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Original article

Analysis of Cerebrospinal Fluid Flowmetry in Evaluating the Efficiency of Endoscopic Third Ventriculostomy in Aqueductal Stenosis

Mohammed Hossam Eldien Abo Shahba[a]; Mohammed El-Gebaly Ahmed Alhady[a]; Hatem Mohammed El Samouly[a]; Islam Mohammed Elshwihi[b]

Department of Neurosurgery, Damietta Faculty of Medicine, Al-Azhar University, Egypt[a].

Department of Neurosurgery, Mansoura New General Hospital, Ministry of Health and Populations, Egypt[b].

Corresponding author: **Mohammed El-Gebaly Ahmed Alhady**
Email: m.gebali@domazhermedicine.edu.eg

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ABSTRACT

Background: Endoscopic third ventriculostomy (ETV) approach was gaining popularity over shunt placement in obstructive hydrocephalus. Postoperative ETV assessment and patients follow up remains a matter of controversy and challenge to ensure efficiency and patency of ventriculostomy.

Aim of the work: To assess whether cerebrospinal fluid (CSF) flow is restored after ETV and similarity to flow in normal aqueduct with patients clinical and ventricular size changes assessment.

Patients and Methods: From April 2016 to April 2019, 30 patients with hydrocephalus due to aqueductal stenosis (AS) were treated with ETV. They were followed up for ventriculostomy patency within the 1st, 6th and 9th month after surgery and compared to 22 persons as a control group of normal aqueductal flow with phase contrast magnetic resonance imaging (PC MRI).

Results: Twenty three (23) patients restored pulsatile bidirectional pattern of CSF flow across the ventriculostomy similar to that of aqueductal flow. While one patient had no flow during the 1st follow up and 6 patients showed initial pulsatile flow then developed flow disturbance during the 2nd follow up period. Absolute stroke volume values showed significant statistical difference between ETV and control groups (p value < 0.001). The value of 85 µl showed sensitivity and specificity of 84.3% and 81.7%, respectively as a cutoff value of ETV efficiency.

Conclusion: ETV is an efficient technique to restores the physiological pulsatile Cerebrospinal fluid flow. Absolute stroke volume was a good predictor of ETV efficiency.

Keywords: Endoscopic; Ventriculostomy; Aqueductal stenosis; Cerebrospinal; Flowmetry.

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INTRODUCTION

Intracranial dynamics driven by the circulation of cerebrospinal fluid (CSF) play a crucial role in healthy brain function. The disturbance of this dynamics reflects on the fluid environment of the cranium, which can lead to multiple complications such as hydrocephalus[1]. Owing to its characteristic anatomy, the cerebral aqueduct represents the commonest location of blockage along the cerebrospinal fluid pathway, and consequently, aqueductal stenosis is considered a common reason of obstructive hydrocephalus[2]. For this complex nature of hydrocephalus, it was defined as a disease associated with disturbances in the cerebro-spinal fluid dynamics[3]. The conventional treatment has been the implantation of ventricular shunt systems; but these systems have inherent tendency for adverse effects including malfunction and infection. The novel technological advancement in the arena of cranial endoscopy has led to a renewed attention in endoscopic third ventriculostomy as the best management for obstructive hydrocephalus[4]. Although third ventriculostomy has gained publicity as a cerebrospinal fluid shunt placement alternative in hydrocephalus owing to aqueductal stenosis, there is still some debate regarding the follow up imaging correlates of clinically successful ETV[5]. Ventriculostomy failure is considered an expected event throughout the follow up period. Although almost failures occur in early times, in a few days to weeks after the procedure, late failure may occur many months after and may present with sudden deterioration[6]. Therefore, patients who had successful third ventriculostomy should be followed up on an ongoing basis. Regular Clinical assessment was considered important in evaluating the efficiency of ventriculostomy inspite of some cases may firstly present with severe clinical consequences during the follow up[7].

