Endoscopic third ventriculostomy and choroid plexus cauterization with a rigid neuroendoscope in infants with hydrocephalus

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OBJECTIVE Combining endoscopic third ventriculostomy (ETV) with choroid plexus cauterization (CPC) has been shown to improve the success rate compared with ETV alone in infants (less than 24 months) with hydrocephalus who were treated in developing countries. The authors sought to evaluate the safety and efficacy of this procedure, using a rigid neuroendoscope, in a single North American center, and to assess whether the ETV success score (ETVSS), the CURE Children's Hospital of Uganda ETVSS (CCHU ETVSS), and other pre- and intraoperative variables could predict success.

METHODS The authors performed a retrospective review of consecutive ETV/CPC procedures performed using a rigid neuroendoscope to treat infantile hydrocephalus. The infants underwent the procedure at Miami Children's Hospital between January 2007 and 2014, with at least one postoperative follow-up. Duration of follow-up or time to failure of ETV/CPC, the primary outcome measure, was documented. A repeat CSF diversion procedure or death was considered as a failure of ETV/CPC. The time to event was measured using a Kaplan-Meier analysis. The authors analyzed ETVSS, CCHU ETVSS, and pre- and intraoperative variables to determine their suitability to predict success.

RESULTS Eighty-five patients (45 boys) with a mean age of 4.3 months (range 1 day to 20 months) underwent ETV/CPC. Etiology included intraventricular hemorrhage of prematurity in 44 patients (51.7%), myelomeningocele (MMC) in 7 (8.2%), congenital aqueductal stenosis in 12 (14.1%), congenital communicating hydrocephalus in 6 (7.1%), Dandy-Walker complex in 6 (7.1%), postinfectious hydrocephalus in 5 (5.8%), and other cause in 5 (5.8%). Six procedure-related complications occurred in 5 (5.8%) patients, including 2 hygromas, 1 CSF leak, and 3 infections. There were 3 mortalities in this cohort. ETV/CPC was successful in 42.1%, 37.7%, and 36.8% of patients at 6, 12, and 24 months follow-up, respectively. The median (95% CI) time to ETV/CPC failure was 4.0 months (0.9–7.1 months). In univariate analyses, both the ETVSS (hazard ratio [HR] 1.03; 95% CI 1.01–1.05; $p = 0.004$) and CCHU ETVSS (HR 1.48; 95% CI 1.04–2.09; $p = .028$) were predictive of outcome following ETV/CPC. In multivariate analysis, the presence of prepontine scarring was associated with ETV/CPC failure (HR 0.34; 95% CI 0.19–0.63; $p < 0.001$). Other variables, such as radiological criteria (prepontine interval, prepontine space, aqueductal stenosis, Third Ventricular Morphology Index) and intraoperative findings (ventriculostomy pulsations, extent of CPC), did not predict outcome.

CONCLUSIONS ETV/CPC is a feasible alternative to ETV and ventriculoperitoneal shunt in infants with hydrocephalus. Both the ETVSS and CCHU ETVSS predicted success following ETV/CPC in this single-center North American cohort of patients.

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KEY WORDS hydrocephalus; endoscopic third ventriculostomy; choroid plexus

ABBREVIATIONS AS = aqueductal stenosis; CCHU = CURE Children's Hospital of Uganda; CPC = choroid plexus cauterization; ETV = endoscopic third ventriculostomy; ETVSS = ETV success score; FOHR = fronto-occipital horn ratio; IVH = intraventricular hemorrhage; MMC = myelomeningocele; PPI = prepontine interval; PPS = prepontine space; TVMI = Third Ventricular Morphology Index; TVW = third ventricle width; VPS = ventriculoperitoneal shunt.

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ENDOSCOPIC third ventriculostomy (ETV) is the treatment of choice for obstructive hydrocephalus in children.^{8,26} However, success rates drop significantly in certain populations, notably infants, patients with a history of prior hemorrhage or infection, or that have previously harbored a ventriculoperitoneal shunt (VPS).^{4,9,11,18,21,24} The ETV success score (ETVSS) has been developed and validated to predict ETV success based on these variables.²⁴ There is strong evidence in sub-Saharan Africa that the addition of choroid plexus cauterization (CPC) to ETV can double success rates in hydrocephalus related to aqueductal stenosis (AS), myelomeningocele (MMC), or Dandy-Walker complex (DWC) and triple success rates in infants with postinfectious or communicating hydrocephalus.^{29,46,49,51,55} The CURE Children's Hospital of Uganda ETVSS (CCHU ETVSS), a scoring system that accounts for the extent of CPC, has since been developed and applied to this patient population.⁵³

