

# Treatment of hydrocephalus following posterior fossa tumor resection: a multicenter collaboration from the Hydrocephalus Clinical Research Network

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# Abstract

## Objective

Persistent hydrocephalus following posterior fossa brain tumor (PFBT) resection is a common cause of morbidity in pediatric brain tumor patients, for which the optimal treatment is debated. The purpose of this study was to compare treatment outcomes between VPS and ETV in patients with persistent hydrocephalus following surgical resection of a PFBT.

## Methods

A post-hoc analysis was performed of the Hydrocephalus Clinical Research Network (HCRN) prospective observational study evaluating VPS and ETV for pediatric patients. Children who experienced hydrocephalus secondary to PFBT from 2008 to 2021 were included. Primary outcomes were VPS/ETV treatment failure and time-to-failure (TTF).

## Results:

Among 241 patients, the VPS (183) and ETV (58) groups were similar in age, extent of tumor resection, and preoperative ETV Success Score. There was no difference in overall treatment failure between VPS and ETV (33.9% vs 31.0%,  $p=0.751$ ). However, mean TTF was shorter for ETV than VPS (0.45 years vs 1.30 years,  $p=0.001$ ). While major complication profiles were similar, compared to VPS, ETV patients had relatively higher incidence of minor CSF leak (10.3% vs. 1.1%,  $p=0.003$ ) and pseudomeningocele (12.1% vs 3.3%,  $p=0.02$ ). No ETV failures were identified beyond 3 years, while shunt failures occurred beyond 5 years. Shunt infections occurred in 5.5% of the VPS cohort.

## Conclusions

ETV and VPS offer similar overall success rates for PFBT-related postoperative hydrocephalus. ETV failure occurs earlier, while susceptibility to VPS failure persists beyond 5 years. Tumor histology and grade may be considered when selecting the optimal means of CSF diversion.

## Introduction

Pediatric posterior fossa brain tumors (PFBT) present commonly with hydrocephalus [1, 2]. In approximately 30% of such patients the hydrocephalus persists following tumor resection, requiring permanent cerebrospinal fluid (CSF) diversion [3–8]. While ventriculoperitoneal shunt (VPS) placement is frequently utilized for PFBT-related hydrocephalus, endoscopic third ventriculostomy (ETV) offers the advantage of avoiding shunt-related complications, particularly in those patients with limited survival prognosis [5, 6, 9–13]. However, there is limited data to guide the surgeon's selection of VPS versus ETV as the optimal treatment modality in these patients [1, 2]. To date, there exists no single study larger than 100 patients comparing the failure rates between ETV and VPS in pediatric patients with PFBT [1]. Also lacking are multicenter studies and those controlling for known risk factors of post-resection

hydrocephalus such as tumor location in the midline, subtotal resection of tumor, and CSF infections[1]. A recent study also found tumor consistency, tumor metastasis, and postoperative ventricular blood on CT to be risk factors of post-resection hydrocephalus [14].

In a recent systematic review and time-to-failure (TTF) analyses of 408 PFBT patients across 12 published studies, there was no significant difference in cumulative failure rates between VPS (29%) and ETV (21%) [1]. The largest included study (N = 91) reported 11% ETV failure rate at a median TTF of 13 days, relative to 13% VPS at a median TTF of 440 days.[11] However, most of the ETVs were performed *prior to* PFBT resection, and the VPS patients represented less than 20% of the study cohort [11]. A retrospective analysis of 53 patients described a 6% ETV failure rate with a median TTF of 10 months, and a 38% VPS failure rate at a 6-month median TTF [15]. Among 6 other studies of 173 patients, the reported failure rates were highly variable, with ETV failure rates ranging from 12–35% (median TTF: 27–94 days) and the VPS failure rate from 22–50% (median TTF: 7-244 days).[16–21] Conclusions from the systematic review, as well as recent literature are limited by the inherent shortcomings of studies with non-uniform inclusion criteria, heterogeneous cohorts, and variable follow-up data [1, 22]. As such, to date, there is limited evidence to guide surgical treatment selection between ETV and VPS in this population.

The objective of this study was to compare the occurrence of and time to failure between ETV and VPS in children with persistent hydrocephalus following PFBT resection. Additionally, we examined relative morbidity and healthcare utilization metrics between the two cohorts.

## Methods

### Patient Population

This was a post-hoc analysis of a multicenter prospective observational study of children who underwent a VPS placement or ETV for treatment of persistent hydrocephalus following PFBT resection at 13 participating Hydrocephalus Clinical Research Network (HCRN) centers between 2008 and 2021. Prospectively collected data were obtained from the HCRN Core Data Project (Registry). Study data was managed using REDCap electronic data capture tools hosted at University of Utah [23]. To address the study's specific aims, relevant clinical variables not already captured prospectively in the HCRN registry were retrospectively retrieved from individual patient records from each site's institutional electronic medical records. Both the prospective and retrospective data were aggregated for analyses. The participating HCRN centers were Alberta Children's Hospital, University of Calgary; BC Children's Hospital, University of British Columbia; Children's Hospital Colorado, University of Colorado; Children's Hospital of Pittsburgh of UPMC, University of Pittsburgh; Children's of Alabama, University of Alabama; Johns Hopkins Hospital, Johns Hopkins University; Monroe Carell Jr. Children's Hospital at Vanderbilt, Vanderbilt University Medical Center; Nationwide Children's Hospital, Ohio State University; Primary Children's Hospital, University of Utah; Seattle Children's Hospital, University of Washington; The Hospital for Sick

Children, University of Toronto; St. Louis Children's Hospital, Washington University; and Texas Children's Hospital, Baylor School of Medicine.

