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Endoscopic third ventriculostomy: a feasible treatment option for pediatric hydrocephalus in a high-risk cohort – a single-center report

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Treating hydrocephalus in young child-primarily either byren and infants is still a demanding procedure with a high rate of surgery-related complications. The improvement of technology in pediatric intensive care has increased the chance of survival in very low birthweight infants, and therefore the risk for patients with posthemorrhagic hydrocephalus (PHH) has also increased. During the past 20 years, endoscopic third ventriculostomy (ETV) has become a reasonable option for treating different types of hydrocephalus, especially in the challenging field of PHH after intraventricular hemorrhage (IVH).[1–6] The reported main factors influencing the outcome of ETV are age at operation and etiology.[2–4 7 8] The success rates of ETV are low in preterm and in infants less than 1 year of age, especially in patients with posthemorrhagic and infection-related hydrocephalus.[4–6 8–10] Outcomes are more favorable in obstructive hydrocephalus, particularly idiopathic aqueductal stenosis in later childhood.[5 6 9 10] Consequently, the reported survival rates after ETV vary up to 90%.[9 10] However, the long-term outcome of ventriculoperitoneal (VP) shunting is not superior to that of ETV. Beyond controversy, children during the first year of life, especially (preterm) neonates, must be considered high-risk patients in terms of failure rates and postoperative infections.[1 11] The aim of the present study was to compare the outcome and risk of failure of ETV with VP shunting in children treated primarily for any kind of hydrocephalus during the first year of life at our institution.

This study was a retrospective comparison of infants (<1 year of age at intervention) with hydrocephalus treated primarily either by ETV or VP shunting between 1999 and 2016 in a Swiss level 1 perinatological center. All children were followed up for 18 months postsurgery. The primary endpoint was time to failure. Failure was defined as the need for surgical revision. Further analysis included a comparison of the success rates, an analysis of revision surgeries and risk factors within a period of 18 months, and a comparison of complications leading to surgical revision. Subcutaneous cerebrospinal fluid (CSF) collection was not considered a complication if it did not lead to revision surgery. The influence of age, prematurity and etiology was analyzed to identify predictors of failure.

In the ETV group, the surgical approach was either via the frontal precoronal burr hole or the lateral aspect of the anterior fontanelle. Typical third ventricle landmarks (mammillary bodies/infundibular recess) were identified during ventriculoscopy using a flexible endoscope in 20 procedures versus a rigid endoscope in three procedures. Ventriculostomy was performed with a Fogarty catheter (2–3 mm). Additional plexus cauterization was not performed in this series. In the VP shunting group, the surgical approach was performed via a frontal (or in one case occipital) burr hole using a programmable shunt valve. A burr hole snap Rickham reservoir was implanted in each child for possible emergency drainage. All procedures were performed by two experienced pediatric surgeons specializing in the field of pediatric neurosurgery.

Descriptive statistics for quantitative variables included the median and first and third quartiles (Q1, Q3). Differences between groups were analyzed using Fisher's exact test for categorical variables and Wilcoxon rank-sum test for quantitative variables. Time to first revision was evaluated by time-to-event

Table 1 Patient characteristics

	VP shunt (n=26)	ETV (n=23)
Age at operation	24.5 (6, 96)	43 (20, 148)
≤4 wk	15 (57.7)	9 (39.1)
2–6 mon	7 (26.9)	10 (43.5)
6–12 mon	4 (15.4)	4 (17.4)
Gestational age at birth (wk)	37.8 (31.9, 38.6) (n=24)	38.3 (29.3, 38.7) (n=21)
Preterm	9 (34.6)	9 (39.1)
Weight (kg)	3.3 (2.8, 4.8)	3.6 (2.8, 6.8)
Gender (male/female)	9 (34.6)/17 (65.4)	11 (47.8)/12 (52.2)
Entity		
Obstructive hydrocephalus	18 (69.2)	13 (56.5)
Posthemorrhagic hydrocephalus	8 (30.8)	9 (39.1)
Postinfectious hydrocephalus	0 (0.0)	1 (4.3)

Categorical values are presentes as number (percentage); quantitative values are expressed as median (Q1, Q3).
Fisher's exact test and results obtained byWilcoxon rank-sum test, p values non-significant.
ETV, endoscopic third ventriculostomy; Q1, first quartile; Q3, third quartile; VP shunt, ventriculoperitoneal shunt.

