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Decreased CSF output as a clinical indicator of cerebral vasospasm following aneurysmal subarachnoid hemorrhage

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ABSTRACT

Objective: Vasospasm is a significant cause of morbidity and mortality among those with aneurysmal subarachnoid hemorrhage (aSAH). Treating increased intracranial pressure by drainage of cerebral spinal fluid through an external ventriculostomy is routine practice. The objective of this study is to evaluate the trends of CSF output in patients who experience vasospasm.

Methods: Electronic medical charts were reviewed to identify two groups of patients with aSAH, 75 consecutive patients who developed vasospasm and 75 matched patients who did not develop vasospasm. CSF output was recorded within 3 days before and 3 days after the occurrence of vasospasm. CSF output was recorded for the same days after SAH in matched patients with no vasospasm.

Results: Total CSF output was lower in patients with vasospasm as compared to patients without vasospasm matched for the same day ($p < 0.001$). In patients with vasospasm, CSF output recordings were significantly higher prior to the occurrence of vasospasm (438 ml/day) than the period following vasospasm (325.7 ml/day), with a consistent decrease in CSF drainage from day 3 before vasospasm to day 3 after vasospasm ($p = 0.012$). Decreasing CSF output was significantly associated with the occurrence of vasospasm ($p = 0.017$). Youden indices demonstrated that daily CSF drainage <160 ml was significantly associated with the occurrence of vasospasm. The sensitivity of this test was 64.79% and the specificity was 55.38%.

Conclusions: In addition to clinical exam findings, observation of a CSF output decline to less than 160 ml/day may be used as additional support for the diagnosis of vasospasm.

1. Introduction

A subarachnoid hemorrhage (SAH) is the release of blood into the subarachnoid space. The most common causes include hemorrhage from a ruptured aneurysm, an arteriovenous malformation (AVM) or traumatic injury such as blunt force injury to the skull. Immediate life threatening consequences of SAH occur from the clotting and hemolysis of blood in the subarachnoid space and the concomitant hydrocephalus that often occurs leading to increased intracranial pressure (ICP) [1–4]. As a result of the increase in ICP, an external ventricular drain (EVD) is placed in SAH patients to allow for drainage of CSF and maintenance of a normal ICP [2]. Cerebral vasospasm is the delayed-onset narrowing of arteries following SAH and is a significant cause of morbidity and mortality in these patients [5]. It has been shown that facilitating the drainage of CSF leads to faster clot evacuation and subsequently a decreased incidence of vasospasm [2]. Vasospasm occurs approximately three days after SAH, peaks between six to eight days and is usually resolved within twelve days [6]. The onset of vasospasm can include symptoms such as increasing headache, progressive confusion and delirium, weakness or lethargy [7]. About one third of patients with aneurysmal SAH will experience clinical vasospasm and approximately one half to two thirds of aneurysmal subarachnoid hemorrhage patients will have angiographic vasospasm. The incidence of cerebral vasospasm is reported to be between 40 and 70% in patients with SAH with 30% of those patients developing delayed cerebral ischemia (DCI), making an adverse outcome more likely [8]. As a result of DCI, patients may display clinical

Abbreviations: aSAH, aneurysmal subarachnoid hemorrhage; AVM, arteriovenous malformation; CBF, cerebral blood flow; CSF, cerebrospinal fluid; DCI, delayed cerebral ischemia; EVD, external ventricular drain; ICP, intracranial pressure; PTA, percutaneous transluminal angioplasty; TCD, transcranial doppler.

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symptoms such as hemiparesis, aphasia, or a decrease in the level of consciousness [9]. Due to the severe complications of vasospasm, Transcranial Doppler (TCD) ultrasound is often used to monitor cerebral blood flow and velocity in SAH patients [10]. The strong correlation between flow velocities in cerebral arteries and cerebral vasospasm severity after SAH makes TCD ultrasound a valuable tool in monitoring vasospasm [10]. Currently, there are three widely-used treatments for vasospasm: percutaneous transluminal angioplasty (PTA) [11], intra-arterial infusion of vasodilators [12,13], and induced hypertension [14]. Previous studies have shown endovascular therapy to have a remarkable safety-efficacy profile with both PTA and nicardipine, a calcium channel antagonist, being equally effective [5]. Induced hypertension involves the elevation of mean arterial pressure with vasopressors and has been shown to be effective in increasing cerebral blood flow (CBF) [4]. At this time, it is difficult to predict which patients will develop vasospasm and when. However, our findings suggest that there is a correlation between CSF output trends and vasospasm. The influence of such a correlation would allow for pre-emptive treatment and decrease the adverse effects of vasospasm. In this study, we evaluated the CSF output trends before and after patients were treated for cerebral vasospasm in order to determine if CSF output can be used as a clinical indicator for impending vasospasm.