However, the socioeconomic milieu, health-care system, etiology, and natural history of hydrocephalus are different between developing and developed countries.^{30,53} It is unclear whether the documented safety and effectiveness of adding CPC to ETV in sub-Saharan Africa applies to infants with hydrocephalus in developed countries.^{5,29,44,50} Furthermore, it is unclear which infants are ideal candidates for this procedure, as the applicability of the ETVSS and CCHU ETVSS and other putative predictors of success have not been studied extensively in North American infants with hydrocephalus.²⁹

We report a single-center, North American experience with ETV/CPC for infantile hydrocephalus. We sought to evaluate the feasibility, safety, and efficacy of ETV/CPC in this mixed cohort of North American infants with hydrocephalus. Our secondary objective was to assess whether the ETVSS and CCHU ETVSS could predict success following ETV/CPC in this cohort of patients. Finally, in an effort to identify which patients are candidates for ETV/CPC, we evaluated whether other preoperative clinical, radiological, or intraoperative variables could predict ETV/CPC success.

Methods

Patient Population

After obtaining institutional ethics board approval, we identified all ETV/CPC procedures performed at Miami Children's Hospital and Jackson Memorial Hospital between July 2007 and May 2014. All infants and young toddlers (aged less than 24 months at the time of surgery) with at least one follow-up were included in the study. For simplicity, this group of patients (age less than 24 months) will be defined as infants in this study.

Patient Selection

There was no standard protocol for patient selection for ETV/CPC or other techniques (ETV, CSF shunting) during the study period. Selection of patients for ETV/CPC was left to the discretion of the treating neurosurgeon. In general, ETV/CPC was considered as a potential first-line treatment for patients with hydrocephalus and known risk

factors of failure following ETV, such as younger age or a history of infection or intraventricular hemorrhage (IVH).

Surgical Technique

The surgical technique for ETV/CPC has been described in detail elsewhere (Fig. 1).⁵ Briefly, the technique involves performing an ETV through a frontal bur hole followed by ipsilateral CPC, septostomy, and contralateral CPC, cauterizing the choroid plexus along the choroidal fissure from the foramen of Monro to the posterior temporal horn using a rigid neuroendoscope (Storz Oi [Karl Storz GmbH & Co. KG], Aesculap, Inc., or Claris [Medtronic]) (Fig. 2). The extent of CPC varied depending on ventricle size and septal anatomy.

Data Collection

We collected several preoperative, intraoperative, and postoperative variables through medical chart review to identify potential predictors of failure. Preoperative variables included patient age, etiology of hydrocephalus, presence of a prior CSF reservoir, prior external ventricular drain or VPS, prior CSF infection, and preoperative imaging ventricular variables, including the fronto-occipital horn ratio (FOHR),^{22,23,33} third ventricle morphology (lamina terminalis and/or tuber cinereum bulging) and Third Ventricular Morphology Index (TVMI),¹² third ventricle width (TVW), prepontine interval (PPI),⁴² prepontine space (PPS; distance from midpons to clivus),⁵ and presence/absence of AS (Fig. 3).⁵

Intraoperative variables were obtained from operative reports and included year of surgery, type of neuroendoscope, details of ETV (preoperative scarring prior to ETV, pulsation of third ventricle floor following ETV), extent of CPC (incomplete or complete), intraoperative bleeding (none, mild, moderate, severe), or neurological injury (e.g., injury to the fornix). To quantify and correlate the extent of CPC with outcome, the extent of subtotal CPC was subdivided into incomplete when CPC was unilateral or bilateral but only extended from the foramen of Monro (FM) to the atrium on one side. While we recognize that the complete choroid plexus (e.g., within the fourth ventricle, roof of third ventricle) cannot be obtained by CPC regardless of the endoscope used, we classified extent of CPC as being complete when CPC extended from the FM to the posterior temporal horn bilaterally (Table 1). Intraoperative bleeding was classified as follows: none, when there was no report of bleeding in the operation report; mild, when the surgeon reported minimal bleeding that was readily controlled with irrigation; moderate, when persistent bleeding requiring additional maneuvers to stop bleeding; and severe, when persistent severe bleeding requiring abortion of the procedure. The prepontine cistern was classified as scarred when the surgeon described abnormal, excessive scarring or arachnoid adhesions in the prepontine cistern following ETV/membrane of Liliequist fenestration, or as normal when the surgeon reported good visualization of the prepontine cistern and/or of the basilar artery after ETV/membrane of Liliequist fenestration.