## **Inclusion Criteria And Exclusion Criteria**

Pediatric patients (age < 17.5 years old at the time of surgery) having undergone resective management (biopsy not included) of PFBT and who received a first time permanent CSF diversion procedure (VPS or ETV) for the treatment of PFBT-related hydrocephalus with a minimum of 6 months follow-up from the index CSF diversion procedure were included. Patients were excluded if 1) VPS placement or ETV was performed prior to resection of the PFBT, or 2) tumor was located in the primary pineal region, or 3) presence of disseminated neoplastic disease or metastatic lesion(s) in the third or lateral ventricle and leptomeninges at the time of CSF diversion, or 4) loculated intraventricular compartments, or 5) presence of diffuse leptomeningeal tumor burden. Perioperative external ventricular drain (EVD) placement was not an exclusion criterion.

## **Study Definitions**

A PFBT was defined as pathology-confirmed neoplasm primarily located within the posterior fossa, including the cerebellar hemispheres, cerebellar vermis, and fourth ventricle, but excluding the pineal region, aqueduct, or posterior third ventricle. Surgical resection included operative interventions performed with the goal of tumor resection (total or partial). Extent of tumor resection, determined by results of the immediate post-operative MRI were categorized: gross total resection (GTR; no radiographic evidence of residual disease); near total resection (NTR, < 1.5 cm<sup>2</sup> disease remaining following resection); subtotal resection (STR, residual tumor measuring greater than 1.5 cm<sup>3</sup>). Persistent hydrocephalus was determined by need for a permanent CSF diversion procedure (VPS or ETV) following PFBT resection. Postoperative CSF leak was defined as one or two episodes of CSF egress from the surgical wound that stops spontaneously, or with simple maneuver, adjustment of drain level, tightening of cerclage stitch, or simple sutures (minor) or persistent CSF drainage, that requires return to operating room for re-suturing/repair of wound, reinsertion of CSF drain, or CSF diversion procedure (major). A pseudomeningocele was defined as a clinically or radiographically evident subdermal CSF collection resulting in some discomfort, or easily palpable, or some threat to wound integrity but responds to simple aspiration and/or wrapping (minor) or significant discomfort, obvious skin deformation, significant threat to wound integrity requiring repeated aspiration and/or wrapping, or additional surgical procedure, i.e. CSF diversion or re-closure of wound (major).

## **Outcome Measures**

The primary outcomes were hydrocephalus treatment failure and TTF. Treatment failure was defined as the need for subsequent surgery for CSF diversion or death due to hydrocephalus in the absence of tumor

progression. TTF was recorded as the duration between the date of index VPS or ETV to the date of first subsequent CSF diversion, or to the date of death, if death was determined to result from hydrocephalus. Secondary outcomes included postoperative complications, including wound infection, wound dehiscence, intracranial hemorrhages (including epidural hematoma, subdural hematoma, and intracerebral hematoma), CSF-culture proven meningitis, CSF leak and pseudomeningocele; number of CSF-diverting surgeries performed within 5 years of initial CSF-diversion; number of hospital admissions for neurosurgery following CSF-diverting procedure within 5 years of index VPS or ETV; and number of CT or MR scans obtained within 5 years following index VPS or ETV.

## Data Analysis

Descriptive statistics including means, standard deviations, and ranges for continuous variables, as well as percentages and frequencies for categorical variables were reported. Wilcoxon rank sum tests were utilized for the comparison of continuous variables and Fisher's exact tests for categorical variables, to compare the VPS and ETV groups. CSF diversion failure-free survival analyses were performed with the Kaplan-Meier method for each group and compared using the log-rank test. All analyses were conducted using SAS 9.4 (SAS Institute).

## Results

As of January 2021, across the 13 participating HCRN sites, 241 patients who underwent CSF diversion for persistent hydrocephalus following PFBT resection met study criteria. 183 (76%) patients received a VPS and 58 (24%) underwent ETV (Fig. 1). The median follow-up time was 6.8 (4.1, 10.5) years.

## Baseline Characteristics

There were no differences between the VPS and ETV groups in the following baseline characteristics: age at treatment (5.6 vs 5.5 years,  $p = 0.80$ ), largest tumor dimension (4.4 vs 4.6cm,  $p = 0.314$ ), relative tumor location within the posterior fossa, extent of resection, Glasgow Coma Scale at time of presentation, ethnicity, race, sex, and complex chronic conditions (Table 1). However, the VPS group, relative to the ETV group, had a greater proportion of patients with high-grade tumors (59% vs 31%,  $p < .001$ ) (Table 1). In terms of CSF diversion features, there were no significant differences in baseline ETV success score ( $p = 0.8$ ) and whether a perioperative EVD was inserted (81% vs 71%,  $p = 0.10$ ) at the time of PFBT surgery. The VPS group had a smaller fronto-occipital horn ratio (0.41 vs 0.48,  $p < .001$ ) (Table 2).

Table 1  
Subject demographics and tumor characteristics

	Initial Permanent CSF-diversion procedure		
	Shunt (N = 183)	ETV (N = 58)	P-value
<b>Age at time of procedure (years)</b>	5.6 [2.5, 9.9]	5.5 [2.3, 11.1]	0.801 <sup>1</sup>
<b>Ethnicity</b>			0.728 <sup>2</sup>
Not Hispanic or Latino	125 (68.3%)	43 (74.1%)	
Hispanic or Latino	22 (12.0%)	5 (8.6%)	
Unknown or Not reported	36 (19.7%)	10 (17.2%)	
<b>Race Collapsed</b>			1.000 <sup>2</sup>
White	114 (62.3%)	38 (65.5%)	
Black or African American	15 (8.2%)	5 (8.6%)	
Other	12 (6.6%)	4 (6.9%)	
Unknown	42 (23.0%)	11 (19.0%)	
<b>Sex</b>			0.759 <sup>2</sup>
Male	108 (59.0%)	36 (62.1%)	
Female	75 (41.0%)	22 (37.9%)	
<b>Complex chronic conditions</b>			0.061 <sup>3</sup>
0	142 (77.6%)	52 (89.7%)	
1	35 (19.1%)	5 (8.6%)	
>=2	6 (3.3%)	1 (1.7%)	
<b>Tumor size*<sup>4</sup></b>	4.4 [3.6, 5.3]	4.6 [3.7, 5.3]	0.314 <sup>1</sup>
<b>Tumor location</b>			0.514 <sup>2</sup>
Cerebellar-midline	37 (20.2%)	17 (29.3%)	
Cerebellar-hemispheric	30 (16.4%)	11 (19.0%)	
Brainstem	22 (12.0%)	5 (8.6%)	
Fourth ventricle	83 (45.4%)	21 (36.2%)	



