Endoscopic third ventriculostomy and repeat endoscopic third ventriculostomy in pediatric patients: the Dutch experience

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OBJECTIVE After endoscopic third ventriculostomy (ETV), some patients develop recurrent symptoms of hydrocephalus. The optimal treatment for these patients is not clear: repeat ETV (re-ETV) or CSF shunting. The goals of the study were to assess the effectiveness of re-ETV relative to initial ETV in pediatric patients and validate the ETV success score (ETVSS) for re-ETV.

METHODS Retrospective data of 624 ETV and 93 re-ETV procedures were collected from 6 neurosurgical centers in the Netherlands (1998–2015). Multivariable Cox proportional hazards modeling was used to provide an adjusted estimate of the hazard ratio for re-ETV failure relative to ETV failure. The correlation coefficient between ETVSS and the chance of re-ETV success was calculated using Kendall's tau coefficient. Model discrimination was quantified using the c-statistic. The effects of intraoperative findings and management on re-ETV success were also analyzed.

RESULTS The hazard ratio for re-ETV failure relative to ETV failure was 1.23 (95% CI 0.90–1.69; $p = 0.20$). At 6 months, the success rates for both ETV and re-ETV were 68%. ETVSS was significantly related to the chances of re-ETV success ($\tau = 0.37$; 95% bias corrected and accelerated CI 0.21–0.52; $p < 0.001$). The c-statistic was 0.74 (95% CI 0.64–0.85). The presence of prepontine arachnoid membranes and use of an external ventricular drain (EVD) were negatively associated with treatment success, with ORs of 4.0 (95% CI 1.5–10.5) and 9.7 (95% CI 3.4–27.8), respectively.

CONCLUSIONS Re-ETV seems to be as safe and effective as initial ETV. ETVSS adequately predicts the chance of successful re-ETV. The presence of prepontine arachnoid membranes and the use of EVD negatively influence the chance of success.

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ENDOSCOPIC third ventriculostomy (ETV) has become the standard treatment for obstructive hydrocephalus.²⁹ Its range of indications has extended to communicative hydrocephalus as well.^{29,49} Unfortunately, to date, no treatment modality guarantees a permanent solution for hydrocephalus.³² Therefore, when primarily treating hydrocephalus, the apparent benefits and disad-

vantages of ETV and shunting have to be weighted and considered.^{10,16,18,30,36,38,41,61} To facilitate neurosurgeons in the process of patient selection for ETV, a predictive model was developed that estimates the chance of ETV success over a 6-month period: the so-called ETV Success Score (ETVSS).^{5,17,20,25,37,47}

When a patient is referred for suspicion of recurrent

ABBREVIATIONS ELD = external lumbar drain; ETV = endoscopic third ventriculostomy; ETVSS = ETV Success Score; EVD = external ventricular drain; IQR = interquartile range; LP = lumbar puncture; re-ETV = repeat ETV.

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hydrocephalus, the neurosurgeon has 2 treatment options: either perform a repeat ETV (re-ETV) or implant a CSF shunt.

A Dutch external validation study of ETVSS found a 78% success rate for the group that underwent re-ETV after an evaluation period of 6 months.⁵ However, the sample size was relatively small, with 18 patients receiving re-ETV. This prompted us to design the current retrospective multicenter study in which data from 6 university neurosurgical centers in the Netherlands were clustered to investigate these findings using a larger sample size. In this paper, we report on the observed effectiveness of re-ETV relative to the observed effectiveness of initial ETV and determine the predictive accuracy of ETVSS in patients undergoing re-ETV. An additional aim is to provide an in-depth analysis of re-ETV patients and the factors that influence the chance of success.

Methods

Study Design

Retrospective data were gathered from the electronic patient records of 6 university medical centers in the Netherlands: Academic Medical Center, Amsterdam (July 1999 to February 2015), VU University Medical Center, Amsterdam (most data obtained between August 2010 and October 2014), University Medical Center, Groningen (April 1998 to November 2014), Radboud University Medical Center, Nijmegen (most between January 2004 and August 2014), Erasmus University Medical Center, Rotterdam (May 1997 to December 2014), and University Medical Center, Utrecht (most between April 2004 and July 2013). The cooperating centers are included in the Dutch Pediatric Neurosurgical Study Group.

The participating neurosurgical clinics are high-volume university hospitals with dedicated neurosurgeons who specialize in pediatric and/or endoscopic procedures. Therefore, the neurosurgeons involved in these procedures (performance or supervision and patient selection) should be considered experienced.