A range of radiological parameters was evaluated, involving ventricular size alterations, flow void signal intensity, and flow patency utilizing dynamic MR studies. Also radionuclide cisternography was found to be precise for evaluating the patency of the ETV stoma [8]. ETV outcome prediction and follow up plans are still a matter of controversy and challenge. Planned follow up and monitoring have the most crucial important role in avoidance of sudden deterioration and expectations of ETV failures[9]. Cine phase contrast MRI was applied for assessing cranial and spinal cerebrospinal fluid flow in addition to analysis of pathologic cerebro-spinal fluid flow dynamics in communicating and obstructive hydrocephalus. It has been often suggested for assessing the patency of ETV and assessing the cerebrospinal fluid dynamics of flow[10].

AIM OF THE WORK

The aim of this study was to assess whether cerebrospinal fluid (CSF) flow is restored after ETV and similarity to flow in normal aqueduct with patients clinical and ventricular size changes assessment.

PATIENTS AND METHODS

From April 2016 to April 2019, 30 patients were treated with ETV. The *inclusion criteria* were: 1) Aqueductal stenosis (obstructive triventricular) hydrocephalus. 2) Patient age more than six months. *Exclusion criteria were*: 1) Obliterated or reduced prepontine cistern. 2) Thick third ventricular floor. 3) Neoplastic mass totally occupies the 3rd ventricle.

All patients' data were compared to 22 healthy persons as a control group of normal aqueductal flow with PCMRI.

The study was done according to the Ethical Committee, and informed written consent was obtained from all participants. The surgery and investigations were clearly explained. Pre-operative assessments of all patients were done through full clinical examination, ventricular size assessment with Evan's index, and conventional MRI. Surgical procedure was done with Lotta ventriculoscope connected to xenon cold light source and three chips digital camera. All patients were operated under general anesthesia in supine position with the head carefully fixed and flexed of 30 degrees. Appropriate scrubbing and draping was done. A curved skin incision centered over 12mm kocher burr-hole was done with a linear dural incision with cauterization of meningeal vessels at cortical point. Cannulation of ventricle and introducing the endoscope with exploration of intraventricular anatomy was done. After that, fenestration was performed in the most thin, avascular part of the tuber cinereum and widened by 3F Fogarty balloon catheter (Figure 1). If there is bleeding external ventricular drain is inserted. A detailed operative report was written and video documentation of the operation.

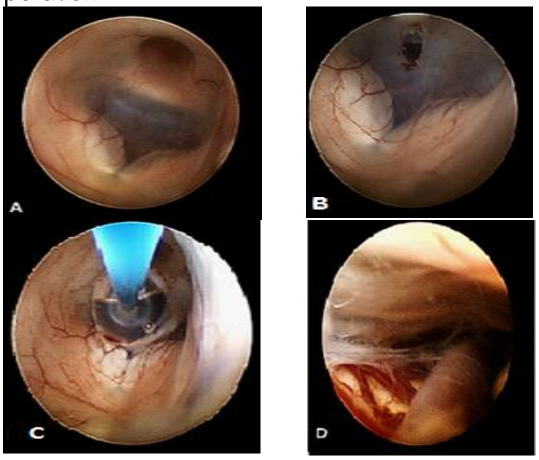

Figure (1): A) E, B,C) Fenestration of the thinnest part of the tuber cinerium with augmentation of the fenestration by fogarty balloon, D) Visualization of the prepontine cistern structures.

All patients were regularly followed up within the first, six and nine month's post-operative through neurological examination, ventricular size assessment, assessment of cerebrospinal fluid flow through the ventriculostomy in patients group and aqueduct of control group carried out on 1.5 T magnetic resonance scanner (Philips Ingenia, Best, Netherland). After the data acquisition, all images were transferred to quantitative (Q) flow analysis software. Qualitative and quantitative assessments were analyzed using mid-sagittal and axial phase images, respectively.

Statistical analysis was done by the Statistical Package for the Social Science (SPSS) for Windows (Standard version 12), (SPSS Inc, Chicago, USA). The normality of data was first tested with one-sample Kolmogorov-Smirnov test. Numerical variables presented as a mean and standard deviation, while categorical variables were showed as frequency and percent. Comparison between groups was done by Chi square or student (*t*) test for qualitative and quantitative data respectively. P value < 0.05 was significant.