	Initial Permanent CSF-diversion procedure		
Other	8 (4.4%)	3 (5.2%)	
Unknown	3 (1.6%)	1 (1.7%)	
<b>Histology</b>			0.005 <sup>2</sup>
Medulloblastoma/ATRT	82 (44.8%)	15 (25.9%)	
Ependymoma	27 (14.8%)	6 (10.3%)	
Pilocytic astrocytoma	49 (26.8%)	33 (56.9%)	
Glioma-other (not pilocytic astrocytoma and not ganglioglioma)	8 (4.4%)	1 (1.7%)	
Glioneuronal tumor (includes ganglioglioma)	4 (2.2%)	0 (0.0%)	
Meningioma/vestibular schwannoma	1 (0.5%)	0 (0.0%)	
Hemangioblastoma	0 (0.0%)	1 (1.7%)	
Choroid plexus tumor	2 (1.1%)	1 (1.7%)	
Dermoid/epidermoid	3 (1.6%)	0 (0.0%)	
Other	6 (3.3%)	1 (1.7%)	
Unknown	1 (0.5%)	0 (0.0%)	
<b>Grade</b>			< .001 <sup>2</sup>
High (WHO 3 or 4)	107 (58.5%)	18 (31.0%)	
Low (WHO 1 or 2)	70 (38.3%)	37 (63.8%)	
Unknown	6 (3.3%)	3 (5.2%)	
<b>Extent of tumor resection</b>			0.481 <sup>2</sup>
Gross total resection (GTR)	103 (56.3%)	30 (51.7%)	
Near total resection (NTR)	36 (19.7%)	10 (17.2%)	
Subtotal resection (STR)	34 (18.6%)	15 (25.9%)	
Unknown	10 (5.5%)	3 (5.2%)	
<b>GCS at tumor presentation<sup>5</sup></b>	15.0 [15.0, 15.0]	15.0 [15.0, 15.0]	0.367 <sup>1</sup>

**Initial Permanent CSF-diversion procedure**

<sup>1</sup> Wilcoxon rank-sum test.

<sup>2</sup> Fisher's exact test.

<sup>3</sup> Cochran-Armitage trend test.

<sup>4</sup>Missing on 44 subjects.

<sup>5</sup>Missing on 90 subjects.

**\*Maximal axial dimension (cm)**

Table 2  
Initial CSF-Diversion Characteristics

	Initial Permanent CSF-diversion procedure		P-value
	Shunt (N = 183)	ETV (N = 58)	
<b>ETV Success Score</b>			0.783 <sup>1</sup>
30	2 (1.1%)	1 (1.7%)	
40	3 (1.6%)	0 (0.0%)	
60	22 (12.0%)	8 (13.8%)	
70	114 (62.3%)	38 (65.5%)	
80	42 (23.0%)	11 (19.0%)	
<b>Fronto-occipital horn ratio (FOR) at initial CSF-diversion<sup>2</sup></b>	.41 [.34, .49]	.48 [.41, .54]	< .001 <sup>3</sup>
<b>Indications of CSF diversion (after tumor resection)</b>			
CSF leak	25 (13.7%)	10 (17.2%)	0.523 <sup>4</sup>
Pseudomeningocele	42 (23.0%)	6 (10.3%)	0.039 <sup>4</sup>
Progressive/persistent ventriculomegaly	101 (55.2%)	26 (44.8%)	0.178 <sup>4</sup>
Elevated ICP readings	31 (16.9%)	8 (13.8%)	0.684 <sup>4</sup>
Symptoms/signs of elevated ICP (including headache, nausea/vomiting, depressed mental state, etc.)	93 (50.8%)	23 (39.7%)	0.175 <sup>4</sup>
<b>Perioperative EVD insertion</b>	149 (81.4%)	41 (70.7%)	0.097 <sup>4</sup>
<sup>1</sup> Cochran-Armitage trend test. <sup>2</sup> Missing on 41 subjects. <sup>3</sup> Wilcoxon rank-sum test. <sup>4</sup> Fisher's exact test.			

<b>Table 3. Post-Initial Permanent CSF Diversion Details</b>			
	Initial Permanent CSF-diversion procedure		
	Shunt (N = 183)	ETV (N = 58)	P-value
<b>Re-intervention for hydrocephalus</b>	62 (33.9%)	18 (31.0%)	0.751 <sup>1</sup>
<b>Time from initial permanent CSF diverting procedure to first re-intervention (years)</b>	1.30 (2.108)	0.45 (0.842)	0.001 <sup>2</sup>
<b>Type of re-intervention</b>			0.125 <sup>1</sup>
Shunt	61 (98.4%)	16 (88.9%)	
ETV	1 (1.6%)	2 (11.1%)	
<b>Number of hospital readmissions for neurosurgical evaluation and/or treatment following initial CSF-diverting procedure<sup>3</sup></b>	1 (2.6) 1 [0, 2]	1 (1.7) 0 [0, 1]	0.185 <sup>2</sup>
<b>Number of brain/head CT or MR scans obtained following initial CSF-diverting procedure<sup>3</sup></b>	17 (10.8) 15 [10, 23]	14 (9.4) 12 [8, 19]	0.025 <sup>2</sup>
<b>Number of CSF-diverting procedures performed after initial CSF-diversion<sup>4</sup></b>	1 (1.2) 0 [0, 1]	1 (1.1) 0 [0, 1]	0.671 <sup>2</sup>
Numeric values are reported as Mean (SD)			
<sup>1</sup> Fisher's exact test.			
<sup>2</sup> Wilcoxon rank-sum test.			
<sup>3</sup> The median follow-up time from initial permanent CSF-diverting procedure is 6.9 [4.1, 10.4] years.			

