Predictors of Shunt-Dependent Hydrocephalus Following Aneurysmal Subarachnoid Hemorrhage

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■ BACKGROUND: **Shunt-dependent hydrocephalus is a common complication of aneurysmal subarachnoid hemorrhage (aSAH). There is a need to identify patients who require ventriculoperitoneal shunt (VPS) insertion so that any modifiable risk factors can be addressed early after aSAH.**

■ METHODS: **Exploratory analysis was performed on 413 patients enrolled in CONSCIOUS-1, a prospective randomized controlled trial of patients with aSAH treated with clazosentan. The association between clinical and neuroimaging covariates and VPS placement was first determined by univariate analysis. Covariates with $P < 0.15$ on univariate analysis were then analyzed in a multivariate logistic regression model. Receiver operating characteristic curve analysis was used to define optimal predictive thresholds. The published literature was reviewed to determine the overall rate of VPS insertion after aSAH.**

■ RESULTS: **Overall, 17.2% (71/413) of patients required VPS insertion. Multivariate analysis demonstrated that insertion of an external ventricular drain (odds ratio, 6.21; 95% confidence interval, 2.51–16.91) and increasing volume of cerebrospinal fluid (CSF) drainage per day (odds ratio, 1.004; 95% confidence interval, 1.000–1.009) were associated with VPS insertion. Receiver operating characteristic curve analysis revealed an optimal daily CSF output threshold of 78 mL was predictive of VPS insertion. Among 41,789 patients with aSAH from 66 published studies, the overall VPS insertion rate was 12.7%.**

■ CONCLUSIONS: **The presence of an external ventricular drain and increased daily CSF output (above 78 mL/day) seems to be predictive of subsequent VPS insertion after aSAH. Although we could not identify modifiable risk factors for needing a VPS, nevertheless, these findings identify patients at greatest risk of VPS placement and inform treatment decisions as well as patient expectations.**

INTRODUCTION

The incidence of shunt-dependent hydrocephalus after aneurysmal subarachnoid hemorrhage (aSAH) ranges from 2% to 48%.[1-7] At present, considerable heterogeneity exists among neurosurgeons with respect to decision making regarding insertion of ventriculoperitoneal shunts (VPS) after aSAH. The variability in institutional policies and treating physician choices regarding shunt-dependent hydrocephalus management was demonstrated by Esposito et al.[8] as a dichotomy between hospital length of stay and shunting rate. Practice styles that prioritize early shunting and discharge tend to have higher shunting rates, whereas those that tend to minimize shunting rates have longer inpatient hospital stays.

It is increasingly important to identify patient factors that may be associated with VPS placement for several reasons. First, shunt-dependent hydrocephalus is associated with a considerable medical burden for the patient as well as health care systems, as nearly half of shunt-related procedures performed in the United States are revisions of previous insertions,[9] with 35%–50% of shunts requiring revision within the first year of placement.[10-12] In patients with VPS placed after aSAH, the revision rate may be as high as 42% in the first 6 months, with a third of these patients requiring multiple revisions.[13] Identifying patients at risk of shunt-dependent hydrocephalus may therefore mitigate unnecessary VPS

Key words
- Hydrocephalus
- Multivariate analysis
- Risk factors
- Shunt
- Subarachnoid hemorrhage

Abbreviations and Acronyms
aSAH: Aneurysmal subarachnoid hemorrhage
CSF: Cerebrospinal fluid
EVD: External ventricular drain
ROC: Receiver operating characteristic
VPS: Ventriculoperitoneal shunt
WFNS: World Federation of Neurosurgical Societies

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placements in low-risk patients. Second, knowledge of the risk of shunt-dependent hydrocephalus may facilitate the management of patient expectations and hospital resources, including duration of hospital stay. Third, with increasing acceptance of stent-assisted coiling, an increasing number of patients are placed on antiplatelet therapy. Early experiences have shown that such agents may be associated with an increased rate of symptomatic intracranial hemorrhage with VPS insertion.[14] Knowledge of the risk of requiring VPS placement may play some role in guiding treatment decisions regarding the procedure to secure the aneurysm.

The objective of this study was to identify clinical and radiographic factors associated with VPS insertion after aSAH in patients enrolled in the Clazosentan to Overcome Neurological iSChemia and Infarction OccUring after Subarachnoid hemorrhage (CONSCIOUS-1) trial.[15] Determining such factors may help influence decision making regarding VPS insertion.