All ETV procedures were performed in accordance with national guidelines, i.e., either by a neurosurgeon or a resident under the direct supervision of a neurosurgeon. ETV failure was defined as any subsequent surgical procedure for CSF diversion, as determined by a neurosurgeon, or death related to hydrocephalus management.¹⁵

The research protocol was submitted to and approved by an ethics committee. Patient consent was not required as we worked with an anonymized retrospective data set and did not use an intervention.

Data Collection

All patients who were younger than 18 years at the time of ETV were eligible for inclusion. The following patient characteristics were collected: etiology (classified as aqueductal stenosis, postinfectious, myelomeningocele, post-intraventricular hemorrhage, tectal tumor, nontectal brain tumor, or other cause), date of birth, sex, date of initial ETV, date of ETV failure (defined as any subsequent surgical procedure for CSF diversion or hydrocephalus-related death), date of re-ETV, date of re-ETV failure (us-

ETV SUCCESS SCORE

$$= \text{Age Score} + \text{Etiology Score} + \text{Previous Shunt Score} \\ \approx \text{percentage probability of ETV success}$$

SCORE	AGE + ETIOLOGY + PREVIOUS SHUNT		
	↓	↓	↓
0	<1 MONTH	POST-INFECTIOUS	PREVIOUS SHUNT
10	1 MONTH TO <6 MONTHS		NO PREVIOUS SHUNT
20		MYELOMENINGOCELE INTRA-VENTRICULAR HEMORRHAGE NON-TECTAL BRAIN TUMOR	
30	6 MONTHS TO <1 YEAR	AQUEDUCTAL STENOSIS TECTAL TUMOR OTHER ETIOLOGY	
40	1 YEAR TO <10 YEARS		
50	≥10 YEARS		

FIG. 1. Calculation of the ETVSS. Reprinted from Kulkarni et al: *J Pediatr* 155:254–259, 259.e1, 2009, with permission from Elsevier.

ing the previously mentioned definition), use of an external ventricular drain (EVD), lumbar puncture (LP), and/or external lumbar drain (ELD) postoperatively, shunt history, and last contact with the neurosurgery or neurology department for follow-up. Patient age was classified as used for the ETVSS score: younger than 1 month, 1 month to younger than 6 months, 6 months to younger than 1 year, 1 year to younger than 10 years, and equal to or older than 10 years.

The ETVSS for each patient's re-ETV was calculated using age, etiology, and previous shunt score (Fig. 1).³⁷ For example, if a 9-month-old patient with hydrocephalus due to aqueductal stenosis who previously underwent CSF shunt placement is selected for an ETV, the chance of ETV success over a period of 6 months is 60% (30 for patient age + 30 for etiology + 0 for previous shunt = 60).

The surgical reports were investigated for intraoperative findings at re-ETV, and these findings were reported in different categories: complete occluded stoma without underlying arachnoid membranes, complete occluded stoma with underlying arachnoid membranes, pinpoint stoma without underlying arachnoid membranes, pinpoint stoma with underlying arachnoid membranes, obstruction due to underlying prepontine arachnoid membranes alone, and no apparent occlusion.

Statistical Analysis

We reported categorical patient characteristics using the number and percentage observed, continuous normally distributed characteristics using the mean and SD, and continuous nonnormally distributed characteristics using

TABLE 1. Demographics of the ETV and re-ETV patients

Characteristic	No. of Patients (%)		
	ETV (n = 624)	Re-ETV (n = 93)	Total (n = 717)
Origin of hydrocephalus			
Aqueductal stenosis	123 (19.7)	19 (20.4)	142 (19.8)
Postinfectious	18 (2.9)	3 (3.2)	21 (2.9)
Myelomeningocele	40 (6.4)	5 (5.4)	45 (6.3)
Intraventricular hemorrhage	44 (7.1)	6 (6.5)	50 (7.0)
Tectal tumor	49 (7.9)	16 (17.2)	65 (9.1)
Other brain tumor (non-midbrain)	195 (31.3)	16 (17.2)	211 (29.4)
Other	155 (24.8)	28 (30.1)	183 (25.5)
Age at procedure			
<1 mo	44 (7.1)	0	44 (6.1)
1–6 mos	110 (17.6)	15 (16.1)	125 (17.4)
6 mos to <1 yr	53 (8.5)	11 (11.8)	64 (8.9)
1–10 yrs	227 (36.4)	34 (36.6)	261 (36.4)
≥10 yrs	190 (30.4)	33 (35.5)	223 (31.1)
Shunt prior to procedure			
Yes	112 (17.9)	25 (26.9)	137 (19.1)
No	512 (82.1)	68 (73.1)	580 (80.9)

