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Predicting slitlike ventricles in children on the basis of baseline characteristics at the time of shunt insertion

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Object. Slit ventricle syndrome (SVS) is a delayed complication of shunt insertion and occurs only in children with slitlike ventricles after shunt placement. Although SVS appears to be related to early shunt placement, its predisposing factors are largely unknown.

Methods. Baseline data in 737 children who had received shunts were obtained from the databases of two previous clinical trials. Ventricular size before shunt placement and at the last routine follow up was measured using the frontooccipital horn ratio (FOHR). Ventricles with an FOHR less than or equal to 0.2 at follow up were classified as slitlike ventricles. A univariate analysis was performed on data obtained in children with more than 1 year of clinical and radiographic follow up to identify risk factors for developing slitlike ventricles. These results were entered into a multivariate analysis to identify independent predictors of slitlike ventricles.

Two hundred forty-four children had more than 1 year of clinical and radiographic follow-up data. The 23 patients (9.4%) who developed slitlike ventricles had shunts inserted at a younger age (42 compared with 134 days, $p = 0.09$) and were more likely to have developed hydrocephalus secondary to infection (37.5%), head injury (25.0%), or aqueductal stenosis (22.2%). Slitlike ventricles were seen in 10.8% of patients with differential-pressure valves, 10.5% of patients with Delta valves, and 3.6% of patients with Orbis-Sigma valves ($p = 0.007$). Regression analysis supported the role of the valve type in developing slitlike ventricles.

Conclusions. Age at shunt insertion and valve type appear to be the modifiable risk factors for developing slitlike ventricles. If the authors of subsequent studies can further validate these conclusions, slow-draining valves and delayed shunt insertion might be used to decrease the incidence of slitlike ventricles and SVS.

Key Words • slitlike ventricle • slit ventricle syndrome • hydrocephalus • predictive factor • ventriculoperitoneal shunt • pediatric neurosurgery

The outcome in patients who develop hydrocephalus has improved dramatically in the modern era of cerebrospinal fluid shunt placement. The insertion of shunts still has several potential complications, however, including SVS. Slit ventricle syndrome is a condition in which children have significant chronic headaches and symptoms suggestive of shunt malfunction as well as ventricles that appear smaller than normal on imaging. Slit ventricle syndrome is distinguished from other shunt-related complications because it occurs in a delayed fashion and only in children with shunt placements whose ventricles appear slitlike on imaging. Although several predisposing factors for the development of SVS have been proposed, its risk factors and causes remain largely unknown.

The treatment of SVS is difficult, and this subgroup of patients often undergoes costly evaluations and repeated surgeries with limited relief. At present, there is no consensus on the management of SVS. Medications, shunt revision, lumboperitoneal shunt insertion, subtemporal decompression, and cranial vault expansion have all been used, but with limited success.

The purpose of this study was to identify risk factors for slitlike ventricles from data obtained in two multicenter randomized trials of hydrocephalus in children. A better understanding of the predisposing conditions and modifiable risk factors may allow us to develop better treatment strategies or decrease the incidence of SVS through preventive measures.

Clinical Material and Methods

Baseline data obtained in 737 children who underwent initial shunt insertion were obtained from the databases of the SDT[3] and ESIT.[7] These data included age at shunt insertion, ventricle size before shunt insertion, valve type, entry site (coronal or occipital), cause of hydrocephalus, and other clinically relevant parameters. Together, these baseline characteristics form the group of potential risk factors for SVS.

In the SDT (1993-1998), 344 children with newly diagnosed hydrocephalus were randomized into groups to re-

Abbreviations used in this paper: CT = computed tomography; DP = differential pressure; ESIT = Endoscopic Shunt Insertion Trial; FOHR = frontooccipital horn ratio; SDT = Shunt Design Trial; SVS = slit ventricle syndrome.

ceive one of three types of shunt valves: a standard DP valve, a Delta Valve, or an Orbis-Sigma valve. In the ESIT (1996-1999), 393 children with newly diagnosed hydrocephalus who were scheduled to receive their first ventriculoperitoneal shunts were randomized to undergo endoscopic or nonendoscopic insertion of a ventricular catheter. In both trials, patients were followed up for a minimum of 1 year or until first shunt failure. In patients without evidence of shunt failure, follow-up examinations were performed at 3 and 12 months (and in some patients at 24 and/or 36 months) after shunt insertion.