The ETVSS^{24,28,32} and CCHU ETVSS⁵³ were calculated for each patient using the appropriate variables (age, etiol-

FIG. 1. Steps involved in ETV/CPC. Right frontal approach. Standard ETV with perforation of tuberculum cinereum (**A–D**) and membrane of Lilliequist (**E**). Cauterization of the right choroid plexus from the foramen of Monro (**F**) toward the ipsilateral atrium (**G** and **H**). Dehiscent septum pellucidum allowing visualization of the CP in the contralateral ventricle (**I**), which is progressively devascularized (**J**) from the posterior temporal horn (**K**) to the atrium (**L**) and foramen of Monro (**M** and **N**), until the CP is completely devascularized (**O**).

ogy, history of prior VPS, extent of CPC). For the CCHU ETVSS, based on ETV/CPC performed using a flexible endoscope, the extent of CPC is defined as none (0 points), partial unilateral (2 points), and complete bilateral (foramen of Monro to tip of temporal horns bilaterally, 4 points). Because a rigid neuroendoscope was used in our study, limiting the CPC from the foramen of Monro to the atrium/posterior temporal horn, patients in whom complete CPC was obtained in our study were given a maximum score of 2 during calculation of the CCHU ETVSS, as there is residual choroid plexus in the temporal horns bilaterally.

Outcome Measures

Failure of ETV/CPC, the primary outcome measure, was defined as a repeated CSF diversion procedure (repeated ETV, reservoir requiring tapping, VPS) or death. Failure of ETV/CPC and the decision to perform a subsequent CSF diversion procedure (repeated ETV, CSF shunt, tapping of CSF reservoir) was made on an individual basis at each neurosurgeon's discretion. In general, this was based on typical clinical presentation of symptomatic raised intracranial pressure and/or neurological or neurodevelopmental stagnation or decline, in association with persistent or worsening ventriculomegaly. However, the symptomatology and presentation were not documented in this retrospective review. Procedure-related complications were also documented.

In patients with failed ETV/CPC undergoing CSF shunting, shunt survival was assessed using the time to event (TTE) method, in which an event was defined as shunt revision (e.g., shunt malfunction, infection) or death. The TTE was measured and calculated using the Kaplan-Meier survival method.

Statistical Analysis

We present the raw data using descriptive statistics. For

continuous variables, we present medians, SDs, and range. For categorical data, we present frequencies and percentages. We created a Kaplan-Meier curve to demonstrate the overall time to ETV/CPC failure. We logarithmically transformed nonnormally distributed quantitative variables. We removed any variable with fewer than 20 observations. We performed univariate Cox regression analysis to determine if ETVSS and CCHU ETVSS were predic-

FIG. 2. Illustration demonstrating the typical maximal extent of CPC obtained with a rigid neuroendoscope, extending from the foramen of Monro to the posterior temporal horn (yellow choroid plexus). There is residual choroid plexus in the temporal horn in addition to the roof of the third and fourth ventricles (red choroid plexus). Copyright Alexander G. Weil. Published with permission.

FIG. 3. Radiological measurements (in millimeters). Preopontine interval (PPI) from the dorsum sellae to the tip of the basilar artery. Preopontine space⁶ from the midpons to clivus. Third Ventricular Morphology Index (TVMI), as calculated by adding the anterior commissure (AC) to tuber cinereum³ line (AC-TC) to the mammillary body to lamina terminalis line (MB-LT), and dividing by the biparietal diameter (BPD) [(AC-TC+MB-LT)/BPD]. The FOHR is calculated by adding the frontal horn (FH) and occipital horn (OH) and divided by 2BPD [(FH+OH)/2BPD]. TVW = width of the third ventricle.

tive of ETV/CPC survival. We performed multivariate Cox regression analysis, adjusting for CCHU ETVSS, to determine the predictive suitability of multiple preoperative MR imaging (FOHR, TVW, TVMI, PPI, PPS, AS) and intraoperative (preopontine scarring, third ventriculotomy pulsations, extent of CPC) variables for ETV/CPC outcome. We created Kaplan-Meier curves to graph the overall time to ETV/CPC failure function. We accepted any variable with a p value of less than 0.05 as a potential predictor of outcome. All statistics were performed in IBM SPSS Statistics version 20 (IBM Corp.).

Results

Patient Population

Between July 2007 and February 2014, 86 consecutive infants underwent ETV/CPC at Miami Children’s Hospital/Jackson Memorial Hospital. Of these, 1 patient who was lost to follow-up was excluded from the study

group. A total of 1, 2, 17, 26, 13, 11, 12, and 3 ETV/CPC procedures were performed in 2007, 2008, 2009, 2010, 2011, 2012, 2013, and 2014 (as of this writing), respectively. There were 45 boys and 40 girls with a mean age of 4.3 months (range 1 day to 20 months) (Table 2). Etiology included IVH of prematurity in 44 patients (51.7%), MMC in 7 (8.2%), congenital AS in 12 (14.1%), congenital communicating hydrocephalus in 6 (7.1%), Dandy-Walker complex in 6 (7.1%), postinfectious in 5 (5.8%), and other cause in 5 (5.8%). Twenty-nine patients (34.1%) had a previously placed reservoir (all IVH prematurity cases), while 5 (5.8%) had a prior VPS and 8 (9.4%) had a prior infection.