Table 2 Median time to revision in both treatment groups

	Estimated time until x% of patients have experienced revision	
	VP shunt (n=26)	ETV (n=23)
Percentage (X%)	Estimated time (d) (95% CI)	Estimated time (d) (95% CI)
20%	111 (6 to 257)	23 (9 to 56)
30%	200 (40 to ∞)	30 (10 to 84)
40%	298 (110 to ∞)	62 (23 to 214)
45%	407 (127 to ∞)	69 (23 to 501)

∞, infinity; CI, confidence interval; ETV, endoscopic third ventriculostomy; VP shunt, ventriculoperitoneal shunt.

analysis and displayed by Kaplan-Meier curves. Multiple Cox regression models were used to investigate the association between intervention and time to revision, adjusted for patient age, gestational age and entity. The results are expressed as hazard ratio (HR) with corresponding 95% Confidence interval (CI). The risk of revision within 18 months after surgery was explored by stepwise multiple logistic regression to identify potential risk factors and to confirm the results obtained by Cox regression. A p value of less than 0.05 was considered statistically significant.

In total, 49 consecutive infants were included in the analysis. In 23 children, hydrocephalus was treated primarily by ETV and in 26 children with a VP shunt. The demographic variables were not distributed significantly (table 1). The median age at operation was 43 days in the ETV group vs 24.5 days in the shunt group (p=0.10). The median weight at operation was 3.6 kg in the ETV group and 3.3 kg in the VP shunt group (p=0.50). A total of 83.7% of children underwent surgery during their first 6 months of life.

The percentage of preterm infants was 39.1% in the ETV group and 34.6% in the VP shunt group (p=1.00). The most frequent entity in all children was obstructive hydrocephalus of different etiologies (n=31, 63.3%). Specifically, 12 children (24.5%) had hydrocephalus due to Chiari malformations, mostly Chiari type 2 malformations (n=11, patients with spinal dysraphism). Six children (12.2%) underwent surgery due to aqueductal stenosis. The remaining etiologies were Dandy-Walker malformations (n=4), cervical meningomyeloceles (n=1), tumor (n=1), arachnoid cysts (n=2) and cases of rare cystic brain lesions (n=5). PHH due to IVH was the cause of disease in 17 children (34.7%), 9 were treated by ETV and 8 by VP shunting. One child with postinfectious hydrocephalus was treated with ETV. The distribution of entities was not significant (ETV vs VP shunting, p=0.45).

During the 18-month observation period, 34.8% (n=8) of ETV procedures and 53.8% (n=14) of VP shunt procedures were successful (no revision surgery). Thus, failure rates of 65.2% in the ETV group (n=15) and 46.2% in the VP shunt group (n=12) were not significantly different within 18 months of observation (p=0.25).

After failed ETV, ten patients received a secondary VP shunt. Revision ETV after failure was performed in five patients, of which two procedures were successful. ETV was never performed after primary shunt failure. The median number of revision surgeries per child was 1 (0, 7) in the ETV group vs 0 (0, 8) in the VP shunt group (p=0.25).

The median time to failure could not be calculated, as the rate of revision surgeries did not reach 50% in the VP shunt group (table 2). The median time to revision surgery in 45% of children was 69 days (95% CI 23 to 501 days) in the ETV group and 407 days (95% CI 127 to ∞) in the shunt group (table 2). Notably, the estimated time until 20% of the children underwent revision surgery was 23 days (95% CI 9 to 56 days) in the ETV group and 111 days (95% CI 6 to 257 days) in the VP shunt group.

A total of 86.7% of all revision surgeries in the ETV group were carried out within 120 days after the initial surgery. As displayed in the Kaplan-Meier failure curves (figure 1), this effect was less pronounced in the shunt group (6 of 12 children received the first revision surgery during the first 120 days).

The time to failure analysis showed a higher risk of ETV failure than VP shunting failure during the complete observation period. Cox regression analysis in which the intervention group was the only factor provided an HR of 1.98 (95% CI 0.93 to 4.26, p=0.078). After adjusting for patient age, gestational age and entity, the HR was 2.63 (95% CI 1.06 to 6.52, p=0.036). During the first 120 days, the risk of ETV failure was higher than that for shunting, with a non-adjusted HR of 3.27 (95% CI 1.26 to 8.63, p=0.017) and an adjusted HR of 6.48 (95% CI 2.04 to 20.56, p=0.002).