Ventricle size prior to the first shunt insertion and at the last routine follow-up examination when the shunt was functioning was measured using the FOHR.[11] The FOHR is an average of the maximum lateral width of the frontal and occipital horns divided by the maximal lateral diameter of the cranium. A normal FOHR, independent of age, is approximately 0.37.[11]

For this study we developed a definition of slitlike ventricles. A committee of three pediatric neurosurgeons reviewed CT images of four different ventricle sizes in children with shunts (FOHRs of 0.3, 0.25, 0.2, or 0.1). The committee was not aware of the measurements and was asked to classify the ventricles as slitlike or not, based on the images only. The committee members consistently classified ventricles with an FOHR less than or equal to 0.2 as slitlike. We therefore used this FOHR (≤ 0.2) as our threshold criterion for slit ventricles.

Previous studies have shown that ventricle size decreases during the first year after shunt insertion[17] and then stabilizes at a size that becomes the patient's baseline ventricle size. Therefore, only children whose shunts did not fail and who had at least 1 year of clinical and radiographic follow-up data were included in the analysis. A univariate analysis was performed to identify factors associated with slitlike ventricles. A logistic regression model was then developed to determine the baseline factors that were associated with slitlike ventricles. The database was developed and analyzed using commercially available software (SPSS version 13.0, SPSS, Inc.).

Results

The individual results of the SDT and ESIT have been published.[3,7] The combined data set contained data from 737 children, of whom 414 had a functioning shunt throughout the follow-up period (no shunt failure). Of those 414 patients, 244 had brain imaging results available for analysis at or beyond 1 year of follow-up monitoring.

The median age of all patients was 42 days. Of the three valve types used, 45.1% of the children received a standard DP valve, 31.1% a Delta valve, and 23.4% an Orbis-Sigma valve. An occipital entry site for the ventricular catheter was used in 62% of patients. Intraventricular hemorrhage and meningomyelocele were the most common causes of hydrocephalus (23.0 and 22.4%, respectively). The mean preoperative ventricular size (the FOHR) was 0.55 (range 0.35–0.90).

Of the 244 patients, 23 children (9.4%) had an FOHR of 0.2 or less at follow up and were classified as the slitlike ventricle group. The univariate analysis revealed that patients who developed slitlike ventricles underwent shunt insertion at a younger age (median of 42 days compared with 134 days, $p = 0.09$) and had a high incidence of hydrocephalus secondary to infection (37.5%), head injury (25%), or aqueductal stenosis (22.2%). Slitlike ventricles were noted in 10.8% of patients who had DP valves, 10.5% of patients with Delta valves, and 3.6% of patients with Orbis-Sigma valves ($p = 0.007$). Site of insertion, preoperative ventricle size, and other parameters had no predictive value. Of these 23 patients, only two developed signs of SVS that required shunt revision.

The factors used for the logistic regression analysis included valve type, age at shunt insertion, and cause of hydrocephalus. The regression analysis supported the role of the valve type as the strongest independent predictor of slitlike ventricles. After controlling for age at shunt insertion and cause of hydrocephalus, children with either a DP or Delta valve were found to be 1.66 times more likely to develop slitlike ventricles than children with an Orbis-Sigma valve.

Discussion

The development of SVS is a delayed complication of shunt insertion, and the interval between first shunt insertion and SVS development can be as long as 6.5 years.[9,15] The incidence of SVS in children with shunts has been reported to be 1 to 37%.[1,8,10,12,16] As the name implies, SVS only occurs in children with slitlike ventricles after shunt insertion. In a series of 370 children with shunts, 64% were reported to have ventricles that appeared slitlike on imaging, but only 11.5% developed SVS.[18] Other investigators obtained similar findings and reported that, although slitlike ventricles can exist in over 50% of children with shunts,[1,16] only 6 to 22% of these children eventually developed SVS.[4,6] In our study of data from 244 children, slitlike ventricles, as noted on neuroimaging, developed in only 23 patients (9.4%), and of these, only two had signs of SVS that ultimately required a shunt revision. These findings may be a function of our shorter follow-up period, lower prevalence of low-pressure valves (7.4% in the SDT compared with $> 22\%$ in the pediatric series by Benzel and coworkers[1]), or variation in the definition of slitlike ventricles (none of the earlier series defined a size for slitlike ventricles).

