










Evaluation of the ETV success score to improve decision making on the management of hydrocephalus secondary to pediatric posterior fossa tumors: A feasibility study

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Introduction: Hydrocephalus is frequently seen in children with posterior fossa tumors (PFT), and endoscopic third ventriculostomy (ETV) prior to tumor resection can improve surgical conditions by treating the hydrocephalus. Moreover, a scoring system predicting the success of ETV could aid in decision-making for this procedure. This study aims to evaluate the efficacy of ETV in the treatment of hydrocephalus related to PFT and to evaluate the accuracy of the ETV success score in predicting ETV success.

Methods: Patients under 18 years of age who underwent ETV before PFT resection between 1996 and 2021 were included in a retrospective study. The ETV success score was retrospectively obtained for all patients, and its predictive capacity was compared to the actual success observed.

Results: Of the 59 surgical cases, a global success rate of 62.7% was observed in the first 6 months following ETV. This rate dropped to 50.8% for those patients reassessed one year after surgery. There was no correlation between the success rate and the histological grade of the tumor or the age of the patient. The ETV success score presented acceptable accuracy at both time points (AUC = 0.671 at 6 months, AUC = 0.649 at one year).

Conclusion: ETV proved to be a safe procedure, capable of treating hydrocephalus in patients with PFT, and the ETV success score is useful for indicating probable success of the endoscopic procedure.

Keywords: hydrocephalus, posterior fossa tumors, endoscopic third ventriculostomy, neuroendoscopy

INTRODUCTION

Posterior fossa tumors (PFT) are prevalent in the pediatric population, especially in patients less than 2 years old. Patients with PFT often present with hydrocephalus due to obstruction of cerebrospinal fluid pathways of caudal egress, including the aqueduct of Sylvius as well as the median and lateral outlets of the fourth ventricle, the Magendie and Luschka foramina, respectively.(1, 2, 3, 4, 5, 6) Overall, hydrocephalus is present in about 80% of all PFT cases.(7) If tumor resection is the first choice of treatment, it is reported that the persistence of hydrocephalus occurs in 16%–33% of cases.(2, 5, 8, 9, 10, 11)

Endoscopic third ventriculostomy (ETV) is a common treatment for hydrocephalus, allowing for reestablishment of the cerebrospinal fluid pathway with no need of hardware and creating better conditions to perform the main

operation of PFT resection.(12, 13, 14, 15) Herein, several studies have advocated this management instead of insertion of a shunt device, external ventricular drainage, or tumor resection alone.(16) However, there is no definitive evidence that ETV is a safe and effective mediator of pre-PFT hydrocephalus, and discrepancies were found in the literature.(4)

The ETV success score (ETVSS) is a validated tool that predicts the success of the procedure for all etiologies of hydrocephalus in the first 6–12 months following ETV.(17, 18) Our goal in this study was to assess the ability of the ETVSS to predict the success of ETV particularly in the setting of PFT, demonstrating its possible utility in medical decision-making for patients with these tumors.



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MATERIALS AND METHODS

Eligibility criteria

In the present study, following the approval by the local ethical committee and reinforced by Brazil government site, a protocol number was generated (#6.283.495), individuals <18 years old who underwent ETV before microsurgical resection of PFT and, therefore, no used the shunt device as the first choice of hydrocephalus's treatment, from 1996 to 2021 were selected for inclusion in this study. All patients were treated at the same pediatric neurosurgery center and operated on by the same team of pediatric neurosurgeons. The STROBE guidelines were used to report this study (19).

Patients with tumors of the pineal region or tectum of mesencephalon and patients with tumors exclusively in the supratentorial compartment were excluded from the analysis in order to assess the effectiveness of ETV on hydrocephalus due to tumors placed on structures exclusively of posterior fossa. Additionally, patients without at least 6 months of follow-up were not considered for this study.

Data collection

Between February and April 2023, the data available in the electronic records of hospitals and private clinics were collected. A databank of all patients operated on between 1996 and 2021 was provided by the neurosurgery team.

In the present study, the following variables were reported: (1) demographic features; (2) anatomic structure affected by the tumor; (3) histology of the tumor; (4) outcome. In addition, all ETVSS were calculated by considering patient age, PFT as etiology of the hydrocephalus, and previous shunt placement. For all patients in the study, the only variable with the potential to impact on the result of the ETVSS was the age of the patients because they received the same score according to ETVSS regarding the etiology of hydrocephalus (PFT) and the absence of shunt device at the beginning of the treatment.