the median and interquartile range (IQR). We examined differences in the groups of patients using the chi-square test. Fisher's exact test was used to assess categorical variables, and the ORs were calculated with the 95% CI. We used the independent 2-tailed t-test and Mann-Whitney U-test to assess continuous normally and nonnormally distributed variables, respectively.

Follow-up was calculated from the date the patient was first operated on to the date at which the patient was seen at the clinic and known to be well, and the date of subsequent treatment or date of death, whichever came first.

Survival curves were calculated using the Kaplan-Meier method. Survival analysis covering the time to ETV failure was performed using a Cox proportional hazards model. The proportional hazards assumption was checked visually with the Kaplan-Meier curves. Stratified ETVSS (low is ≤ 40 ; moderate is 50–70; high is ≥ 80) and "ETV versus re-ETV" were entered into a multivariable Cox proportional hazards model because the literature supports the elements

TABLE 2. Number of patients per institution

Institution	No. of Patients (%)	
	ETV Patients	Re-ETV Patients
Erasmus University Medical Center, Rotterdam	189 (30.3)	37 (39.8)
University Medical Center, Groningen	202 (32.4)	36 (38.7)
Radboud University Medical Center, Nijmegen	97 (15.5)	8 (8.6)
University Medical Center, Utrecht	42 (6.7)	7 (7.5)
Academic Medical Center, Amsterdam	62 (9.9)	3 (3.2)
VU Medical Center, Amsterdam	32 (5.1)	2 (2.2)

FIG. 2. Flowchart for selecting the patients with ETV and re-ETV enrolled in this study.

of the ETVSS as the most important confounders.³⁷ This model was used to provide an adjusted estimate and 95% CI of the HR for re-ETV failure relative to ETV failure.

Successful cases with less than 6 months of follow-up were excluded from testing of the predictive adequacy of the ETVSS, as this score predicts the chances of ETV success over a 6-month period. We determined the predictive adequacy of ETVSS by comparing the predicted probability of re-ETV success between patients with successful and failed re-ETV treatment using the independent t-test. Model discrimination was quantified by the area under the receiver operating characteristic curve (hereafter called the c-statistic) with 95% CI, and the correlation coefficient between ETVSS and chance of re-ETV success was calculated using Kendall's tau coefficient with the 95% bootstrapped CI based on 1000 replications. We performed the same analysis for the initial ETV procedure on all patients who underwent surgery during the aforementioned dates at the cooperating centers.

We performed all data analyses using IBM SPSS Statistics for Windows (version 23.0; IBM Corp.) and considered p values less than 0.05 as statistically significant.

Results

Demographics

A total of 624 ETV patients and 93 re-ETV patients were included for analysis. See Table 1 for the baseline demographics, Table 2 for the number of ETV and re-ETV cases performed by each institution, and Fig. 2 for the flowchart for patient selection.

In 5 patients, a third ETV was performed; in 3 of these patients no subsequent treatment was needed and 2 patients received a shunt. Seven patients were excluded from the analysis; these patients had a patent ventriculostomy site and no other obstruction was found during neuroen-

TABLE 3. Survival tables for ETV and re-ETV

Yrs After Treatment	% Cumulative Survival (95% CI)	
	ETV	Re-ETV
0.5	67.6 (63.9–71.3)	67.6 (57.9–77.3)
1	62.7 (58.8–66.6)	65.1 (55.2–75.0)
3	55.2 (51.0–59.4)	50.3 (39.1–61.5)
5	51.5 (47.0–56.0)	44.3 (32.5–56.1)
7	45.9 (40.9–51.0)	44.3 (32.5–56.0)

doscopy. Three patients died of hydrocephalus-related causes: 2 patients had an earlier failure of ETV, after which they received a shunt that subsequently failed but they were referred too late and died. The remaining patient, who had a nonpremature birth with neonatal cerebral hemorrhage (resulting in hydrocephalus that was treated with a shunt), was a severely mentally challenged, spastic child with infantile encephalopathy, who, at the age of 17 years, was admitted to the intensive care unit with suspected aspiration of blood and obstructed airways, gastroscopy, and multiple other diagnoses. This patient developed bradycardia, after which MRI of the cerebrum showed a trapped fourth ventricle and compression of the brainstem. ETV with aqueduct stenting proved insufficient and eventually the patient died.