## Failure Rates, Time-to-failure (Ttf) And Resource Utilization

There was no difference in overall treatment failure between VPS and ETV (33.9% vs 31.0%,  $p = 0.751$ ). The mean TTF was shorter for ETV than for VPS (0.45 years vs 1.30 years,  $p = 0.001$ ) (Table 3). No ETV failures were observed after 3 years, while VPS failures continued to occur up to 6 years after the initial surgery, albeit at a lower rate compared to the first three years following shunt placement (Fig. 2).

## Postoperative Complications And Resource Utilization

Postoperative complications were similar between ETV and VPS, with two exceptions.

Relative to VPS, the ETV group experienced a higher rate of minor CSF leak (10% vs 1%,  $p = 0.003$ ) and pseudomeningocele (12% vs 3%,  $p = 0.017$ ). There were no significant differences in other reported complications including hyponatremia, hygroma, new neurologic deficits, seizures, wound infection or systemic infection or postoperative hemorrhage. There were no reports of ascites, bowel perforation, brain infarct, cardiopulmonary issues, diabetes insipidus, endocrinological disturbances in either group (Online Resource 1). Shunt infections occurred in 10 (5.5%) patients in the VPS cohort. The mean number of hospital readmissions and number of CSF-diverting procedures after index CSF-diversion were similar between both cohorts ( $p = 0.185$  and  $p = 0.671$ , respectively), however the mean number of subsequent CT and MR scans performed following index CSF-diversion was higher following VPS than ETV ( $17 \pm 10.8$  vs  $14 \pm 9.4$ ,  $p = 0.025$ ) (Table 3).

## Discussion

A common cause of morbidity in the pediatric population is hydrocephalus related to PFBT.[1–8, 24] While a majority of PFBT-related hydrocephalus resolves following tumor resection, up to a third of patients require permanent CSF diversion [3–6, 8]. The historical mainstay treatment of hydrocephalus in children has been placement of a VPS, albeit with reportedly high failure rates [25]. More recently, ETV has been popularized as an alternative to VPS, given its advantage of avoiding lifelong shunt-related complications and dependence[25–27]. In this study, we demonstrate that both ETV and VPS are effective means of CSF diversion with favorable safety profiles in patients with persistent hydrocephalus following PFBT resection. Aggregated over time, the cumulative failure rate between ETV and VPS is similar in this cohort (31% vs 34%). Indeed, by 6-months following index surgery, the failure rate is statistically equivalent between the two procedures. However, ETV failures occur earlier – most within the first 6-months, while VPS failures occur in a more protracted fashion, with the risk of failure extending beyond 5 years of initial shunt placement.

The current WHO pediatric tumor grading system concatenates tumor histology and molecular features to assign a grade (1 through 4), which is further dichotomized into low-grade (grades 1 or 2) and high-grade (grades 3 or 4) [28]. Tumor grade not only informs disease severity, but it also aids with prognostication and guides the need for adjuvant chemotherapy and/or radiotherapy [28]. After PFBT resection, a majority of patients with low-grade tumors undergo serial radiologic surveillance alone, while those with high-grade tumors require additional postoperative adjuvant therapy [29, 30]. A critical determinant of the efficacy of adjuvant therapy in high-grade PFBTs is the timing of initiation of the treatment following tumor resection [29, 31–33]. Early initiation helps to both reduce time for tumor regrowth and maximize the potential recurrence and survival benefit of the adjuvant therapy [29, 34, 35]. Conversely, delayed initiation, especially for longer than 6 months is an independent predictor of worse outcomes [29, 31–35]. Indeed, recent clinical trials such as the Children's Oncology Group ACNS0332 trial and the St Jude's SJMB12 trial, which assessed treatment outcomes of PFBT mandated starting therapy within 31 and 36 days of tumor resection, respectively [34, 35]. In this study, while the overall treatment

failure or relative risk of treatment failure were equivalent between VPS and ETV beyond 6 months, most ETV failures occurred within the first 6 months of surgery, posing a risk for interfering with adjuvant therapy for high-grade PFBT patients. Accordingly, tumor grade (suspected or confirmed) may reasonably be considered when choosing VPS vs ETV for CSF diversion in post-resection hydrocephalus. It may be prudent to favor VPS in patients with high-grade lesions who a) need expedited and uninterrupted adjuvant therapy, and b) are less likely than their low-grade counterparts to survive long enough to experience delayed shunt malfunction. In this cohort, there were no ETV failures after 3 years, but VPS failures continued to occur beyond 5 years after the initial surgery. Therefore, in patients with low-grade PFBT ETV may be the preferred modality, thereby avoiding shunt-related complications and dependence which persist life-long.

Interestingly, approximately two-thirds of the patients in this study who underwent ETV had low-grade tumors and a similar proportion who had placement of VPS had high-grade tumors, which may reflect a practice pattern possibly attributed to what surgeons already suspect about failure times between the two procedures based on non-tumor-related-hydrocephalus data. Indeed, the majority of the recent ETV data show that over 90% of failures occur within the first 6 months of surgery, and shunt failures have been known to occur in a delayed fashion, but the risk of failure persists across the lifespan of the patient. While avoidance of a shunt may seem optimal in PFBT patients, the shorter TTF of ETV may make VPS a better option in patients with high-grade lesions requiring post-resection therapy.