When evaluating the effectiveness of ETV, success is defined as the remission of symptoms related to intracranial hypertension. Failure occurs in the case of liquoric leakage, or if symptoms such as headache, vomiting, and impairment of consciousness do not improve. In this study, the actual success of each procedure was compared to the success predicted by the ETVSS at time points of 6 months and one year after the procedure. Therefore, the ETVSS was retrospectively applied to each patient of the study.

Given that this study covered a large range of time in which some aspects of the surgical techniques have changed

(such as using peel-away sheathes for ventricular puncture), the potential impact of the learning curve was also analyzed.

Surgical technique

The patient was placed in the supine position, with the head neutrally positioned over the horseshoe. The entry point was chosen based on imaging examination (CT scan or MRI) and the predicted difficulty of the neuroendoscopy was determined based on the cortical mantle width, size of the Monroe foramen, and relationship between the tuber cinereum and basilar tip. Usually, entry was obtained through Kocher's point, giving access to the frontal horn of the lateral ventricle.(Figure 1)

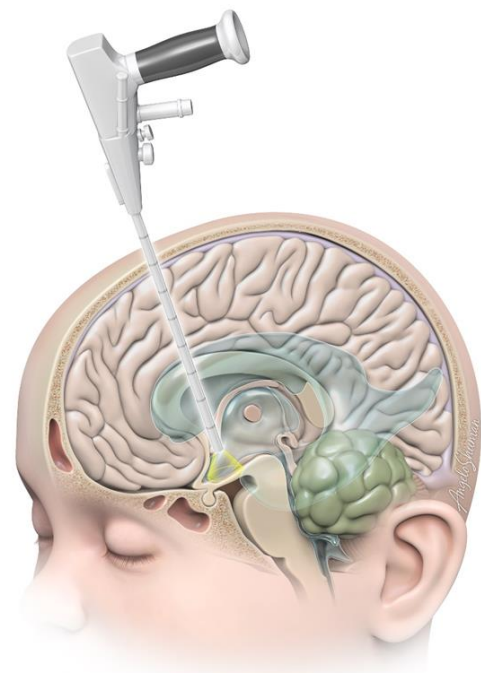


Figure 1 – Illustration of neuroendoscope positioning on the floor of the third ventricle, before fenestration of the tuber cinereum. The posterior fossa tumor exerts a mass effect on the posterior fossa, increasing the risk of upper herniation due to imbalance between supra and infratentorial pressure.

After shaving hair from the area, an arch incision with anterior concavity was made behind the burr hole in order to minimize the risk of liquoric leakage and infection. The burr hole was made with a drill, and the dura was coagulated and opened with a number 11 scalpel. This step was followed by a ventricular puncture using a peel-away sheath, and the leakage of liquor was avoided to minimize risk of upper herniation of the diencephalon. The neuroendoscope was then inserted into the ventricle. After recognition of ventricular landmarks was established, the tuber cinereum and the Liliequist membrane were fenestrated and the ETV was completed. Finally, the neuroendoscope was withdrawn

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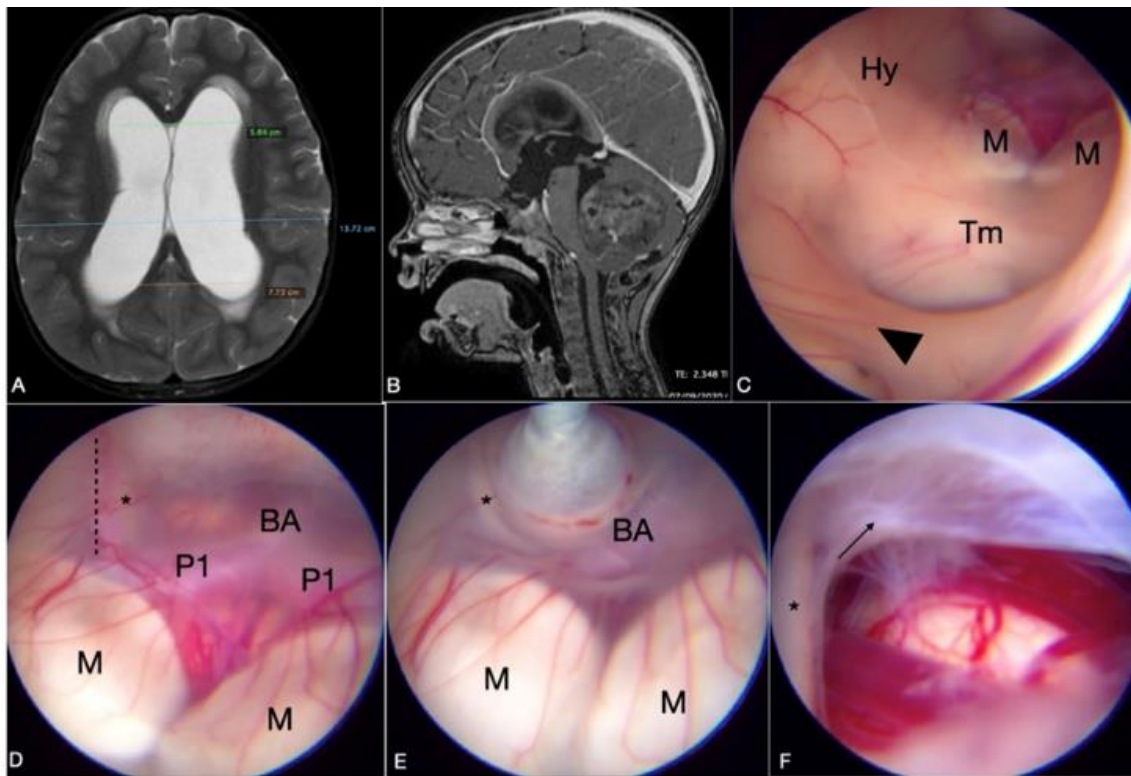