RESULTS

From April 2016 to April 2019, thirty patients were treated with ETV. The age of this studied group was ranged from 1 to 45 years with a mean age 13.5 (± 11.9) years. The control group was ranged from 1 to 42 years with a mean age 15.2 (± 12.7) years. Among The studied group 18 (60%) patients were males and 12 (40%) patients were females. In the control group, there were 12 (54.6%) males and 10 (45.4%) females with insignificant difference (p = 0.694) between the study and control groups.

Primary AS was diagnosed in 17 (56.7%) patients, while secondary AS was diagnosed in 13 (43.3%) patients. The common presenting symptoms were headache in 14 (46.7%) patients, blurring of vision 9 (30%) patients, vomiting 8 (26.7%) patients, education problems 8 (26.7%) patients, somnolence and confusion 5 (16.7%) patients, diplopia 4 (13.3%) patients, seizures 4 (13.3%) patients, gait disturbance 2 (6.7%) patients and urinary incontinence 2 (6.7%) patients. Among the neurological signs, papilledema was found in 14 (46.7%) patients, eye gaze disorders 9 (30%) patients, shunt malfunction 9 (30%) patients, neurodevelop-mental delay 8 (26.7%) patients and cranial nerve palsies 3 (10%) patients.

ETV was done in all patients, ETV with shunt removal in 7 (23.3%) patients, ETV with endo-scopic biopsy in 4 (13.3%) patients and ETV with external ventricular drain (EVD) in one (3.3%) patient. The most common intraoperative complications recorded were forniceal injury in 3 (10%) patients and intraventricular hemorrhage in 1 (3.3%) patient.

During the whole clinical follow up period, 11 (36.7%) patients showed total clinical improvement, and 12 (40 %) patients showed partial clinical improvement with minor residual presenting symptoms or signs, while one (3.3%) patient showed no clinical improvement. Six (20%) patients showed initial clinical improvement and then developed clinical worsening during the secind follow up period (Figure 2).

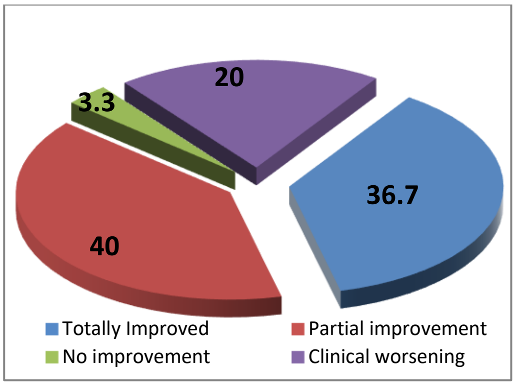

Figure (2): Postoperative clinical outcome among the studied group

The postoperative ventricular sizes were assessed for each patient and compared to the preoperative size revealed that 16 (53.3%) patients with evident ventricular size reduction (P < 0.001), while 8 (26.7%) patients showed no significant ventricular size reduction (P 0.297), with increased ventricular size in 6 (20%) patients (Table 1). The mean values were found to be as follow; absolute stroke volume (ASV) was 60 (±10) µl, peak diastolic velocity (PDV) equal 3.49 (±0.53) and peak systolic velocity (PSV) equal 3.31 (±1.43).

The scheduled flowmetric assessment for patients group was done in three consecutive intervals respectively with mean flowmetric values as shown in [Table 2]. The first follow up showed adequate qualitative (Figure 3) and quantitative data of flow (Table 2) through the ventriculostomy in 29 (96.7%) patients and one (3.3%) patient had inadequate flow. During the second follow up, 23(76.7%) patients had adequate flow while 6 (20%) patients showed inadequate flow. During the third follow up, all the 23 (76.7%) patients showed adequate flow. During follow up period, the patients group showed bidirectional craniocaudal and caudo-cranial pattern (Figure 4) of flow in 23 (76.7%) patients which is similar to CSF flow in control group, while a loss of this bidirectional flow pattern across the ventriculostomy was noticed during follow up in 7 (23.3%) patients.