Seventy-six patients (89.4%) had preoperative MRI data. The median (SD) FOHR was 0.57 (0.07). The median³⁹ TVMI was 0.26 (11.90). The median³⁹ PPI and PPS were 1.67 mm (1.90 mm) and 3.54 mm (2.70 mm), respectively. AS could be assessed in 75 of the 76 patients with imaging, and AS was present in 43 patients (57.3%). The median³⁹ ETVSS and CCHU ETVSS were 40 (12.76) and 2 (0.96), respectively.

ETV and CPC were performed in all patients; extent of CPC was reported in 84 patients and was complete in 58 patients (69.0%) and incomplete in 26 (31.0%) (Table 3). Because extent of CPC was reported in a subtotal of patients but performed in all patients, the extent of CPC component of the CCHU ETVSS was 2 for all patients. Preopontine cistern status was reported in 83 patients and was described as scarred in 25 (30.1%). Third ventricle pulsations were absent in 7 (13.2%), present but moderate in 17 (32.0%), and excellent in 29 (54.7%) of the 53 cases in which it was reported. Intraoperative hemorrhage was absent in 70 patients (82.3%), minimal in 13 (15.3%), and moderate in 2 (2.4%). There were no reports of inadvertent neurological injury.

TABLE 1. Extent of CPC definitions

Extent of CPC	Incomplete (current study)	Complete (current study)	Complete (Warf et al., 2010)
Intraoperative description of CPC	Unilateral CPC or bilateral with 1 side complete and 1 extending to FM or atrium	Bilateral CPC from FM to posterior TH	Bilateral CPC from FM to tip of TH
CCHU ETVSS extent CPC grade	2	2	4

FM = foramen of Monro; TH = temporal horn.

TABLE 2. Preoperative characteristics of 85 patients undergoing ETV/CPC

Characteristic	Data*
Age at surgery in mos	
<1	16 (18.8)
1–6	49 (57.6)
6–12	17 (20)
12–24	3 (3.5)
Etiology	
IVH of prematurity	44 (51.8)
MMC	7 (8.2)
Congenital AS	12 (14.1)
Congenital communicating hydrocephalus	6 (7)
DWC	6 (7)
Postinfectious	5 (5.9)
Other etiology	5 (5.9)
Prior CSF hardware	
Prior reservoir	29 (34.1)
Prior shunt	5 (5.8)
Prior infection	8 (9.4)
Preop MR images available	76 (89.4)
Preop MR image score, median (SD)	
FOHR	0.57 (0.07)
TVMI	0.26 (11.9)
PPI	1.67 (1.9)
PPS	3.54 (2.7)
Presence of AS (n = 75)	43 (57.3)
Scoring system, median score (SD)	
ETVSS	40 (12.76)
CCHU ETVSS	2 (0.96)

DWC = Dandy-Walker complex.

* Data given as number of patients (%) unless otherwise indicated.

ETV/CPC Outcome

ETV/CPC was successful in 42.1%, 37.7%, and 36.8% of patients at 6, 12, and 24 months of follow-up, respectively (Fig. 4). The median (95% CI) time to ETV/CPC failure was 4.0 months (0.93–7.07 months). In univariate analyses, both the ETVSS (hazard ratio [HR] 1.03, 95% CI 1.01–1.05, $p = 0.004$) and CCHU ETVSS (HR 1.48; 95% CI 1.04–2.09; $p = 0.028$) were predictive of outcome (Table 4). In multivariate analysis, when adjusting for CCHU ETVSS, the presence of prepontine scarring was associated with ETV/CPC failure (HR 0.34; 95% CI 0.19–0.63; $p < 0.001$). Other variables, such as radiological criteria (PPI, PPS, AS, TVMI) and intraoperative findings (ventriculostomy pulsations, extent of CPC), did not predict success (Table 5).