Figure 2 – The MRI as well as the neuroendoscopy of a 4 years old boy with medulloblastoma occupying the fourth ventricle was displayed here. Ventriculomegaly (Evan's Index = 0.42 / Frontoccipital Horn ratio = 0.49) and transependymal exudation were seen in an axial MRI T2 (A). Ballooning of third ventricle on sagittal MRI post gadolinium (B); A translucent Tuber cinereum was showed on C and D and the ostomy of tuber cinereum and Lilliequist membrane (Single black thin arrow) by Forgarty 4-F catheter were depicted on E and F, respectively. Left oculomotor nerve (*); Basilar artery (BA); Posterior artery (P1); Posterior communicating artery (dot line); Tegmentum of midbrain (Tm); Mammillary bodies (M); Interthalamic adhesion (Arrow head) Hypothalamus (Hy).

from the ventricle and the burr hole was blocked with geof foam and bone fragments embedded with fibrin glue. The skin was closed with separated stiches. (Figures 1 and 2)

Statistical analysis

The software SPSS version 20 (IBM, Armonk, NY, USA) and Microsoft Excel 2010 (Microsoft Corporation, Redmond, WA, USA) were used for data analysis. Differences were considered significant at a P value < 0.05.

Furthermore, a receiver operating characteristic (ROC) curve was designed in order to test the ability of the ETVSS to discriminate the success from the failure of the technique in two timepoints; 6-month and 12-months. Traditionally, an ETVSS higher than 0.7 is considered enough as a clinical prediction rule. Herein, we identified the cutoff point of the ETVSS regarding the improved prediction of the actual success of

RESULTS

The study included 59 children who underwent ETV prior to PFT resection. The sample set was composed of 19 males (65.5%, $p = 0.926$) and the mean age was 7.1 years (SD = 4.7).

The majority of patients in the sample were diagnosed with high-grade tumors (33 patients, 56%). This included 16 patients with medulloblastoma, 9 with diffuse glioma of the pons, 7 with grade III ependymoma, and 1 with a teratoma. Low-grade tumors in this study included 16 pilocytic astrocytomas, 7 grade II ependymomas, 1 ganglioglioma of the fourth ventricle, 1 hemangioblastoma of the cerebellum, and 1 grade II glioma of the fourth ventricle. Overall, the patients with low-grade tumors had a higher success rate of ETV (56.7%) than those with high-grade tumors (43.3%, $p = 0.047$).

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Anatomically, the tumors were distributed solely on the cerebellum parenchyma in 26 patients (44.1%), invaded the fourth ventricle floor in 21 patients (35.6%), and were exclusive to the brainstem in 5 patients (20.3%). This distribution did not have a statistically significant impact on the ETV success rate ($p = 0.638$).

Concerning the timeframe of this study and its impact on ETV success, the comparison of effectiveness between the periods no show significance ($p=0.409$). The impact of age on the success of ETV is presented in Table 1.

Table 1- ETV success rate stratified by patient age.

	N	SUCCESS (%)	P-VALUE
<2 YEARS	12	5 (13.5)	0.084
>2–10 YEARS	34	21 (56.8)	
>10 YEARS	13	11 (29.7)	

Overall, no fatalities were observed during the neuroendoscopic procedure. One patient with hydrocephalus secondary to diffuse glioma of the pons presented with intraoperative hemorrhage after ostomy of the tuber cinereum, leading to a failure of ETV. After shunt placement, the patient was discharged with no additional deficits.

