	
Age on visit				0.02
Median (Q1, Q3)	56.0 (48.0, 63.0)	45.0 (40.0, 56.0)	55.0 (46.0, 62.0)	
Aneurysm location, no.[a] (%)				0.06
Anterior circulation	10 (35.7)	7 (70.0)	17 (44.7)	
Posterior circulation	18 (64.3)	3 (30.0)	21 (55.3)	
Aneurysm diameter (mm)[a]				0.59
Median (Q1, Q3)	7.0 (5.0, 9.5)	6.2 (4.6, 7.5)	6.7 (5.0, 9.1)	
Modified Fisher score				0.48
Median (Q1, Q3)	4.0 (3.0, 4.0)	4.0 (4.0, 4.0)	4.0 (3.0, 4.0)	
Glasgow Coma Scale				0.51
Median (Q1, Q3)	11.0 (6.0, 14.0)	7.5 (4.0, 13.0)	9.0 (4.0, 14.0)	
IVH, no. (%)				0.98
Absent	3 (10.3)	1 (10.0)	4 (10.3)	
Present	26 (89.7)	9 (90.0)	35 (89.7)	
Vasospasm, no. (%)				0.03
Absent	14 (48.3)	1 (10.0)	15 (38.5)	
Present	15 (51.7)	9 (90.0)	24 (61.5)	
ICP during clamp				0.39
Median (Q1, Q3)	7.8 (4.3, 13.2)	10.7 (7.3, 14.7)	9.0 (4.3, 14.3)	
Days to clamp trial[a]				0.58
Median (Q1, Q3)	13.0 (10.0, 18.0)	15.0 (8.0, 20.0)	14.0 (10.0, 19.0)	
mRS at discharge				0.24
Median (Q1, Q3)	4.0 (3.0, 4.0)	4.0 (3.0, 5.0)	4.0 (3.0, 4.0)	
mRS at 1 year[a]				0.71
Median (Q1, Q3)	4.0 (2.0, 4.0)	3.5 (2.0, 5.0)	4.0 (2.0, 5.0)	

dVPS delayed ventriculoperitoneal shunt, *eVPS* early ventriculoperitoneal shunt, *ICP* intracranial pressure, *IVH* intraventricular hemorrhage, *mRS* modified Rankin scale, *Q1* first quartile, *Q3* third quartile

[a] Refers to the loss of some patient data during follow-up for the following variables: total number available for aneurysm location in eVPS ($n=28$), total ($n=38$); aneurysm diameter eVPS ($n=24$), dVPS ($n=8$), total ($n=32$); days to clamp trial eVPS ($n=27$), total ($n=37$); mRS at 1 year eVPS ($n=19$), total ($n=29$)

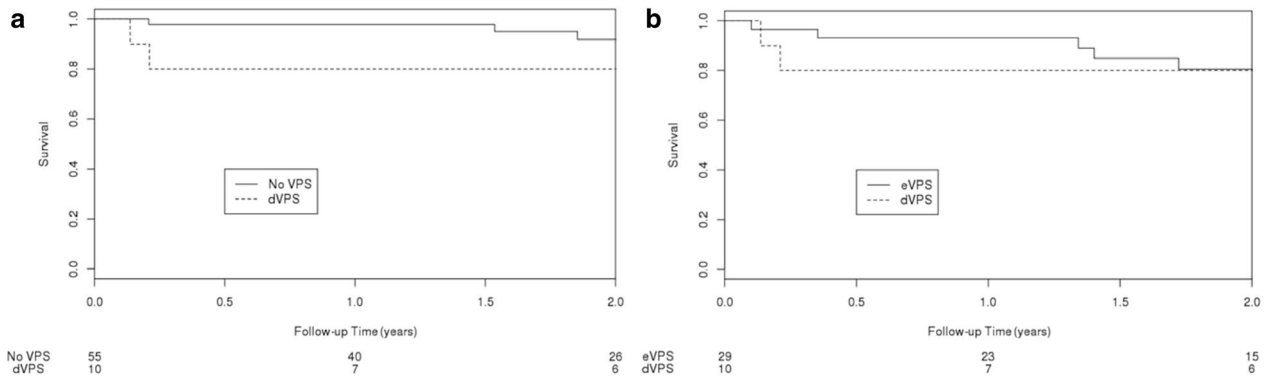

Fig. 2 Kaplan–Meier survival estimates. **a** This graph compares patients with delayed ventriculoperitoneal shunting (dVPS) and patients who passed their clamp trial and did not require a ventriculoperitoneal shunt (no VPS). There was no significant difference at 2 years ($P=0.14$), but there was significantly higher survival in the no VPS group at 6 months ($P=0.02$), and 1 year ($P=0.02$), **b** this graph compares the patients in the dVPS group with patients who had early ventriculoperitoneal shunting (eVPS). There was no significant difference at 2 years ($P=0.78$), 6 months ($P=0.22$), or 1 year ($P=0.22$)

investigating short- and long-term outcomes of hydrocephalus after aSAH [7].