Beyond tumor grade, it remains unclear if any other baseline patient or tumor characteristics are informative for selecting VPS vs ETV in PFBT patients who develop persistent hydrocephalus following tumor resection [7, 10, 24, 28, 36, 37]. The largest systematic review to date comparing patients who underwent VPS or ETV in PFBT patients demonstrated no intergroup differences in age, sex, cerebral metastases, extent of resection, tumor grade, and tumor histology.[1] In the current cohort, while we also did not find any between-group differences in age, sex, tumor size, relative posterior fossa tumor location, extent of resection, and ETV Success Scores [27], we did find differences in tumor grade and histology. In addition, we found that preoperative ventricular size (hydrocephalus severity) was statistically different between the VPS and ETV groups, wherein patients treated with VPS had relatively smaller ventricles than those treated with ETV. Future studies rigorously testing additional baseline characteristics – including clinical and radiographic factors not examined here – may help elucidate pre-operative variables which can predict differential success between the two procedures.

Independent of oncologic treatment and follow-up, the long-term management of hydrocephalus represents an additional burden for patients, their families, and the healthcare ecosystem.[38] We identified no differences between VPS and ETV in the mean number of hospital readmissions and number of CSF-diverting procedures after index CSF-diversion. However, the mean number of subsequent CT and MR scans performed following the index VPS was significantly higher than following ETV. It remains unclear the proportion of those images that yielded any clinical interventions. While future studies are required to elucidate the cost-effectiveness of ETV vs VPS in PFBT patients, it does appear

from this data that cost may also be taken into consideration when deciding between VPS and ETV, especially in regions with limited resource and barriers to healthcare access.

The findings of this study must be interpreted in the context of several limitations. This was a post-hoc analysis of multi-institutional data. Surgeon bias may have influenced which operation was offered to patients at any given center. The presence or degree of bias could not be accounted for in this analysis. We did not find any difference in ETV Success Score between VPS and ETV patients. However, there may exist radiographic factors present on pre-CSF-diversion studies which influenced ETV success – or surgeon-derived perception of likelihood of success – which were not measured. A dedicated radiomics study may help determine which patients are most likely to benefit from either procedure.

In conclusion, both ETV and VPS are safe and effective treatments for PFBT-related postoperative hydrocephalus, with similar overall success rates. Future studies may help elucidate which procedure is best suited to individual patients based upon preoperative clinical and radiographic variables.

## Abbreviations

CSF: cerebrospinal fluid; DCC: Data Coordinating Center; ETV: endoscopic third ventriculostomy; FOR: fronto-occipital horn ratio; HCRN: Hydrocephalus Clinical Research Network; PFBT: posterior fossa brain tumor; TTF: time-to-failure; VPS: ventriculoperitoneal shunt

## Statements & Declarations

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## **Competing Interests**

None of the sponsors participated in design and conduct of this study; collection, management, analysis, and interpretation of the data; or preparation, review, or approval of this manuscript. Its contents are solely the responsibility of the authors and do not necessarily represent the official view of the sponsors.

## **Author Contributions**

Michael C. Dewan, Abhaya V. Kulkarni, John C. Wellons, John R.W. Kestle contributed to study conception and design. Acquisition of data was completed by Jay Riva-Cambrin, Michael Cools, Albert M. Isaacs, Ryan Jafrani, Jonathan Pindrik, Eric M. Jackson, Brendan Judy, Elena Kurudza, Michael M. McDowell, Todd C. Hankinson, Susan Staulcup, Jason Hauptman, Koko Hall, Mandeep Tamber, Alex Cheong, Nebras M. Warsi, Benjamin Saccomano, Brandon G. Rocque, Rita Snyder. Analysis and interpretation of data was done by Hailey Jensen, Richard Holubkov, Ron Reeder, Michael C. Dewan, Abhaya V. Kulkarni. The first draft of the manuscript was written by Michael C. Dewan.

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## **Data Availability**

The data is currently only available to members of the Hydrocephalus Clinical Research Network. There is no public use dataset available.

## **Ethics Approval**



This study was performed in line with the principles of the Declaration of Helsinki. Approval for the study was granted by the IRB/REB at each participating institution. The study has a waiver of patient consent.