The overall success rate of ETV was 62.7% at 6-month follow-up but dropped to 50.8% by one year after the ETV. Receiver operating characteristic (ROC) curves representing the ability of the ETSS to predict this rate at the two time points are displayed in the Figures 3 and 4.

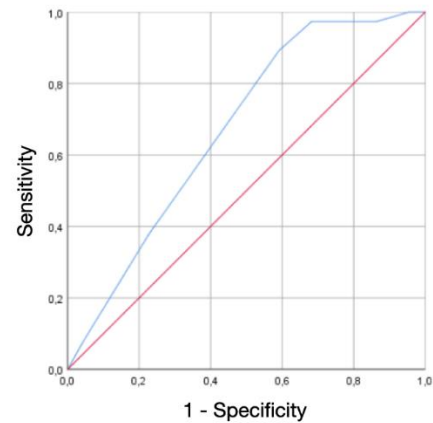


Figure 3 – The receiver operating characteristic (ROC) curve displays the accuracy of the endoscopic third ventriculostomy scoring system (ETVSS) in predicting ETV success during the six first months after the procedure, with an area under the curve of 0.671 ($p = 0.029$).

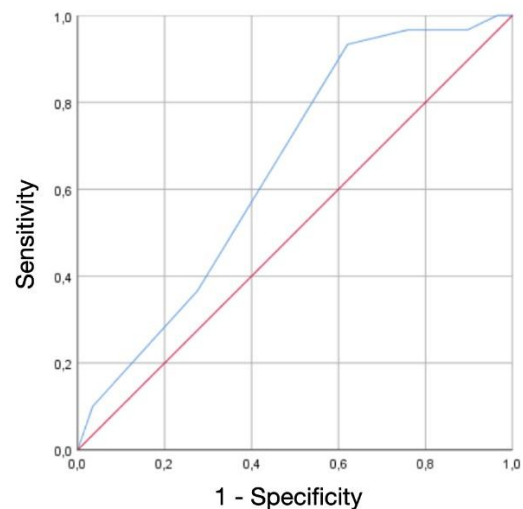


Figure 4 – The ROC curve demonstrating accuracy of the ETSS one year after the ETV procedure, with an area under the curve of 0.649 ($p = 0.050$).

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DISCUSSION

In this single-institutional experience, ETV has been adopted as the main option to manage hydrocephalus prior to PFT resection. This allows providers to temporize and plan a more effective surgery with no intracranial hypertension, warranting less bleeding, optimizing the tumor resection to achieve better oncologic results, and preventing hydrocephalus after tumor resection. Overall, ETV was successful in approximately six out of every ten patients. However, a year after surgery, the success persisted in only about half of all cases. Similarly, Srinivasan et al. (20) designed a comparative study of ETV and non-ETV groups in this context and found 32% shunt dependence in the ETV group and 22% shunt dependence in the non-ETV group. There is a general paucity of evidence in the literature regarding the neuroendoscopic management of hydrocephalus specifically in the setting of PFT; the findings of this study indicate that ETV before tumor resection is beneficial, particularly when ETVSS is applied in medical decision-making (Table 2).

Table 2- Failure rates of ETV on the management of hydrocephalus due to pediatric posterior fossa tumors

STUDY	YEAR	N	FAILURE RATE
SAINT-ROSE ET AL. (15)	2001	67	6%
RUGGIERO ET AL. (16)	2004	20	15%
BHATIA ET AL. (13)	2009	37	13.5%
EL BELTAGY ET AL. (14)	2010	40	37.5%
EL-GHANDOUR (27)	2011	32	6.2%
AZAB ET AL. (12)	2013	17	11.8%
SRINIVASAN ET AL. (20)	2020	31	21%
FURTADO ET AL.	2023	59	37.3%

Failure of ETV can arise due to technical problems during the procedure, postoperative issues, complications during tumor removal surgery, and changes in cerebrospinal fluid (CSF) absorption during oncologic treatment. Intraoperatively, failure is linked to bleeding, blockage of the ostomy, and the Lilliequist membrane not being

fenestrated.(21) Infections of the central nervous system during the two postoperative periods (ETV and tumor resection) can impact CSF absorption. Less frequently, fragments of tissue generated during tumor removal can block the ostomy in the tuber cinereum, which is known as the “snow globe effect.” (22)