Analysis of the absolute stroke volume values of the first follow up were done in relation to the ETV outcome at the end of the study using receiver operating characteristic (ROC) curve (Figure 5) revealed that 85µl value point had a sensitivity and specificity of 84.3% and 81.7% respectively as a cutoff point for ETV efficiency prediction

Table [1]: Ventricular size assessment among the studied group (SD; standard deviation). The flowmetric assessment was done for the control group.

Ventricular size changes	Reduction (n=16)	No reduction (n=8)	Increased (n=6)
Preoperative (mean ±SD)	39.4 % (±9.6)	50.2% (±10.8)	38.3% (±7.5)
Postoperative (mean ±SD)	34.3% (±9.9)	50.4% (±13.6)	48.7% (±5.4)
p-value	< 0.001*	0.297	< 0.001*

Table [2]: CSF flowmetric data of the patients group

Follow up	**Flow parameters**	**No. of patients**	**Adequate Flow Group**		**Inadequate Flow Group**		**P value**
			Flow values **(Mean ± SD)**	No.	Flow values **(Mean ± SD)**	No.	
1st Follow Up	SV(µl)	30	160 (±90)	29	6 (±0.0)	1	0.024*
	PDV(cm/sec)		4.34 (±1.43)		0.2 (±0.0)		0.002*
	PSV(cm/sec)		3.98 (±2.01)		0.22 (±0.0)		0.014*
2nd follow up	SV(µl)	29	185 (±86)	23	20 (±10)	6	<0.001*
	PDV(cm/sec)		4.37 (±1.62)		0.70 (±0.26)		<0.001*
	PSV(cm/sec)		4.53 (±1.5)		0.26 (±0.5)		<0.001*
3rd Follow Up	SV(µl)	23	179 (±81)	23	-	0	
	PDV(cm/sec)		4.37 (±1.09)		-		
	PSV(cm/sec)		3.95 (±2.2)		-		

SV; stroke volume, PDV; peak diastolic velocity, PSV; peak systolic velocity, µl; microliter, cm/sec; centimeter per second

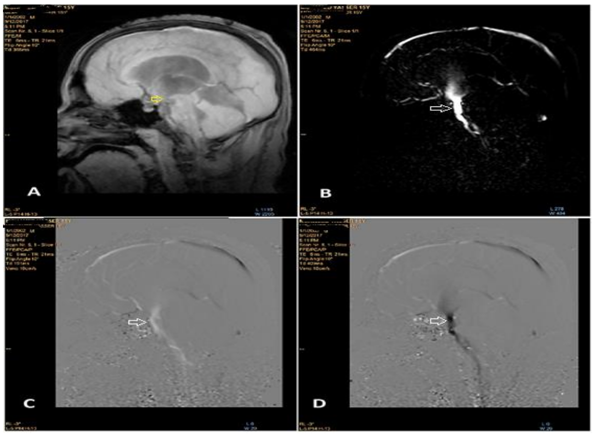

Figure (3): Cine MR images show the qualitative data of CSF flow**,** (A) Re-phased, (B) magnitude, (C-D) phase images showed bidirectional ETV CSF flow.

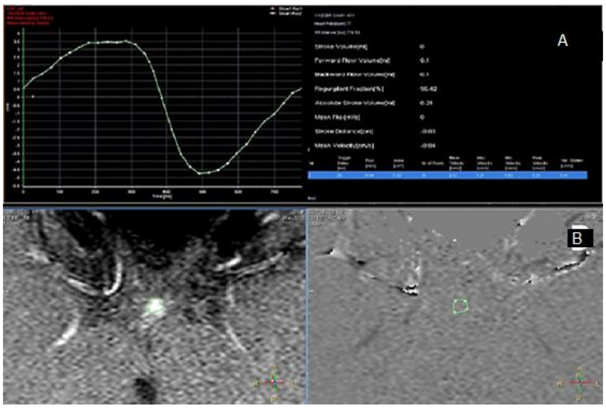

Figure (4): A) Bidirectional curve of flow show the quantitative data of flow, B) axial cine image shows the region of interest for ETV.