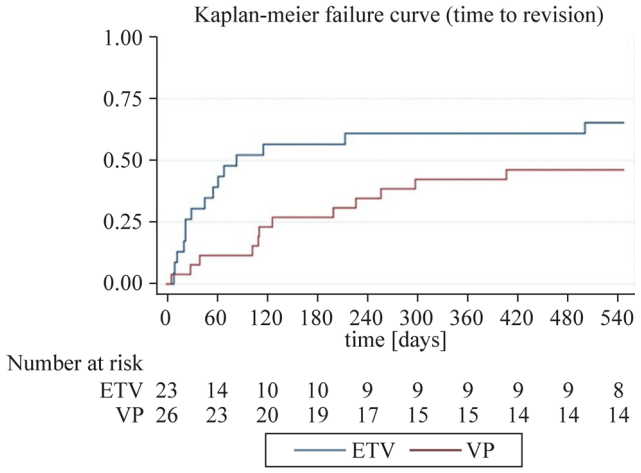

Figure 1 Kaplan Meier failure curve: time to revision. ETV, endoscopic third ventriculostomy; VP, ventricular peritoneal shunt.

Stepwise multiple logistic regression, which was performed to explain the probability of revision surgery by intervention, patient age, prematurity and/or gestational age and entity (or etiology of any kind), indicated that patient age is a potential risk factor for failure, with younger children having a higher risk. Similar to the increased risk of failure of ETV, this is even more pronounced for revision events within 120 days after surgery and is in line with the results obtained from the Cox regression analysis (modeling time to revision surgery). The entity of obstructive hydrocephalus did not differ from the posthemorrhagic entity in terms of risk of revision (all estimates for OR or HR comparing both entities were close to 1).

In summary, the independent risk of failure is higher for ETV and for younger children, particularly over a period of 120 days after the initial surgery. Etiology was not a predictor of failure.

Within the observation period, there was no major bleeding or lethal complication. The median number of revision surgeries per child was 1 (0, 7) in the ETV group vs 0 (0, 8) in the VP shunt group, thus leading to 30 revision procedures in the ETV group vs 25 procedures in the VP shunt group (p=0.21). The data displayed in table 3 indicate the number and cause of revisions in both groups and in the group of children switched to VP shunt after failed ETV to attribute complications to the corresponding procedure.

Overall, complications related to the shunt procedure were more frequent with an infection rate of 22.2% (n=8) and a rate of CSF leakage of 27.8% (n=10). The number of obturated ETVs leading to revision was comparably high (n=10, 52.5%).

This study demonstrates high but not significantly different failure rates in both treatment groups (65.2% for ETV vs 46.2% for VP shunting, p=0.25) and a remarkably shorter time to failure in the ETV group, with failure defined as the need to repeat the respective procedure. The independent risk of failure of ETV being significantly higher specifically during the early phase (120 days after the initial surgery) remains clinically relevant. Our results revealed young age as a risk factor for failure. However, after a second ETV, 43.5% of patients remained free of a VP shunt system in a high-risk cohort of children during the first year of life.

This cohort comprised a population of 49 children who underwent surgery during early infancy, with 36.7% born prematurely. The most common etiologies were obstructive hydrocephalus (63.3%) and PHH (34.7%). Reportedly, neonates with PHH due to IVH are considered a group with high complication rates and expected shunt dependencies up to 81.7%, so-called a high-risk cohort, also in terms of infection rates.[5 11–13]

Our data show that 65.2% of the ETV group (vs 46.2% of the VP shunt group) underwent at least one revision

Table 3 Complications leading to revision procedure during 18 months of follow-up

Initial therapy	VP shunt (n=26)	ETV (n=23)	
	25 revisions in 12 children	30 revisions in 15 children	
Therapy at the time point before revision	**Still treated with VP shunt**	**Switched to VP shunt**	**Still treated with ETV**
	25 revisions in 12 children	11 revisions in 5 children	19 revisions in 15 children
Cause of revision* (more than one may apply)			
Obstruction of catheter or ETV	6 (24)	4 (36.4)	10 (52.6)
CSF leakage	6 (24)	4 (36.4)	3 (15.8)
Catheter displacement	3 (12)	0 (0)	0 (0)
Infection	5 (20)	3 (27.3)	3 (15.8)
Dysfunctional valve	2 (8)	0 (0)	0 (0)
Unknown	7 (28)	2 (18.2)	3 (15.8)

* Data are presented as number (percentage).
CSF, cerebrospinal fluid; ETV, endoscopic third ventriculostomy; VP shunt, ventriculoperitoneal shunt.