Postoperative MRI was available for review in 75 patients (88.2%) at a mean follow-up of 2.9 months (range 1–72 months). The median FOHR³⁹ was 0.49 (0.11). The median TVMI³⁹ was 0.18 (0.05). In patients with successful ETV/CPC, the median³⁹ FOHR was 0.52 (0.09) compared with 0.45 (0.12) in patients who failed ETV/CPC and

TABLE 3. Intraoperative variables in 85 patients undergoing ETV/CPC

Variable	No. (%)
ETV	
Performed	85 (100)
Prepontine cistern status (n = 83)	
Scarring present	25 (30.1)
Ventilation of third ventricle (n = 53)	
Excellent	29 (54.7)
Mild	17 (32)
None	7 (13.2)
Septostomy (n = 84)	
Performed or already present	77 (90.6)
Extent of CPC (n = 84)	
Incomplete	26 (31)
Complete	58 (69)
Intraoperative bleeding (n = 85)	
None	70 (82.3)
Mild	13 (15.3)
Moderate	2 (2.4)
Severe	0 (0)

were subsequently treated by placement of CSF shunts ($p < 0.005$). In patients in whom ETV/CPC was successful, the median³⁹ TVMI was 0.20 (0.05) compared with 0.16 (0.05) in patients subsequently treated with placement of CSF shunts for ETV/CPC failure ($p < 0.001$).

There were 6 procedure-related complications in 5 patients (5.8%), all occurring in the first half of the study period (before May 2010) (Table 6). Two patients developed subdural hygromas, one of which was symptomatic requiring aspiration. Three patients developed meningitis, 1 in the context of a CSF leak. All of these patients had a history of IVH of prematurity with CSF reservoir prior to ETV/CPC. Two of the infections occurred within 2 weeks following ETV/CPC and both required subsequent VPS placement. In the third case, meningitis occurred after VPS placed 2 weeks after ETV/CPC. The VPS infection was treated with VPS removal, CSF reservoir placement, and serial CSF aspirations; however, the patient developed a cerebral abscess requiring surgical evacuation. This patient died 2 months postoperatively. Overall, there were 3 deaths (3.5%) in this series; these occurred at 2, 8, and 26 months after surgery. Two of the mortalities occurred 6 weeks and 21 months after a VPS was placed for ETV/CPC failure. The other mortality was a newborn with hydranencephaly who died of cardiorespiratory arrest 8 months after ETV/CPC.

Shunt Survival After Failed ETV/CPC

Of the 49 patients with failed ETV/CPC, 48 underwent VPS; of these, 46 had follow-up after shunting. Overall, CSF shunting was successful in 95.6%, 95.6%, and 87.0% of patients at 6, 12, and 24 months follow-up, respectively (Fig. 5). The median (95% CI) time to ETV/CPC failure

FIG. 4. Kaplan-Meier survival curve of time to ETV/CPC failure. Figure is available in color online only.

was 60.4 months (52.8–68.0 months). The “events” included 1 death; shunt infections in 2 patients (4.4%), 1 of which occurred from a perforated appendicitis; and shunt malfunctions, due to obstruction, in 3 patients (6.6%; 5 revisions).

Discussion

We report a single-center North American experience with ETV/CPC for hydrocephalus of infancy. Our first objective was to evaluate the safety and efficacy of this procedure for North American infants with hydrocephalus. Our secondary objective was to assess whether the ETVSS, the CCHU ETVSS, or other factors could predict success, to identify ideal candidates for ETV/CPC.

Is ETV/CPC Safe?

For it to be considered as a first-line treatment for infantile hydrocephalus, the complication profile of ETV/CPC must be equivalent to or better than that of ETV or CSF shunting. The complication profile in this study compares favorably to prior series of ETV/CPC in both North American^{5,29,50} and developing countries.⁴⁶ (Table 7). Our study corroborates others in suggesting the addi-

tion of CPC does not lead to an increase in complications compared with ETV performed alone in infants, where the reported rate of meningitis is 0%–12.0%, including CSF leak in 0%–8.5%, hemorrhage in 0%–4.3%, and hygroma in 0%–4.7%.^{1,10,11,13,14,17,20,34,45} However, the mortality rate of 3.5% in our series is not negligible, and, although similar to that reported by Kulkarni et al. (8.3%),²⁹ it is higher than mortality reported in series of infants undergoing ETV/CPC in other North American centers (0%),⁴⁴ in Uganda (1.0%), and following ETV alone worldwide, where it is closer to 0%.^{1,2,10,11,13,14,20,34,45} However, comparison between cohorts of patients undergoing ETV/CPC, ETV, or CSF shunting from different studies and centers is severely lim-

TABLE 5. Multivariate analysis of variables for ETV/CPC success adjusted for CCHU ETVSS

Characteristic	HR	95% CI	p Value
Preoperative			
PPI	1.001	0.850–1.179	0.987
PPS	0.941	0.828–1.069	0.348
TVW	1.034	0.979–1.092	0.227
TVMI	1.015	0.996–1.036	0.130
FOHR	0.067	0.001–7.842	0.067
Intraoperative			
Extent of CPC	1.030	0.550–1.928	0.928
Prepointe scarring	0.344	0.189–0.625	<0.001*
Third ventricular floor pulsation	1.451	0.651–3.235	0.363

*Statistically significant.