Several techniques were used for the ETV procedures. The most commonly used was a dumbbell-shaped balloon for dilating the stoma; other methods used included thulium laser ablation of the third ventricle floor and a “black” fiber tip/diode laser combination for controlled tissue ablation.⁶²

The median follow-up duration for the ETV procedures was 31.4 months (IQR 1.6–49.7 months), and the median

TABLE 4. Hazard ratios from the multivariable Cox proportional hazards model

Variable	HR	95% CI	p Value
Re-ETV relative to ETV	1.23	0.90–1.69	0.20
ETVSS			
High ETVSS (≥ 80)	Ref	Ref	Ref
Low ETVSS (≤ 40)	4.24	3.09–5.81	<0.001
Moderate ETVSS (50–70)	2.08	1.61–2.70	<0.001

Ref = reference.

follow-up duration for the re-ETV procedures was 14.8 months (IQR 1.2–49.9 months).

The median age at the initial ETV was 4.8 years (IQR 0.5–11.6 years), and the mean ETVSS for the initial ETV was 67 (SD 17). The median age at re-ETV was 6.1 years (IQR 1.0–12.4 years), and the mean ETVSS for re-ETV was 71 (SD 16). There were 5 patients older than 18 years at re-ETV (19, 19, 21, 22, and 26 years).

The median time between ETV and re-ETV was 10.6 months (IQR 3.8–29.4 months). The median time between ETV and failure was 1.4 months (IQR 0.6–9.2 months), and the last failure occurred after 11.8 years. The median time between re-ETV and failure was 1.7 months (IQR 0.5–14.7 months), and the last failure occurred after 8.0 years.

See Table 3 for the success rates for ETV and re-ETV over time and Fig. 3 for the Kaplan-Meier survival curves. The hazard ratios are shown in Table 4.

Validity Evidence for Predictive Modeling

For the initial ETV procedure, the mean ETVSS was significantly higher for successful cases than for failed

FIG. 3. Kaplan-Meier survival curves for ETV and re-ETV. $p = 0.58$, log-rank test. Cum = cumulative. Figure is available in color online only.

TABLE 5. Characteristics of re-ETV success and failure at 6 months*

Characteristic	No. of Patients (%)		
	Success (n = 57)	Failure (n = 29)	Total (n = 86)
Origin of hydrocephalus			
Aqueductal stenosis	11 (19.3)	8 (27.6)	19 (22.1)
Postinfectious	1 (1.8)	1 (3.4)	2 (2.3)
Myelomeningocele	3 (5.3)	2 (6.9)	5 (5.8)
Intraventricular hemorrhage	4 (7.0)	2 (6.9)	6 (7.0)
Tectal tumor	13 (22.8)	1 (3.4)	14 (16.3)
Other brain tumor (non-midbrain)	8 (14.0)	5 (17.2)	13 (15.1)
Other†	17 (29.8)	10 (34.5)	27 (31.4)
Age at re-ETV			
<1 mo	0	0	0
1–6 mos	5 (8.8)	8 (27.6)	13 (15.1)
6 mos to <1 yr	6 (10.5)	5 (17.2)	11 (12.8)
1–10 yrs	22 (38.6)	11 (37.9)	33 (38.4)
≥10 yrs	24 (42.1)	5 (17.2)	29 (33.7)
Sex			
Male	31 (54.4)	15 (51.7)	46 (53.5)
Female	26 (45.6)	14 (48.3)	40 (46.5)
Shunt prior to re-ETV			
Yes	11 (19.3)	14 (48.3)	25 (29.1)
No	46 (80.7)	15 (51.7)	61 (70.9)
Closed ventriculostomy site‡			
Yes	30 (56.6)	8 (27.6)	38 (46.3)
No	23 (43.4)	21 (72.4)	44 (53.7)
Additional subarachnoid membranes§			
Yes	17 (32.1)	19 (65.5)	36 (43.9)
No	36 (67.9)	10 (34.5)	46 (56.1)
LP or ELD placement¶			
Yes	13 (24.5)	7 (24.1)	20 (24.4)
No	40 (75.5)	22 (75.9)	62 (75.6)
EVD placement**			
Yes	2 (3.7)	9 (31.0)	11 (13.3)
No	52 (96.3)	20 (69.0)	72 (86.7)

* Seven patients were lost to follow-up or died within 6 months and were excluded from analysis.