Our data regarding the incidence of acute hydrocephalus requiring an EVD after aSAH are similar to other publications (mean [range], 25% [6–67%]) [1–5]. These data also suggest that hydrocephalus occurrence may increase with the severity of the illness and may be associated with worsened functional status. Delayed hydrocephalus after hospitalization could also result in lack of neurologic improvement, requiring hospital readmission for VPS placement. In our study, 21% of our aSAH patients with acute hydrocephalus required VPS prior to discharge, which is similar to the other studies [1, 2]. However, the novel finding in our study is that up to 15% of patients who initially passed their EVD clamp trial later required VPS after discharge, which we found to be higher than previously reported [1, 2].

This study is important because it demonstrates several findings around CSF physiology and hydrocephalus after aSAH. Two or more unsuccessful EVD clamp trials appear to be associated with increased risk of delayed hydrocephalus and possible VPS over the first 6 months. The strength of this study is that our center uses a standardized approach to EVD weaning and clamping compared to other aSAH-related hydrocephalus and VPS literature, which could eliminate considerable variation that may exist in a neurosurgeon's choice in timing, duration, and methods. There is, however, no standardized algorithm for deciding which patients need to be shunted, highlighting the need for this study. Klopfenstein et al. [20], for example, found no difference in the rate of chronic hydrocephalus requiring VPS when randomizing patients to a 96-h compared to a *rapid* 24-h wean. When assessing patients who were discharged from the hospital with no VPS, patients who failed 2 or more clamp trials during admission had a higher risk of returning with delayed hydrocephalus requiring VPS, when compared with patients who never required VPS ($P \leq 0.01$). Also, when comparing number of EVD weaning attempts and ultimate VPS, delayed hydrocephalus occurred in approximately 8% of patients who passed their first clamp trial, compared to 14% who failed their first trial and 80% who failed 2 or more. With this information, it seems that repeated unsuccessful EVD clamp trials have diminishing returns, and predict higher rates of VPS.

Another important finding from this study is the observation that dVPS patients have poorer early outcomes compared to patients not requiring VPS. Our dVPS group had higher mRS at discharge ($P = 0.02$), yet no difference by 1 year ($P = 0.10$). It is generally known that VPS is associated with worsened early outcomes in patients with aSAH [21]. Our data demonstrate Kaplan–Meier survival estimates with higher mortality at 6 months ($P = 0.02$) and 1 year ($P = 0.02$), but no significant difference at 2 years ($P = 0.14$). This worsened outcome could potentially be explained by the increased incidence of symptomatic vasospasm as these patients typically present with lethargy and focal neurologic deficit.

Posterior circulation aneurysms are reported to have a nearly twofold greater risk of rupture and subsequent shunt dependency than anterior circulation aneurysms [2, 8], and our results revealed a trend toward increased risk of dVPS in patients with posterior circulation aneurysms ($P = 0.06$). It has been reported that patients older than 60 years are at increased risk of hydrocephalus requiring VPS [22–24]. Interestingly, our study showed a trend toward younger patients being more likely to develop delayed hydrocephalus. It is possible that there are age-related factors as brain volume, compliance/elastance, as well as subarachnoid space volume and arachnoid granulation differences with changes in CSF flow that may predispose to delayed hydrocephalus. The clinical imaging available for this study was inadequate to visualize CSF flow patterns or arachnoid granulations. Future studies could investigate additional advanced neuroimaging and clinical risk factors for delayed hydrocephalus.

Vasospasm appeared to be associated with dVPS in our study. Vasospasm is a delayed neuroinflammatory response, with a well-known association with aSAH, as high levels of selectins and other inflammatory molecules are found in the CSF of these patients [25, 26]. While previous studies identified vasospasm as a factor for overall shunt risk [2, 23, 24, 27, 28], our data reveal that symptomatic vasospasm has a significantly higher incidence in dVPS patients compared to eVPS patients (90% vs 52%; $P = 0.03$). Also, there is likely variability in the size of arachnoid granulations from patient to patient [29], and it is possible that patients with small arachnoid granulations are more prone to chronic hydrocephalus secondary to inflammatory scarring and subarachnoid protein debris obstruction of these granulations. In theory, CSF diversion of SAH blood products could reduce the neuroinflammation obstructing the arachnoid villi, which may reduce the risk of subsequent hydrocephalus. A larger prospective study would be needed to draw conclusive data regarding a true correlation between vasospasm and delayed hydrocephalus.

Most of the patients with delayed hydrocephalus in this series had a clinical presentation similar to NPH, including gait impairment, urinary issues, and cognitive decline or plateau. The mean time to presentation was over 3 months after discharge, indicating a gradual process in most cases. Only one patient with delayed hydrocephalus presented with coma by the time of presentation

at 188 days after discharge. While this is an extreme case from our series, it highlights the importance of high clinical suspicion and need for early recognition of this entity in patients deemed to be at risk. All patients with dVPS had radiographic evidence of hydrocephalus with ventriculomegaly in conjunction with clinical findings, which resolved after VPS (Fig. 3). Consideration may be made to implement serial non-contrast head CTs in high-risk patients during follow-up visits, for up to 6 months. This may identify developing hydrocephalus in these patients before it becomes severe and may warrant a more detailed cognitive assessment to supplement the standard neurologic examination completed in the clinic.