TABLE 4. Univariate analysis of scoring system variables for ETV/CPC success

Scoring System	HR	95% CI	p Value
ETVSS	1.013	1.010–1.054	0.004
CCHU ETVSS	1.477	1.043–2.092	0.028

TABLE 6. Postoperative variables in 85 patients undergoing ETV/CPC

Characteristic	Data
Complications, n (%)	
Infection	3 (3.5)
Hygroma	2 (2.3)
CSF leak	1 (1.2)
Postoperative MRI available, n (%)	75 (88.2)
Mean follow-up in mos (range)	2.9 (1–72)
Median FOHR (SD)	0.49 (0.11)
Median TVMI (SD)	0.18 (0.05)

ited by differences in the patient populations. Differences in mortality are likely heavily influenced by this selection bias, as patients undergoing ETV/CPC suffer from more complex underlying conditions (e.g., IVH of prematurity, hydranencephaly) than those undergoing standard ETV. The mortality is related to these underlying conditions, as none of the mortalities in our series were directly related to the ETV/CPC procedure itself: 2 occurred after VPS placement and 1 was related to the underlying condition (e.g., hydranencephaly) of the child.

What Is the Role of ETV/CPC?

The success rate of ETV/CPC in this single-center cohort is similar to that of many other North American studies.^{5,29,50} The 12-month success rate of 37% is lower than that recently reported by Kulkarni et al. (52%) and Stone

and Warf (57%), both of which were North American studies.^{29,44} However, comparison between studies is limited by differences in patient population and nonstandardized methodology and criteria for undergoing a repeated CSF diversion procedure.^{29,44} For example, compared with Kulkarni et al., our series had a higher proportion of patients younger than 6 months (76% vs 56%), more patients with prior IVH of prematurity (52% vs 25%), and a lower predicted success rate based on the median CCHU ET-VSS (2 vs 4) and ET-VSS (40 vs 50).²⁹ Also, compared with Stone and Warf, our series had a higher proportion of patients with unfavorable risk factors, such as age less than 6 months (76.4% vs 68.0%), preoperative scarring (30.1% vs 16.5%), and more patients with IVH of prematurity (51.8% vs 27.5%), limiting direct comparison of outcome data.

This study found that ETV/CPC has a failure profile similar to ETV, with a higher rate of early postoperative failure compared with shunting.^{16,21,25} The 6- and 12-month ETV/CPC success rates of 41% and 38%, respectively, in our series are inferior to the VPS survival rates of 62% and 47%, respectively.^{19,25} However, while the ETV/CPC success rate stabilizes at 37% after 2 years, shunt survival rates drop to 41% by 4 years and 20% by 12 years, suggesting that any difference in efficacy between ETV/CPC and shunting may become very small in the long term.^{19,29}

Some authors have questioned the relative contribution of CPC in improving success rates for ETV in infants.⁴¹ The overall success rate of ETV/CPC performed across several North American centers has not systematically been superior to that reported for ETV.^{1,10,11,13,14,16,17,20,34,45} However, comparisons of results of ETV/CPC from our single center to historical controls of ETV alone for infantile hydrocephalus, including more recent studies, are significantly

FIG. 5. Time to shunt failure. Kaplan-Meier survival curve of CSF shunt survival after failed ETV/CPC. Figure is available in color online only.