† See Table 6 for a list of conditions.

‡ Four missing values.

§ Four missing values.

¶ Four missing values.

** Three missing values.

cases at 6 months: 72 (SD 15) versus 57 (SD 18) ($p < 0.001$). The c-statistic for the 6-month follow-up was 0.74 (95% CI 0.70–0.79). The ETVSS of the initial ETV was significantly related to the chances of ETV success ($\tau = 0.36$; 95% bias corrected and accelerated CI 0.29–0.42; $p < 0.001$).

For the re-ETV procedure, the mean ETVSS was significantly higher for successful cases than for failed cases at 6 months: 76 (SD 13) versus 63 (SD 16) ($p < 0.001$). The c-statistic for the 6-month follow-up was 0.74 (95%

TABLE 6. Conditions included in the “other” category for origin of hydrocephalus (n = 27)

Etiology	No. of Patients (%)
Walker-Warburg syndrome	1 (3.7)
Dandy-Walker syndrome	6 (22.2)
Arachnoid cyst	12 (44.4)
Unknown	1 (3.7)
3rd ventricle cyst	3 (11.1)
Neurofibromatosis Type 1	1 (3.7)
4th ventricle outlet syndrome	1 (3.7)
Vein of Galen malformation	2 (7.4)

CI 0.64–0.85). The ETVSS of re-ETV was significantly related to changes of re-ETV success ($\tau = 0.37$; 95% bias corrected and accelerated CI 0.21–0.52; $p < 0.001$).

Successfully Versus Unsuccessfully Treated Re-ETV Patients

For the 93 re-ETV patients, an in-depth analysis was conducted (see Tables 5 and 6 for the demographics of the failed and successful cases). Seven patients had less than 6 months of follow-up or died before 6 months (not hydrocephalus related) and were excluded from the analysis in this section. Only 1 patient received additional choroid plexus cauterization at re-ETV; 2 months after the procedure, the patient received a CSF shunt.

In the successfully treated patients, the median age at re-ETV was significantly higher than in unsuccessfully treated patients at 6 months of follow-up: 8.2 years (IQR 1.8–13.5 years) versus 1.6 years (IQR 0.4–8.6 years) ($p = 0.002$).

The median time between ETV and re-ETV did not differ significantly between successful and unsuccessful cases: 12.1 months (IQR 5.6–29.4 months) versus 7.6 months (IQR 1.6–29.7 months) ($p = 0.17$).

Shunting Prior to Re-ETV

The failure rate for patients with a shunt prior to re-ETV was 56% (14 of 25 patients). Of the 25 patients with a shunt prior to re-ETV, only 10 patients received the shunt between the initial ETV and re-ETV surgery. Of these 10 patients, the re-ETV of 8 patients (80%) failed within 6 months. Of these 8 patients, 6 patients had subarachnoid membranes and 1 patient had massive prepontine adhesions. The remaining 15 patients already had received a shunt prior to the initial ETV.

Effect of Intraoperative Findings

In 4 patients, intraoperative findings were missing from documentation; thus, data from 82 patients were available for analysis. If the ventriculostomy site was closed and reopened, the patient had a significantly higher chance of success than when no closed ventriculostomy site was found during surgery. Based on the OR, the odds of success were 3.4 times higher (95% CI 1.3–9.1; $p = 0.01$).

When additional subarachnoid membranes were ob-

served during re-ETV surgery, the patient had a significantly greater chance to need subsequent hydrocephalus treatment within 6 months. Based on the OR, the odds of failure were 4.0 times higher (95% CI 1.5–10.5; $p = 0.004$).

Effect of Postoperative Management

Two patients underwent EVD placement after intraoperative bleeding. One patient had multiple thick prepontine arachnoid membranes, and the CSF of the other patient was a bit cloudy (suspected infection). In the remaining cases, no specific reasons for leaving an EVD was mentioned, and therefore we considered the EVD as being for escape reasons (i.e., to divert CSF in an emergency). It is not clear whether these escape EVDs were planned or whether it was the intraoperative call of the surgeon. When an EVD was placed, the patient had a significantly higher chance of needing subsequent hydrocephalus treatment within 6 months. Based on the OR, the odds of failure were 9.7 times higher (95% CI 3.4–27.8; $p = 0.001$).