The pediatric neurosurgeon should keep in mind that endoscopic procedures have risks. The more dangerous consequences of this operation include intraoperative tumor bleeding and upper herniation of the diencephalon due to imbalance of pressure among the supra and infratentorial compartments.(23) For this reason, ETV should be performed only by experienced neurosurgeons, with precautions taken to avoid leaving excess CSF during the ventricle puncture and throughout the endoscopic navigation.(18, 24) The present study reported no upward herniation, and the only intraoperative bleeding was handled by irrigation. To our knowledge, the shunt option has more associated risks. These are often related to hardware (infections and malfunctioning), with other issues being potential peritoneal dissemination of the tumor, (25) tumor bleeding, and upper herniation due to hyper drainage. Recently, Dewan et al. (8) performed a systematic review and metaanalysis comparing patients that underwent either ETV or shunt placement to treat hydrocephalus secondary to PFT, and found that 17% of patients in the ETV group experienced complications, versus 31% of shunted patients ($p = 0.012$). Adverse events included infections, shunt malposition, extra-axial hemorrhages, and cranial nerve palsies.

In order to estimate the risk of developing definitive hydrocephalus even after tumor removal, Riva-Cambrin et al. (26) validated a scoring system and found that age of less than 2 years at diagnosis of PFT, presence of papilledema, high degree of hydrocephalus by ventriculomegaly on imaging, presence of cerebral metastases, and histopathological type (medulloblastoma, ependymoma, and dorsally exophytic brainstem glioma) were indicative of a higher risk. This scoring system has the capability to guide the medical decision-making process and estimate hydrocephalus risk. However, other concerns linked to tumor removal with intracranial hypertension or risks of shunt complications were not taken into consideration. Despite the fact that the Canadian Preoperative Prediction Rule for Hydrocephalus indicates an age of less than 2 years as the main predictor for developing definitive hydrocephalus after tumor resection, in the present study, we did not see a statistically significant difference from other age groups ($p = 0.084$). Moreover, there was no difference in hydrocephalus risk between tumors with different histology ($p = 0.047$). Here, the ETVSS displayed more accuracy in the context of hydrocephalus linked to PFT if the neurosurgeon

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intended to evaluate the chance of success of ETV as a modality of treatment.

As the main advantage of ETV is to control hydrocephalus with no need of hardware and no risk of peritoneal dissemination, the utility of ETVSS in predicting the actual success rate would be crucial for decision-making.

The main limitation of the current study is the retrospective nature of the data collection. The ability to control variables is potentially damaged, especially considering the long term over which some patients have been treated. Conversely, the data come from a single institution and are aligned to the learning curve of the main neurosurgeon, who operated on the majority of the cases. This represents an advantage in evaluating the outcome by decreasing the bias of different surgeons using multiple techniques.

CONCLUSION

In summary, before attempting the management of hydrocephalus secondary to PFT, the pediatric neurosurgeon should consider the pros and cons. The first option of removing the tumor with no prior intervention could be the best option to treat both conditions simultaneously. However, operating under hydrocephalic conditions can risk increased bleeding due to intracranial hypertension.

Overall, ETV can be performed safely by experienced hands, and controlling hydrocephalus makes the tumor resection an elective procedure that is more feasible and has a higher chance of success. Moreover, the ETVSS plays a worthwhile role in decision-making and has an acceptable prediction accuracy.

Therefore, even though there are risks inherent in ETV, this option of treatment leads to fewer complications than shunt placement and offers better surgical conditions than resecting the tumor without prior intervention. However, prospective and controlled studies would enhance this evidence.

ACKNOWLEDGMENTS

DISCLOSURES

Ethical approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Hospital Vila da Serra Ethics Committee, CAAE: 71105923.3.0000.5134

Consent to participate

The patients gave consent to use their information and images for research purposes. *Consent for publication*

The patient gave consent to use his information and images for publication.

Conflict of interest

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

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CONTRIBUTIONS

-Leopoldo Mandic Ferreira Furtado: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing

-José Aloysio da Costa Val Filho: Methodology, Supervision, Validation

-Aieska Kellen Dantas dos Santos: Investigation, Methodology

-Jaime Xavier de Oliveira Neto: Formal Analysis, Methodology, Visualization

-Márcio Júnior Pena: Data curation, Methodology, Writing – original draft

-Cristiano Frattesi Bernardes: Data curation, Methodology, Writing – original draft

-Mariana Gonçalves Lima de Paula: Data curation, Methodology, Writing – original draft

-Anne Ribeiro Magalhães: Conceptualization, Data curation, Formal Analysis, Funding acquisition, Investigation, Methodology

-Alice Izabel Costa Silva: Conceptualization, Data curation, Funding acquisition, Investigation, Methodology, Data curation, Methodology, Writing – original draft

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