2. Materials and methods

2.1. Patient selection and outcomes

The study protocol was approved by the University Institutional Review Board. A patient list of consecutive patients with aneurysmal subarachnoid hemorrhage (aSAH) was generated based on ICD-9 codes. Electronic medical charts were reviewed to identify two groups of patients with aSAH: patients who developed clinical vasospasm and patients who did not develop clinical vasospasm post aSAH. Clinical vasospasm was defined as a worsening in neurologic status that could not be attributed to any other factor including rebleeding, hydrocephalus, intracerebral hematoma and metabolic factors. The presence of arterial vasospasm was confirmed with a cerebral angiogram in all patients as evidence of >30% arterial luminal narrowing. 116 consecutive patients with clinical vasospasm post aSAH were identified between January 2007 and December 2012. All patients had an EVD. Initially, the drainage is set at 15–20 cm H2O. Hourly CSF outputs were collected and combined to determine the daily CSF output. Daily CSF output levels were evaluated within three days prior to the occurrence of clinical vasospasm and within three days after vasospasm. Patients with missing CSF output levels were excluded from the study (n = 42). 75 patients with clinical vasospasm meeting the study criteria were included. Blinded to the outcomes of the study, 75 patients with aSAH who did not develop clinical vasospasm were matched in a 1:1 fashion to patients with vasospasm based on patient age, gender, Hunt and Hess, and Fisher grades. Hunt and Hess and Fisher grades were determined by the treating neurosurgeon.

The primary outcome of this study was to evaluate trends of CSF output in patients who develop vasospasm after aSAH and identify any potential associations between CSF drainage and the occurrence of vasospasm. Secondary outcomes included (1) sensitivity and specificity analysis of CSF output in predicting the occurrence of clinical vasospasm and (2) an evaluation of other factors that may be associated with the occurrence of vasospasm.

2.2. Statistical analysis

Data are presented as mean and range for continuous variables, and as frequency for categorical variables. Patients who did and did not experience vasospasm were matched based age, gender, H&H and Fisher grades and days of CSF output measurement blinded to all other outcomes. Analysis was carried out using Wilcoxon paired rank sum test and McNemar's test as appropriate. Univariate conditional (matched) analysis was used to test covariates predictive of vasospasm. The following factors were tested: age, sex, smoking, hypertension, Hunt and Hess grade, Fisher grade, aneurysm location and CSF output. Interaction and confounding was assessed through stratification and relevant expansion covariates. Factors predictive in univariate analysis ($p < 0.20$) [15] were entered into a multivariate conditional logistic regression analysis. Regression models were assessed using area under the receiver operating characteristic curve (AUC). Youden Indices were calculated to determine cutoffs for the dichotomized continuous variable CSF output that yielded the optimal discrimination of vasospasm (sensitivity, specificity, positive predictive value, negative predictive value). P-values of ≤ 0.05 were considered statistically significant. Statistical analysis was carried out with Stata 10.0 (College Station, TX) [15].

Table 1
Baseline characteristics.

	Vasospasm	No vasospasm	P value
Mean patient age	54	53.4	0.72
Women	70.7%	70.7%	1
Men	29.3%	29.3%	1
Smoking	33.3%	63.5%	<0.001
Hypertension	44%	49%	0.52

Table 2
Hunt and Hess grades.

	Vasospasm	No vasospasm	Percent
1	2	2	2.7
2	7	7	9.3
3	40	39	53.3
4	24	25	32
5	2	2	2.7

Table 3
Fisher grades.

	Vasospasm	No vasospasm	Percent
1	0	0	0
2	9	9	12
3	12	12	16
4	54	54	72

3. Results

3.1. Baseline characteristics

The mean patient age was 54 years. Baseline characteristics of patients with and without vasospasm are detailed in Table 1. 70.7% of patients were women and 29.3% men. The only significant difference between the two groups was a higher percentage of smokers in the no vasospasm group ($p < 0.001$). The majority of patients had Hunt and Hess grade 3 (53%) (Table 2). SAH was Fisher grade 2 in 12% of patients, Fisher grade 3 in 16% and Fisher grade 4 in 72% (Table 3). In patients with vasospasm, 17.3% of aneurysms were located in the posterior circulation versus 14.8% in patients without vasospasm (P = 0.68). Aneurysm locations are detailed in Table 4.

3.2. CSF output

CSF output was recorded within 3 days before and 3 days after the occurrence of vasospasm (Table 5). CSF output was recorded for