Performing an LP or ELD after re-ETV did not influence the chance of success at 6 months ($p = 0.97$).

Discussion

In the present study we observed a 7-year success rate for re-ETV of 44.3% (95% CI 32.5%–56.0%). One large study from the CURE Children's Hospital of Uganda on 215 pediatric patients reported corresponding findings with a 7-year success for re-ETV of 51%.⁴⁵ The population of this group is not necessarily equal to the patient population found in the Western world (e.g., more cases of postinfectious hydrocephalus). The few published studies with 20–40 patients have reported reasonably good success rates between 63% and 81%.^{5,43,44,50,56} In other reports with fewer patients, the success rates range from 0% to 100%.^{21,23,26,28,31,33,34,48,53,60,64}

Whereas some conclude that re-ETV should be considered in all patients who are referred with recurrent symptoms, others mention that re-ETV remains controversial. We think it is worthwhile to give ETV another chance in selected patients. Our primary motivation for this suggestion is to avoid shunt dependency. Also, the chances of ETV success and re-ETV success are similar; the adjusted estimate of the hazard ratio for re-ETV failure relative to ETV failure is 1.23 (95% CI 0.90–1.69).

Effect of Time

There is great heterogeneity among the patient populations in the aforementioned studies (not all are pediatric populations), and it is rare to find the method used to calculate the follow-up duration.

In the literature on re-ETV, there seems to be a trend toward lower success rates in younger patients.³⁷ This does not come as a surprise, as similar findings have been reported for initial ETV procedures.^{3,34} In the ETVSS proposed by Kulkarni et al., 50% of the total score is estimated by age alone.³⁷

We also found that the patients in whom re-ETV was successful at 6 months after treatment were significantly older than unsuccessfully treated patients, but they did not have a longer time between their initial and re-ETV

than unsuccessfully treated cases. However, on face value the suggestion is that longer duration might be associated with success. The lack of a statistically significant finding might be a statistical power issue of this cohort. Other authors have suggested that re-ETV seems worthwhile for patients with late failure of their ETV.^{44,45} Furthermore, as has been extensively reported in the literature on initial ETV, we found that 64% of failures occurred within the first 6 months after re-ETV.^{21,26,35,42,53,55,63}

Another reason for choosing ETV over shunt treatment is the apparent difference in concern among the parents of children with hydrocephalus.⁴⁰ Although the comfort of parents could be a reason to prefer ETV over shunting, it can also make parents less cautious (i.e., provide a false sense of security), as there is no certainty of a cure for hydrocephalus, and late failure of ETV does occur with potential devastating results.^{14,19,27,60} In our study, the latest failures occurred 12 years after ETV and 8 years after re-ETV.

Shunt Placement and Re-ETV

A priori, one might argue that a shunt might allow a patient to age and thus increase the chance of re-ETV success (as age is a major factor in success). On the other hand, for initial ETV it has been shown that the chance of success diminishes if a shunt is placed prior to ETV surgery.³⁷ In our cohort, 8 of 10 patients who received a shunt between ETV and re-ETV experienced failure of the re-ETV within 6 months. In 7 of 8 of these patients, subarachnoid membranes or even massive prepontine adhesions were found during re-ETV surgery. It is unclear whether there is a causal relationship between shunt implantation and the formation of subarachnoid membranes. This might be an interesting topic for a (prospective) follow-up study.

Intraoperative Findings

Some intraoperative and preoperative factors have been postulated to have predictive effects on ETV outcome (e.g., third ventricle floor thickness, prepontine scarring).^{2,12,19,50,52,67,69} A thicker third ventricle floor has been negatively associated with ETV success,⁵⁹ but unfortunately we could not retrospectively analyze this aspect. The presence of cisternal scarring has been negatively associated with success of the first ETV.⁶⁷ We found that the presence of subarachnoid membranes and younger patient age had a negative effect on the chance of success. Similar findings were previously reported.^{19,50}

We found a positive effect of observed closure of the ventriculostomy site at re-ETV on the chance of short-term success. Other authors suggested that re-ETV should be considered if closure of the ventriculostomy site by gliosis and scarring is found during the second neuroendoscopic procedure.^{6,8,11,46,54}