## References

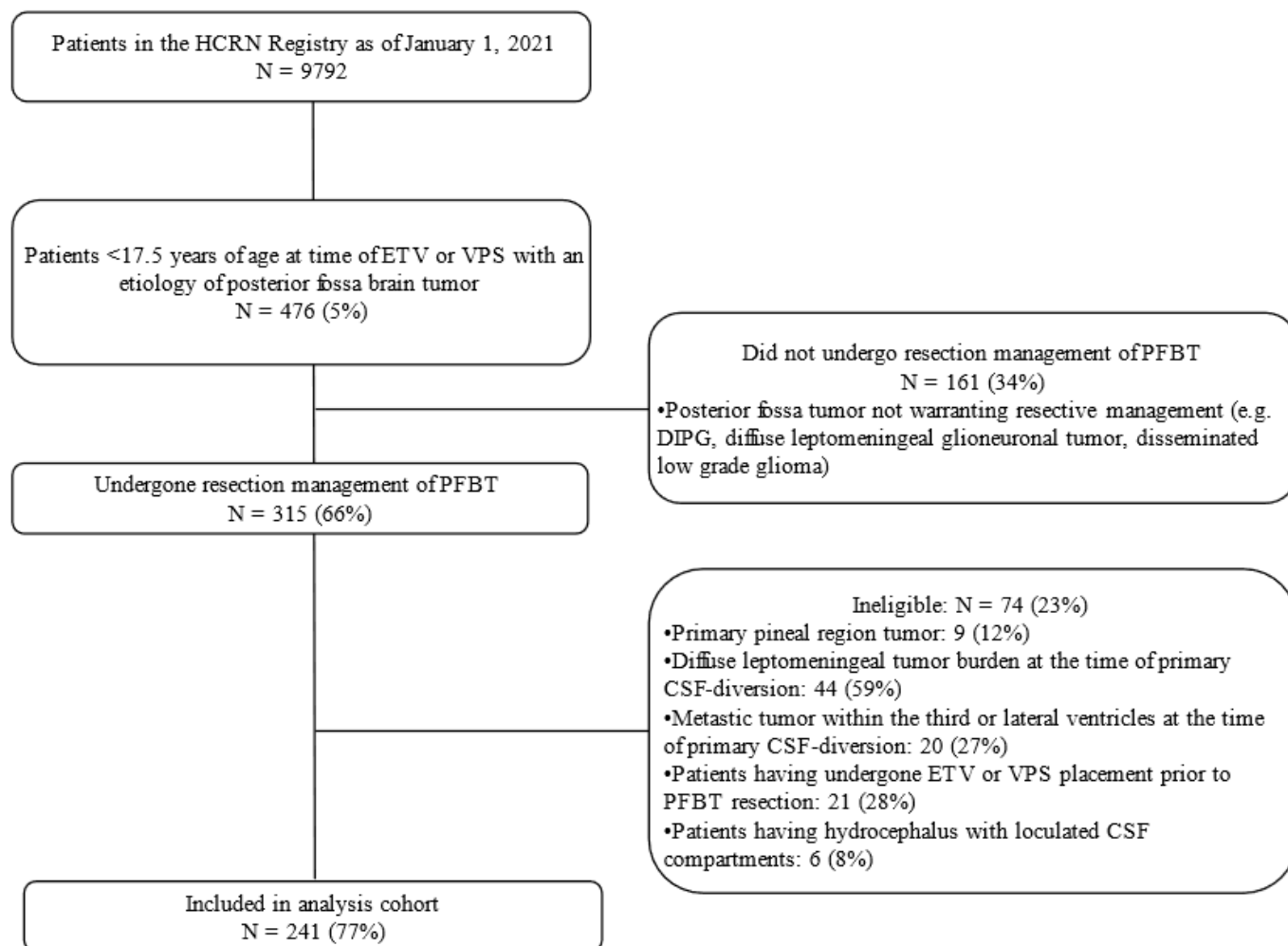
1. Dewan MC, Lim J, Shannon CN, Wellons JC 3rd (2007) The durability of endoscopic third ventriculostomy and ventriculoperitoneal shunts in children with hydrocephalus following posterior fossa tumor resection: a systematic review and time-to-failure analysis. *J Neurosurg Pediatr* 19(5):578–584. 10.3171/2017.1.PEDS16536
2. Lin CT, Riva-Cambrin JK (2015) Management of posterior fossa tumors and hydrocephalus in children: a review. *Childs Nerv Syst* 31(10):1781–1789. 10.1007/s00381-015-2781-8
3. Dias MS, Albright AL (1989) Management of hydrocephalus complicating childhood posterior fossa tumors. *Pediatr Neurosci*, vol. 15, no. 6, pp. 283-9; discussion 290, 1989, doi: 10.1159/000120484
4. Raimondi AJ, Tomita T (1981) Hydrocephalus and infratentorial tumors. Incidence, clinical picture, and treatment. *J Neurosurg*, vol. 55, no. 2, pp. 174 – 82, doi: 10.3171/jns.1981.55.2.0174
5. Schneider C, Ramaswamy V, Kulkarni AV, Rutka JT, Remke M, Tabori U et al (2015) Clinical implications of medulloblastoma subgroups: incidence of CSF diversion surgery. *J Neurosurg Pediatr* 15(3):236–242. 10.3171/2014.9.PEDS14280
6. Tamburrini G, Pettorini BL, Massimi L, Caldarelli M, Di Rocco C (2008) Endoscopic third ventriculostomy: the best option in the treatment of persistent hydrocephalus after posterior cranial fossa tumour removal? *Childs Nerv Syst* 24(12):1405–1412. 10.1007/s00381-008-0699-0
7. Bognár L, Borgulya G, Benke P, Madarassy G (2003) Analysis of CSF shunting procedure requirement in children with posterior fossa tumors. *Childs Nerv Syst*, vol. 19, no. 5–6, pp. 332-6, Available: <https://www.ncbi.nlm.nih.gov/pubmed/12709823>
8. Foreman P, Samuel McClugage, Naftel r, Griessenauer R, Ditty CJ, Agee BJ BS, et al (2013) Validation and modification of a predictive model of postresection hydrocephalus in pediatric patients with posterior fossa tumors. *J Neurosurg Pediatr* 12(3):220–226. 10.3171/2013.5.PEDS1371
9. Cochrane DD, Kestle JR (2003) The influence of surgical operative experience on the duration of first ventriculoperitoneal shunt function and infection. *Pediatr Neurosurg* 38(6):295–301. 10.1159/000070413
10. Morelli D, Pirotte B, Lubansu A, Detemmerman D, Aeby A, Fricx C (2005) Persistent hydrocephalus after early surgical management of posterior fossa tumors in children: is routine preoperative endoscopic third ventriculostomy justified? *J Neurosurg* 103(3):247–252
11. Sainte-Rose C, Cinalli G, Roux FE, Maixner R, Chumas PD, Mansour M et al (2001) Management of hydrocephalus in pediatric patients with posterior fossa tumors: the role of endoscopic third ventriculostomy. *J Neurosurg* 95(5):791–797. 10.3171/jns.2001.95.5.0791
12. Takahashi Y (2006) Long-term outcome and neurologic development after endoscopic third ventriculostomy versus shunting during infancy. *Childs Nerv Syst* 22:1591–1602. 10.1007/s00381-