surgery within the observation period. The independent risk of the ETV procedure was higher and the median time to revision surgery was remarkably shorter in this group. These results are consistent with the literature, since reported failure rates of VP shunting amount up to 40% in this age group 12 months after shunt implantation.[9 10 14 15] Drake *et al*[12] described an ETV survival rate of 65% 1 year after intervention in children aged 6.5 years; thus, it was not a high-risk cohort, as in our study. Independently validated through multiple studies, the ETV Success Score can be applied to assess the outcome.[4–6 16] The relevant predictors are the etiology of hydrocephalus, the presence of a previous shunt and the age at intervention. As the success rate in our study was 34.8% within 18 months, we found it important to mention the decreasing risk of ETV failure over time, which has been previously described.[9 10 14] Drake *et al* postulated that age at operation is the most important predictor of ETV-related survival and therefore suggested carefully indicating ETV in neonates and young infants.[12] Additionally, various studies described the association of etiology to shunt or ETV failure, mostly revealing a poor outcome for individuals with PHH or postinfectious hydrocephalus and higher success rates for obstructive conditions, for example, those caused by a single aqueductal stenosis.[2 7 8 17 18]

A deficiency in CSF absorption in infants is postulated to be a pathophysiological cause of the association of younger age and ETV failure. Until the age of 3 months, the ETV failure rate is supposed to be higher than that in later infancy due to immaturity of the glymphatic system and arachnoid villi.[2 19] This hypothesis is also supported by our study because the multiple logistic regression analysis revealed age as a predictor of failure in both treatment groups. Diverse findings in this field demonstrate that the mechanisms of CSF dynamics are still not well understood and indicate that the indications for both procedures, VP shunting and ETV, should be carefully considered in this particular age group.[20]

IVH is a common and serious complication, especially in premature infants. A majority of those with IVH develop PHH, which is associated with high morbidity and mortality.[18] Effective treatment for this group of patients is still not clearly defined throughout the literature. However, the role of ETV in the treatment of PHH is being increasingly emphasized.[1 17 18 20] A large percentage of the literature states that PHH is significantly associated with increased failure rates for ETV.[5 9 10 14 16] Luther *et al*[20] and Bock *et al*[18] recently described a positive association between the level of IVH and shunt failure, which was not shown for ETV. One hypothesis for this correlation is the fact that high-grade IVH may lead to proteinaceous and cellular debris, which may obstruct implanted catheters.[15] Neuroendoscopy includes not only the possibility of ETV but also additional procedures, such as choroid plexus cauterization and neuroendoscopic lavage, in cases of PHH or aqueductoplasty in an obstructive condition. Neuroendoscopic lavage is described to significantly reduce ventricular size, overall shunt rate and complications of PHH.[21] Thus, neuroendoscopic treatment has gained attraction, especially as a treatment for PHH and obstructive hydrocephalus (especially aqueductal stenosis) to obviate lifelong shunt dependency in infants.[9 10 14 19 22–26] Although ETV is effective in the treatment of PHH and very low birthweight infants with comorbidities, it is described to have a much higher initial failure rate than VP shunting, consistent with our results.[18 20] In accordance with previous studies, our findings revealed patient age as a potential risk factor for ETV and VP shunt failure.[2 5 6 9 12] Ventricular catheter obstructions are described to be the most common cause of VP shunt failure, consistent with our results, which indicated that obstruction caused a majority of all VP shunt-related complications (n=10, 27.8%).[15] Consistent with our data neonatal patients during the first year of life do have higher rates of shunt infection due to weakness in their immune response, another reason why children during early infancy are called a high-risk cohort and why foreign materials should be avoided wherever possible.[11] Consequently, an infection rate of 15.8% (n=3) in the ETV group might be attributed to foreign material (Rickham reservoir), which was also implanted in this group.

The results of this study show a significantly higher risk of ETV failure than VP shunt failure. However, the risk of ETV failure specifically decreases after 120 days after the initial surgery and therefore must be expected to become progressively lower over time.[9 10 14] In contrast, the risk of VP shunt failure increases over time due to possible lifelong complications, such as infection, catheter obstruction and displacement, a dysfunctional valve, or chronic complaints due to overdrainage.[6 15 20 23] It is therefore postulated that after the early high-risk period, patients who undergo ETV could experience a long-term treatment advantage over patients who receive a VP shunt. This study was limited by the small number of patients and its retrospective nature. Because the observation period was only 18 months, data regarding long-term complications and ETV/VP shunt-related survival were not collected.

To our knowledge, this is the first study to investigate the outcome of VP shunting and ETV in the treatment of early childhood hydrocephalus in infants less than 1 year of age regarding the entire spectrum of infantile hydrocephalus. ETV provides a treatment option for any kind of hydrocephalus. However, this study revealed a higher risk of failure for the ETV procedure and for younger children, yet 43.5% of infants remained free of a shunt device within the 18-month observation period. As failure rates are high for both treatment options, considerations regarding the particular (re)intervention still remain a case-by-case decision. To establish treatment algorithms and guidelines in the future, more long-term follow-ups and prospective trials with regard to neurocognitive outcomes and related long-term complications are needed.[13]

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