Several risks factors for SVS have been proposed in the last 20 years. These risk factors include the cause of hydrocephalus, patient age at shunt insertion, baseline ventricle size, previous shunt revisions, and valve type.[1,16,19] In our study using slitlike ventricles as a surrogate outcome for SVS, we found after a univariate analysis that patients who developed slitlike ventricles tended to have had their shunts inserted at a younger age and had a high incidence of hydrocephalus secondary to infection, head injury, and aqueductal stenosis. Slitlike ventricles were also seen more commonly in patients who had DP and Delta valves than in those with Orbis-Sigma valves. Multivariate regression analysis supported the role of valve type as the strongest predictor of the development of slit ventricles.

Regarding the effect of shunt valves on the development of SVS, it has been suggested that DP valves lead to a faster collapse of ventricles and that insertion of valves with antisiphon (Delta) or flow-control (Orbis-Sigma) devices may result in slightly larger ventricles after shunt insertion.[19] On the basis of their experience in the SDT, Tuli and cowork-

ers[17] found that the reduction in ventricle size over time appeared to be slower for the Orbis-Sigma valve than for the Delta or DP valves, but these observations were not found to be statistically significant. In a large multicenter prospective cohort, the Orbis-Sigma valve was reported to reduce the incidence of overdrainage,[5] and in the SDT the Orbis-Sigma valve was associated with fewer cases of overdrainage than the DP or Delta valves. The findings in our current analysis appear to be further suggestive evidence that the Orbis-Sigma valve is associated with a lower incidence of slit ventricles.

Our observation of an association between slit ventricles and younger age has been previously suggested. Oi and Matsumoto[13,14] believed that the immature brain and cranium of infants, coupled with low intracranial pressure and dampened ventricular pressure after shunt insertion, could lead to SVS and possibly microcephaly, as well as synostosis.

In our study, patients with slitlike ventricles were more likely than other patients to have hydrocephalus secondary to infection. Subependymal and periventricular gliosis[13,14] or gliotic adhesions between the collapsed ventricular walls[2] have been suggested as causes of low compliance (stiffness) in slit ventricles. Gliosis is a well-known consequence of ventriculitis that can certainly occur in the setting of infantile meningitis. Thus, postinfection gliosis may explain our observed association between infection and slit ventricles.

Our study has several limitations. The first limitation is the use of a surrogate outcome, slitlike ventricles, to determine SVS. An ideal study would use SVS as the outcome of interest, but this would be very difficult because SVS is rare and occurs in a very delayed fashion after shunt insertion. We acknowledge that a CT finding of slit ventricles does not mean that a child will develop SVS; many will not, but children with slit ventricles as noted on CT are the ones at risk for SVS, and the object of this work is to predict, and possibly prevent, slit ventricles (as noted on neuroimaging) as a means of reducing the incidence of SVS.

The second limitation is that our predictive model needs further testing. To validate our observations, they should ideally be tested in another large population of children with hydrocephalus in a future study.

Third, despite the use of a pooled database from two large multicenter trials, the incidence of slit ventricles was low and therefore provided only a small sample of patients with slit ventricles, limiting our statistical power and ability to detect meaningful associations.

Finally, incomplete imaging results were common in our study. Of the 414 patients in the database who had no shunt failure and were clinically well at last follow up, only 244 had imaging results at that time. Thus, we may have underestimated or overestimated the incidence of slit ventricles.

Conclusions

Age at shunt insertion and valve type appear to be the modifiable risk factors for slit ventricles. If the authors of further studies validate these conclusions, slow-draining valves and delayed shunt insertion might be used to decrease the incidence of slit ventricles.

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