13. Taylor WA, Todd NV, Leighton SE (1992) CSF drainage in patients with posterior fossa tumours. *Acta Neurochir (Wien)* 117:1–2. 10.1007/BF01400627
14. Zhang N, Zhang D, Sun J, Sun H, Ge M (2022) Contribution of tumor characteristics and surgery-related factors to symptomatic hydrocephalus after posterior fossa tumor resection: a single-institution experience. *J Neurosurg Pediatr* 31(2):99–108. 10.3171/2022.10.PEDS22281
15. El-Ghandour NM (2011) Endoscopic third ventriculostomy versus ventriculoperitoneal shunt in the treatment of obstructive hydrocephalus due to posterior fossa tumors in children. *Childs Nerv Syst* 27(1):117–126. 10.1007/s00381-010-1263-2
16. Azab W, Al-Sheikh T, Yahia A (2013) Preoperative endoscopic third ventriculostomy in children with posterior fossa tumors: an institution experience. *Turk Neurosurg*, vol. 23, no. 3, pp. 359 – 65, 2013, doi: 10.5137/1019-5149.JTN.7035-12.1
17. Bhatia R, Tahir M, Chandler CL (2009) The management of hydrocephalus in children with posterior fossa tumours: the role of pre-resectional endoscopic third ventriculostomy. *Pediatr Neurosurg*, vol. 45, no. 3, pp. 186 – 91, 2009, doi: 10.1159/000222668
18. El Beltagy MA, Kamal HM, Taha H, Awad M, El Khateeb N (2010) Endoscopic third ventriculostomy before tumor surgery in children with posterior fossa tumors, CCHE experience. *Childs Nerv Syst* 26(12):1699–1704. 10.1007/s00381-010-1180-4
19. Ray P, Jallo GI, Kim RY, Kim BS, Wilson S, Kothbauer K et al (2005) Endoscopic third ventriculostomy for tumor-related hydrocephalus in a pediatric population. *Neurosurg Focus* 19(6):E8. 10.3171/foc.2005.19.6.9
20. Roujeau T et al "Shall we treat hydrocephalus associated to brain stem glioma in children. *Childs Nerv Syst*, vol. 27, no. 10, pp.1735–9, doi: 10.1007/s00381-011-1538-2
21. Ruggiero C, Cinalli G, Spennato P, Aliberti F, Cianciulli E, Trischitta V et al (2004) Endoscopic third ventriculostomy in the treatment of hydrocephalus in posterior fossa tumors in children. *Childs Nerv Syst* 20:11–12. 10.1007/s00381-004-0938-y
22. Salah M, Elhuseny AY, Youssef EM (2022) Endoscopic third ventriculostomy for the management of hydrocephalus secondary to posterior fossa tumors: A retrospective study. *Surg Neurol Int* 13:65. 10.25259/SNI\_971\_2021
23. Harris P, Taylor R, Minor B, Elliott V, Fernandez M, O'Neal L et al (2019) The REDCap consortium: Building an international community of software platform partners. *J Biomed Inform* 95:103208. 10.1016/j.jbi.2019.103208
24. Riva-Cambrin J, Detsky AS, Lamberti-Pasculli M, Sargent MA, Armstrong D, Moineddin R et al (2009) Predicting postresection hydrocephalus in pediatric patients with posterior fossa tumors: Clinical article. *J Neurosurgery: Pediatr* PED 3(5):378–385. 10.3171/2009.1.PEDS08298
25. Kulkarni AV, Riva-Cambrin J, Butler J, Browd SR, Drake JM, Holubkov R et al (2013) Outcomes of CSF shunting in children: comparison of Hydrocephalus Clinical Research Network cohort with historical controls: clinical article," (in eng). *J Neurosurg Pediatr* 12(4):334–338. 10.3171/2013.7.Peds12637

26. Kulkarni AV, Drake JM, Kestle JR, Mallucci CL, Sgouros S, Constantini S et al (2010) Endoscopic third ventriculostomy vs cerebrospinal fluid shunt in the treatment of hydrocephalus in children: a propensity score-adjusted analysis. *Neurosurgery*, vol. 67, no. 3, pp. 588 – 93, doi: 10.1227/01.NEU.0000373199.79462.21
27. Kulkarni AV, Drake JM, Kestle JR, Mallucci CL, Sgouros S, Constantini S (2009) Endoscopic Third Ventriculostomy in the Treatment of Childhood Hydrocephalus. *J Pediatr* 155(2):254–259. <https://doi.org/10.1016/j.jpeds.2009.02.048>. e1, doi
28. Roujeau T, Di Rocco F, Dufour C, Bourdeaut F, Puget S, Rose CS et al (2021) The 2021 WHO Classification of Tumors of the Central Nervous System: a summary," *Neuro-Oncology*, vol. 23, no. 8, pp. 1231–1251, 2021, doi: 10.1093/neuonc/noab106
29. Kann BH, Park HS, Lester-Coll NH, Yeboa DN, Benitez V, Khan AJ et al (2016) Postoperative Radiotherapy Patterns of Care and Survival Implications for Medulloblastoma in Young Children. *JAMA Oncol* 2(12):1574–1581. 10.1001/jamaoncol.2016.2547
30. Chin AL, Moding EJ, Donaldson SS, Gibbs IC, Soltys SG, Hiniker SM et al (2018) Survival impact of postoperative radiotherapy timing in pediatric and adolescent medulloblastoma. *Neuro Oncol* 20(8):1133–1141. 10.1093/neuonc/noy001
31. Zeltzer PM, Boyett JM, Finlay JL, Albright AL, Rorke LB, Milstein JM et al (1999) Metastasis stage, adjuvant treatment, and residual tumor are prognostic factors for medulloblastoma in children: conclusions from the Children's Cancer Group 921 randomized phase III study. *J Clin Oncol* 17(3):832–845. 10.1200/jco.1999.17.3.832
32. Bailey CC, Gnekow A, Wellek S, Jones M, Round C, Brown J et al (1995) Prospective randomised trial of chemotherapy given before radiotherapy in childhood medulloblastoma. International Society of Paediatric Oncology (SIOP) and the (German) Society of Paediatric Oncology (GPO): SIOP II. *Med Pediatr Oncol* 25(3):166–178. 10.1002/mpo.2950250303
33. Kortmann RD, Köhl J, Timmermann B, Mittler U, Urban C, Budach V et al (2000) Postoperative neoadjuvant chemotherapy before radiotherapy as compared to immediate radiotherapy followed by maintenance chemotherapy in the treatment of medulloblastoma in childhood: results of the German prospective randomized trial HIT '91. *Int J Radiat Oncol Biol Phys* 46(2):269–279. 10.1016/s0360-3016(99)00369-7
34. Khan RB, Patay Z, Klimo P, Huang J, Kumar R, Boop FA et al (2021) Clinical features, neurologic recovery, and risk factors of postoperative posterior fossa syndrome and delayed recovery: a prospective study. *Neuro Oncol* 23(9):1586–1596. 10.1093/neuonc/noab030
35. Leary SES, Packer RJ, Li Y, Billups CA, Smith KS, Jaju A et al (2021) Efficacy of Carboplatin and Isotretinoin in Children With High-risk Medulloblastoma: A Randomized Clinical Trial From the Children's Oncology Group. *JAMA Oncol* 7(9):1313–1321. 10.1001/jamaoncol.2021.2224
36. Due-Tønnessen BJ, Helseth E (2007) Management of hydrocephalus in children with posterior fossa tumors: role of tumor surgery. *Pediatr Neurosurg*, vol. 43, no. 2, pp. 92 – 6, 2007, doi: 10.1159/000098379