TABLE 7. Literature review of ETV/CPC or CPC for pediatric hydrocephalus

Authors & Year	Country	Procedure (n)	Total No. of Cases	Patient Age	Etiology (n)	Success Rate	Mortality (cause)	Complication (n)
Pople & Ettles, 1995	New Zealand	CPC (104)	104	2 yrs (median 5 mos)	Communicating, obstructive, MMC, idiopathic	38%	10%	None
Warf, 2005	Uganda	ETV (284), ETV/CPC (266)	550	Mean 14 mos, median 5 mos	Postinfectious (320), posthemorrhagic (5), MMC (73), other (152)	66% ETV/CPC vs 47% (ETV) for age <12 mos	1%	<1% infection
Warf & Campbell, 2008	Uganda	ETV/CPC (115)	115	Mean 3 mos (range ± 2 mos)	MMC (115)	76%	1.1%	None
Warf et al., 2011 ⁵⁰	USA	ETV/CPC (10)	10	Mean -1.6 wks (range -11 to 11 wks)	IVH prematurity (10)	40%	0%	None
Warf et al., 2011 ⁵¹	Uganda	ETV/CPC (45)	45	Mean 5 mos	DWC (45)	74%	N/A	N/A
Sandberg et al., 2012	USA	ETV/CPC (3), CPC (5)	8	N/A	Congenital severe HCP/hydranencephaly (8)	50% (at mean 15-mo follow-up)	50% (75% successful ETV/CPC)	None
Warf et al., 2012 ⁵⁵	Uganda	ETV/CPC (23), ETV (12)	35	Mean 3.5 mos	Congenital AS (35)	81.9% ETV/CPC vs 48.6% ETV	0%	None
Warf, 2013	Uganda	ETV (16), ETV/CPC (48)	64	Mean 6.1 mos (all <24 mos)	Congenital communicating hydrocephalus (64)	65.2% ETV/CPC vs 20% ETV	0%	Ventriculitis (1)
Kulkarni et al., 2014	USA/Canada	ETV/CPC (36)	36	All <24 mos	IVH prematurity (9), AS (8), MMC (4), other (15)	52% (12 mos)	8.3%	Infections (2)
Chamiraju et al., 2014	USA	ETV/CPC (24), ETV (3)	27	Mean 7 wks cGA (range -4 to +34 wks)	IVH prematurity	37%	0%	None
Shitsama et al., 2014	Kenya	CPC (33)	33	Mean 8 wks (range 0-144 wk)	Extreme hydrocephalus (22), hydranencephaly (11)	43.3%	18%	None
Ogiwara et al., 2014	Japan	ETV/CPC (12), CPC (6)	18	Mean 8 mos (range 0.4-24 mos)	IIVH (5), postinfectious (2), MMC (3), AS (1), hydroencephaly (1), other (6)	50% overall (42% ETV/CPC, 33% CPC alone)	0%	None
Stone & Warf, 2014	USA	ETV/CPC (91)	91	Mean 4.7 mos, median 3.2 mos	MMC (23), IVH (25), AS (23), DWC (6), postinfectious (6), congenital (5), congenital cyst (3)	57% (12 mos)	0%	CSF leak (1), SIADH (1)
Bankole et al., 2015	Nigeria	ETV/CPC (22)	22	M:F ratio (2.5:1); 91% <1 yr	MMC (8), postinfectious (4), non-postinfectious (10)	68% (mean 13 mos, range 6-12 mos)	0%	None

cGA = corrected gestational age; N/A = not applicable; SIADH = syndrome of inappropriate antidiuretic hormone.

limited by many uncontrolled variables.¹⁶ In many studies, the success rate of ETV/CPC has also not been shown to be superior to the success rate predicted by the ETVSS, which predicts success following ETV alone.^{5,29,50} For example, the mean ETVSS was 40% in our series, which is roughly equivalent to the actual predicted 6-month ETV/CPC success of 42.1%. This would suggest a modest benefit at best. However, a more recent North American study of 91 infants undergoing ETV/CPC found that the 6-month success rate of 59% exceeded the 45% rate predicted by the ETVSS.⁴⁴ Furthermore, some authors have shown stand-alone CPC (without ETV) to be a relatively efficient treatment with good (38%) long-term efficacy in children with hydrocephalus.³⁶ Finally, a study by Warf in sub-Saharan Africa strongly suggests an important role for CPC, as it has been found to almost double the efficacy of ETV in patients with MMC, AS, and DWC, and to triple efficacy in cases of postinfectious or communicating hydrocephalus.^{47,49,51,55} The finding of a dose response of CPC, in which more extensive CPC improves success rate over less extensive CPC, as reported by Warf, also supports the role of CPC and is the basis for the CCHU ETVSS.⁵³

Selecting a Candidate for ETV/CPC

This is the first study to show that the ETVSS can predict success following ETV/CPC. It is also the first study to show that the CCHU ETVSS can predict success after ETV/CPC in a North American cohort of infants. The ETVSS was specifically designed and validated to predict success in patients undergoing ETV.²⁶ The CCHU ETVSS was developed based on data from ETV/CPC performed using a flexible endoscope on children at the CCHU in sub-Saharan Africa.⁵³ This scale includes an assessment of the extent of CPC, in addition to age and etiology; however, since all our patients had an extent of CPC score 2 (incomplete), only etiology and age were contributing factors. Overall, this suggests that age and etiology are likely important determinants of success. A recent study has shown postinfectious hydrocephalus to be associated with ETV/CPC failure.⁴⁴ Although these findings suggest that both these scoring systems can predict which patients will fail and help patient selection in patients treated at our center, whether these results are generalizable to other centers remains unknown.²⁹ A recent multi-institutional study of 36 infants undergoing ETV/CPC failed to demonstrate any impact of age or etiology.²⁹ Both the ETVSS and CCHU ETVSS also failed to predict success, suggesting that further studies are warranted to verify if our results are generalizable.²⁹

Not surprisingly, prepontine scarring predicted ETV/CPC failure, as has been shown by other authors when assessed on preoperative MRI⁵⁰ and during surgery.^{44,52} This suggests that in the presence of prepontine scarring, the CPC may not decrease CSF production sufficiently to treat the hydrocephalus, underscoring the important role the concomitant ETV plays in ETV/CPC.