Choroid Plexus Cauterization

Combination with choroid plexus cauterization might give better results than ETV alone, as was shown in a cohort from the previously mentioned Uganda-based authors.^{65,68} In another study, it was shown that even when ETV could not be performed and the procedure had to be converted

to a CSF shunt, the implanted shunt had a better chance of success if choroid plexus cauterization was performed.⁶⁶ It may be that ETV with choroid plexus cauterization has the largest effect in a subset of patients (e.g., patients with myelomeningocele).^{4,70} However, the possible favorable influence of choroid plexus cauterization in combination with ETV in developed countries is still being researched and debated and is beyond the scope of this study.^{7,13,39,51,57,58,71}

Postoperative Management

Usage of an EVD had a negative effect on the chance of re-ETV success. It seems likely that a perioperative event made the surgeon proceed with caution but deterred the surgeon from converting to an internal shunt (e.g., bleeding during endoscopy or suspect infection). Postoperatively administering LP or ELD did not influence the chances of re-ETV success. The retrospective nature of our study is an obstacle in this aspect. It is not clear whether the postoperative use of LP or ELD are always well documented.

Predictive Model

We performed an additional analysis of ETVSS and found that the score adequately predicts the chance of success for patients undergoing re-ETV. The ETVSS of the successful cases was significantly higher than the ETVSS of the unsuccessful cases. The c-statistic ranges from 0.5 (no discrimination) to 1.0 (perfect discrimination).⁹ As a rough guideline, values between 0.7 and 0.9 indicate moderate accuracy.^{1,22} The c-statistic for ETVSS for re-ETV of 0.74 (95% CI 0.64–0.85) was comparable to the findings of other validation studies on initial ETV procedures, including a study by our group in which we found an ETVSS of 0.82 (95% CI 0.71–0.92).^{5,37,47} Kendall's tau coefficient showed a significant correlation between ETVSS and chances of both ETV and re-ETV success. The fact that ETVSS predicts the chances of re-ETV success as accurately as the chance of initial ETV success is another argument for the comparability of these 2 procedures. ETVSS takes few variables into account that have been shown over and over again to have an effect on the chance of short-term success of ETV, and now we show that these same factors can be used to predict the chance of re-ETV success.

Limitations and Future

The results of our study should be interpreted with caution due to limitations of its retrospective design. Because of this retrospective nature, we could not focus on some aspects that might be of importance. The thickness of the third ventricle floor has already been mentioned. Another is the motive for choosing re-ETV over shunt implantation (this is rarely clearly stated in documentation) with the possibility of selection bias. The decision-making process of the treating surgeons when selecting cases for re-ETV (or ETV) was beyond our control, but surgeons will have their own algorithm and will only select patients who they think will benefit from ETV or re-ETV. The relatively small sample of re-ETV cases is also a limitation. Finally, this study used a Dutch study population and the extent to which our results are generalizable to world-wide practice is not certain.

The description of flow void on postoperative MRI is missing in our analysis. Again, the retrospective design is a limiting factor. It has been postulated that if a patient returns with symptoms of raised intracranial pressure and the disappearance of flow void artifacts (where it was shown before on MRI), re-ETV should be considered.⁸ In other cases, shunt implantation may be a better option. Within our group, opinions differed on follow-up MRI regarding the duration of routine patient surveillance and under whose supervision this surveillance should take place (neurologist, pediatrician, neurosurgeon, or general practitioner).

One of the more notable findings was the diverse pattern of practice when the initial ETV failed. We intend to reveal these patterns with a survey study in which we target pediatric neurosurgeons who face the difficulties of treating pediatric hydrocephalus on a regular basis.

Conclusions

Re-ETV seems to be as safe and effective as initial ETV.^{24,56} The factors related to the success of re-ETV are similar to those related to the success of initial ETV (e.g., patient age and etiology of hydrocephalus). Other elements that negatively influence the chance of success are the presence of preoperative arachnoid membranes, use of EVD after the endoscopic procedure, and a short time interval between initial and re-ETV. The avoidance of lifelong shunt dependency in successful re-ETV cases is important, and therefore we recommend performing re-ETV in selected patients. ETVSS adequately predicts the chance of success and can be used for patient selection for re-ETV.

Appendix

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Author Contributions

Conception and design: Breimer, Hoving. Acquisition of data: Breimer, Dammers. Analysis and interpretation of data: Breimer,

Hoving. Drafting the article: Breimer. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Breimer. Statistical analysis: Breimer, Brusse-Keizer. Study supervision: Hoving.

Supplemental Information

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