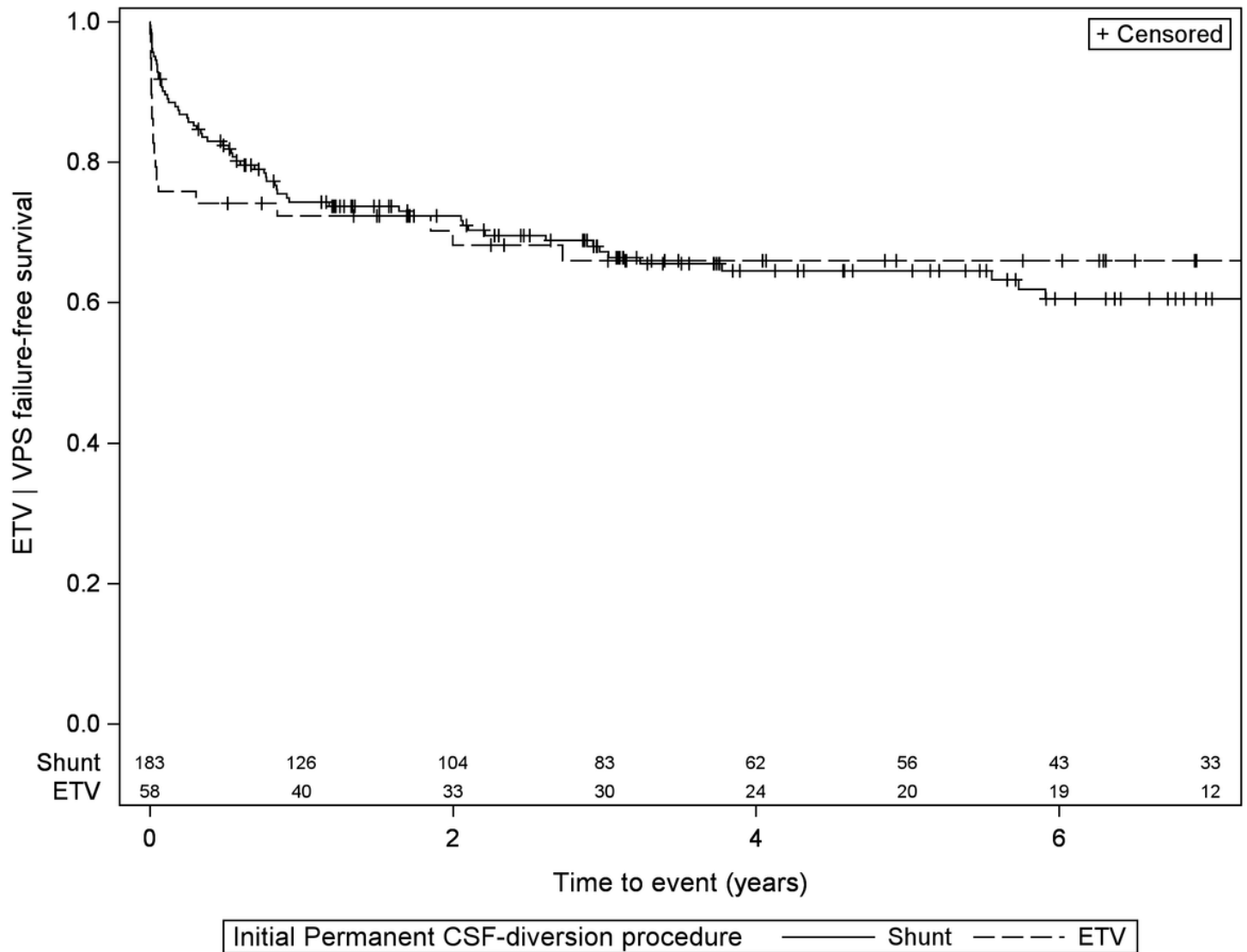
37. Kumar V, Phipps K, Harkness W, Hayward RD (1996) Ventriculo-peritoneal shunt requirement in children with posterior fossa tumours: an 11-year audit. Br J Neurosurg 10(5):467–470. 10.1080/02688699647096
38. Simon TD, Riva-Cambrin J, Srivastava R, Bratton SL, Dean JM, Kestle JR et al (2008) Hospital care for children with hydrocephalus in the United States: utilization, charges, comorbidities, and deaths. J Neurosurg Pediatr 1(2):131–137. 10.3171/PED/2008/1/2/131

## Figures



**Figure 1**

CONSORT diagram (Screening population)



**Figure 2**

Kaplan-Meier Analyses of VPS or ETV failure-free survival

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