Does Extent of CPC Matter?

How much of the choroid plexus must be cauterized for a successful ETV/CPC is unknown. The extent of CPC necessary to improve success rate is also controversial.^{5,44}

Some authors consider subtotal CPC with a rigid neuroendoscope to be sufficient,⁵ while others advocate performing complete CPC with a flexible neuroendoscope to optimize efficacy.^{44,49} In support of Warf's findings, Kulkarni et al. recently found a trend ($p = 0.0501$) for improved success rate, above that predicted by the ETVSS, following near-complete CPC (greater than 90%) in a mixed etiology cohort of 36 North American infants undergoing ETV/CPC.²⁹ A more recent North American study in 91 infants showed a higher 57% 12-month success rate in infants undergoing ETV/CPC, using a flexible neuroendoscope, suggesting a possible added benefit of complete CPC.⁴⁴ However, the extent of CPC was assessed subjectively by the operating neurosurgeon, which is known to be an unreliable assessment in the tumor literature, with frequent overestimation of extent of resection.⁵⁶ None of these studies on ETV/CPC has evaluated the extent of CPC in an objective, independent, or blinded fashion using objective biomarkers (e.g., MRI to evaluate the choroid plexus postoperatively). Finally, the literature on ETV/CPC for infantile hydrocephalus related to IVH of prematurity shows a 40% success rate regardless of whether flexible endoscope-guided complete CPC or rigid endoscope-guided subtotal CPC is performed.^{5,50} While the ultimate goal of ETV/CPC is to alter the balance of CSF production and absorption sufficient enough to avoid a CSF diversion, the optimal extent of CPC may be different for each patient, with some patients requiring a more extensive CPC than others.

Defining Success

Although our primary end point of shunt independence is the most commonly used end point to assess efficacy of ETV or ETV/CPC,²⁴ it does not provide information on the patient's functional outcome. Although unavailable in this retrospective chart review, neurocognitive outcome and health-related quality of life may have been more informative and relevant end points.^{27,41} Is it better to live with shunt-independent ventriculomegaly following a successful ETV/CPC than to survive with small- to normal-sized shunted ventricles, with the well-established long-term risk of shunt infection, malfunction, and reoperation?^{7,43} Avoiding multiple shunt infections and surgical revisions should be a primary objective in infants with hydrocephalus, as they have been shown to correlate with a worse neurocognitive outcome.^{31,37} Furthermore, several authors have shown that in the absence of raised intracranial pressure, ventriculomegaly does not impair neurodevelopment.^{15,54} This is supported by Warf et al., who demonstrated comparable neurocognitive outcomes in hydrocephalic MMC children undergoing ETV/CPC or CSF shunting.⁵⁴

Some authors have questioned whether the CPC, which alters CSF composition and physiology in unknown ways, can predispose patients who fail and go on to have shunts placed to a higher rate of complications.⁴¹ The rate of shunt failure in the patients shunted after failed ETV/CPC was comparable to other series looking at shunted patients following failed CPC³⁶ and within the range expected following primary shunt placement.^{7,19} Although these data are anecdotal, they are supported by a recent study in sub-Saharan hydrocephalic infants that showed that the addition

of CPC to ETV did not affect shunt survival and infection rate compared with patients in whom a shunt was placed primarily or after ETV alone.⁴⁸

Study Limitations

There are multiple limitations to this study that are inherent to its retrospective nature, small sample size, and heterogeneous patient population. The nonblinded data collection introduces a bias. Although this is a consecutive series of patients undergoing ETV/CPC, other patients underwent either ETV or CSF shunting at our institution during the study period, introducing a selection bias. Because of this, and because it is a single-center experience, whether the results are generalizable to other centers with different surgeons, techniques, and patient populations with hydrocephalus is unknown.

Conclusions

ETV/CPC is a feasible alternative to ETV and VPS in infants with hydrocephalus. Both the ETVSS and CCHU ETVSS predicted success following ETV/CPC in this single-center North American cohort. The presence of pre-pontine scarring may reduce success after this procedure.

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Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Bhatia, Weil, Ragheb. Acquisition of data: Weil, Fallah. Analysis and interpretation of data: Weil, Fallah. Drafting the article: Weil, Fallah. 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: Bhatia. Statistical analysis: Fallah. Study supervision: Bhatia, Ragheb.

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