Optimal timing of VPS after aSAH is a topic of intense debate. Neurosurgeons have previously been concerned that ultra-eVPS placement after aSAH and catheter placement into a ventricle with hemorrhage and high CSF protein could lead to shunt failure and revision. On the other hand, waiting 21 days or longer before VPS can be concerning for prolonged length of stay and risk of developing ventriculitis. Studies have found that intraventricular hemorrhage and proteinaceous CSF do not necessarily preclude successful VPS placement, and earlier VPS can be considered rather than delaying VPS unnecessarily in these patients [30, 31]. Our data do not report any significant differences in intraventricular hemorrhage presence when comparing eVPS versus dVPS ($P=0.98$).

A limitation of this study is that we utilized standard of care neuroimaging in neurosurgical practice, which was commonly non-contrast head CT to monitor for ventriculomegaly. While this makes the data more applicable and practical, standard imaging cannot assess for microscopic (communicating) hydrocephalus similar to NPH. Overall, the pathophysiology of delayed hydrocephalus after aSAH (especially 30–90 days later) remains poorly understood, particularly since these patients appear to tolerate EVD weaning and removal during the acute phase. While giant arachnoid granulations can be seen best on magnetic resonance imaging (MRI) sequences, such as T2-weighted and fluid-attenuated inversion recovery, and on contrast-enhanced CT images [32], these are not always utilized in the immediate or follow-up clinic settings. Advanced imaging techniques, such as thin-cut and flow-sensitive MRI, should be considered in future studies and may reveal patients with smaller-than-average arachnoid granulations and impaired CSF outflow [33–35]. Further, MRI techniques evaluating CSF flow patterns for other neurologic diseases, and although not routinely performed for aSAH patients, could also be considered. Finally, the use of advanced MRI and CSF flow studies may help practitioners determine whether patients who are borderline or who marginally pass their EVD clamp trial will benefit from eVPS [36–39]. However, this application would need to be investigated further in clinical trials or animal models.

We acknowledge that our study is primarily limited by its retrospective single-center design and that our results should be validated in a prospective multicenter study. Delayed hydrocephalus is an uncommon occurrence in our practice, but one we feel is worth reporting for greater awareness in other centers. Finally, this study was limited by the inability to assess the volume of CSF drained per day. Intermittent CSF drainage during initial or repeated clamp trials could provide clues to subsequent delayed hydrocephalus and failure. However, failing more than one EVD clamp trial increased the odds of delayed hydrocephalus (dVPS in 7.8% of patients who passed the initial EVD clamp trial, 14.3% who failed the initial trial, and 80.0% who failed 2 or more trials).

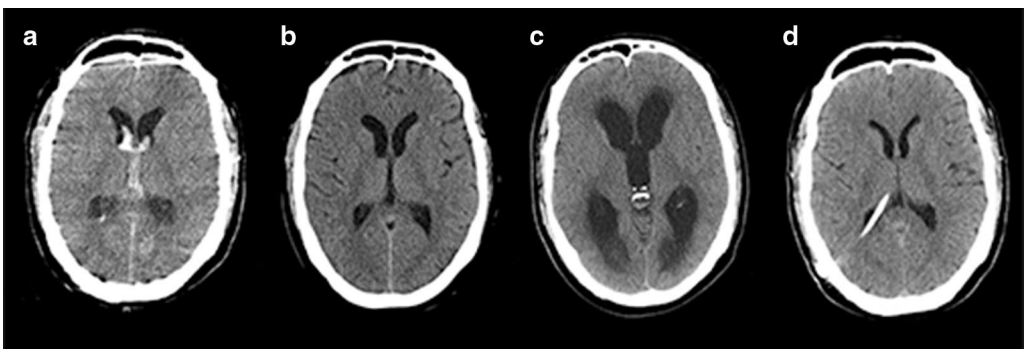

Fig. 3 Computed tomography (CT). **a** Non-contrast head CT at time of admission demonstrating modified Fisher score 4 subarachnoid hemorrhage and early signs of hydrocephalus with ventricular dilation, **b** same patient CT completed immediately after successful removal external ventricular device, **c** thirty-six days after discharge, this same patient presented with nausea, vomiting, and headache. Head CT revealed marked ventricular enlargement, **d** CT completed after ventriculoperitoneal shunt placement for this same patient

Conclusion

Patients with aSAH who failed their initial or subsequent EVD clamp trial appeared to have increased risk of developing delayed hydrocephalus requiring VPS. Additionally, the majority of patients who presented with delayed hydrocephalus also suffered symptomatic vasospasm. These apparent associations should be further explored in a larger prospective study.

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Author Contributions

OOA contributed to conception/design, data collection/analysis/interpretation, manuscript writing/critical revision, tables/figures. TGV-B contributed to data collection, tables/figures. NH contributed to manuscript writing/critical revision. SG contributed to data collection. NM contributed to data collection. RGT and MTT contributed to manuscript critical revision. WDF contributed to conception/design, manuscript critical revision. All authors approved the final article.

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