METHODS

Study Population

A post hoc analysis was performed on the 413 patients enrolled in the CONSCIOUS-1 trial, a prospective, randomized, double-blinded phase IIb trial investigating the endothelin-receptor antagonist clazosentan in patients with aSAH.[15] Patients were enrolled in the trial between January 2005 and March 2006. The clinical trial methods and results have been published.[15] The trial was registered (https://clinicaltrials.gov NCT00111085).

Clinical Assessment

The primary outcome in this post hoc analysis was whether patients had VPS insertion. Clinical and demographic information was obtained from the trial data. Patients were graded on the World Federation of Neurosurgical Societies (WFNS) scale.[16] Patients were followed up at 12 weeks after aSAH, with clinical outcome assessed using the extended Glasgow Outcome Score and the modified Rankin Scale.[17,18]

Radiology

Using the initial noncontrast head computed tomography scan, the subarachnoid clot burden was evaluated using the Hijdra scale.[19] Intraventricular hemorrhage was evaluated using a modification of the Graeb score: 0 (no blood), 1 (sedimentation, but less than 25% filled), 2 (moderately-filled), or 3 (completely filled) for each of the 4 ventricles with a maximum score of 12.[20,21]

Statistics

Descriptive statistics were reported as means and frequencies. Ordinal variables were described with median values and interquartile range. Comparisons of ordinal variables used the nonparametric Mann-Whitney U test. Fisher's exact test was used to compare proportions and the χ^2 test was used for categorical variables. Univariate analysis was performed to determine associations between VPS placement and the clinical and imaging variables. Variables with $P < 0.15$ were entered into a multivariate logistic regression model. Statistical significance was set at $P < 0.05$. Receiver operating characteristic (ROC) curve analysis was performed to determine the optimal threshold for continuous variables that were found to be significant after multivariate analysis. The statistical analysis was performed using R Statistical software.

LITERATURE REVIEW

PubMed was searched on 15 March 2015 with the search strategy ("subarachnoid hemorrhage" OR "subarachnoid haemorrhage") AND "shunt." This search strategy yielded a total of 482 articles; 90 of these articles actually represented clinical studies investigating the use of shunts after aSAH. References were also checked for relevant studies. Twenty-eight studies were identified that utilized multivariate analysis to identify risk factors for VPS insertion after aSAH.

RESULTS

Patients

Patient characteristics are displayed in Table 1. VPS was associated with worse clinical outcome at 12 weeks based on the extended Glasgow Outcome Score and modified Rankin Scale.

Univariate Analysis

On univariate analysis (see Table 1), factors associated with VPS insertion after aSAH were older age, history of hypertension, increased heart rate on admission, WFNS score of IV–V, ventriculomegaly or more severe intraventricular hemorrhage on initial imaging, external ventricular drain (EVD) insertion, greater volume of cerebrospinal fluid (CSF) drainage per day, longer length of stay in a critical care unit, greater subarachnoid clot burden, slower rate of subarachnoid clot clearance, and ventriculitis/meningitis.

Multivariate Analysis

In the multivariate logistic regression model, we included variables that were associated with VPS placement after aneurysm rupture on univariate analysis with $P < 0.15$ (Table 2). Of these, only EVD insertion (odds ratio, 6.21; 95% confidence interval, 2.51–16.91; $P < 0.001$) and CSF volume (milliliters) drained per day (odds ratio, 1.004; 95% confidence interval, 1.000–1.009; $P = 0.033$) were associated with VPS insertion.

ROC Curve Analysis

The only significant continuous variable associated with VPS insertion on multivariate analysis was the volume of CSF (milliliters) drained per day. To establish the optimal threshold for CSF drainage that may be associated with shunt-dependent hydrocephalus, we used ROC analysis (Figure 1). An optimal CSF drainage volume threshold of 78 mL/day provided 81% sensitivity and 72% specificity. This was associated with 39% and 95% positive and negative predictive values, respectively. The area under the curve was 0.80.

DISCUSSION

Using detailed prospective clinical trial data, this exploratory analysis found that EVD insertion and larger daily volume of CSF drainage from an EVD independently predicted shunt-dependent hydrocephalus after aSAH. The current study is the first to