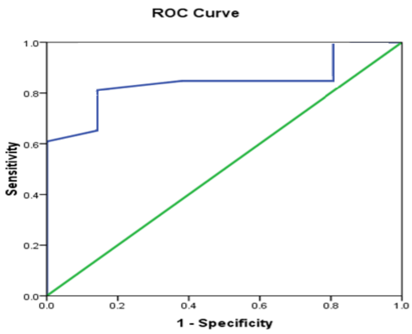

Figure (5): ROC curve showing the sensitivity and specificity relation

DISCUSSION

Monitoring the patients following ETV procedure remains a matter of controversy and challenge to ensure efficiency and patency of ventriculostomy. It is considered sometimes difficult to rely on clinical symptoms and signs of hydrocephalus, especially in younger patients, as it is difficult to establish until it reaches critical levels[9]. In addition to clinical outcome assessment to evaluate the efficiency of the ETV a range of image parameters have been assessed, including ventricular size changes, flow void signal intensity, and flow patency using cine PC MR. Also radionuclide cisternography was found to be sensitive for ETV patency assessment but very invasive and difficult to perform in routine practice [8].

In this study, clinical results showed 12 (40%) patients showed partial clinical improvement and one (3.3%) patient with no clinical improvement. Bargalló et al.[11] reported that, 17 (44.7%) patients with partial clinical improvement and 6 (15.8%) patients not improved. So, patients presented with post-operative residual or vague non informative symptoms about the state of ETV were confusing and challenging until it reaches critical clinical levels. The same authors stated that ventricular size changes not correlates with clinical results and therefore, conventional anatomical imaging follow up is just helpful for exclusion of the increase in the ventricular size[11].

In the current study, 16 (53.3%) patients showed significant ventricular size reduction (P value <0.001), and 7 (23.3%) patients of them showed partial clinical improvement. On the other hand, 8 (26.7%) patients showed no ventricular size reduction, 7 (23.3%) patient of this group showed clinical improvement. Bargalló et al.[11] reported that, the ventricular reduction was found only in 39.5% of the patients, and on correlating with clinical improvement, they found that patients which improved completely only 38% had ventricular size reduction. Nikas et al.[12] stated that the proportion of subjects who did not present ventricular reduction in a reported series showed a range between 11% and 38%.

For qualitative evaluation of ETV stoma, a strong pulsatile movement of cerebrospinal fluid flow might be viewed in sagittal cine image which is greatly consistent with demonstrating patency of the ETV stoma and for detection of flow obstruction by membrane or cyst[13].

In adequate flow group, ventriculostomy pattern of flow was similar to normal aqueductal flow as it is cardiac related pulsatile motion, but in contrast the flow signal was higher in ETV. While in those patients with subtle or no flow, ventriculostomy showed disturbed waveform of flow in the interpeduncular cistern associated with turbulence of the CSF flow due to stoma occlusion and this is in agreement with the Bargalló et al.[11] and Schroeder et al.[14] who qualitatively assessed the flow pattern and signal intensity through ventriculostomy and basal cistern.

In the present work, the absolute stroke volume measured across the ETV stoma of all adequate flow patients (mean 175 (±85) µl and median 145µl) were significantly higher in comparison to the stroke volume through the aqueduct (mean 60 (±10) µl and median 70 µl) of control group. We also observed that patients with the higher stroke volume values were maintained high during the whole follow-up period which is close to Bargalló et al. [11] who reported that, the ETV patient's median stroke volume equal 137µl in comparison to 80µl in healthy individuals and Schroeder et al.[14] stated that the mean systolic stroke volume in ETV patient's equal 86.5 (± 56) µl was higher than the flow in aqueduct after aqueductoplasty which equal 20 (±12) µl and in healthy individuals aqueduct 28 (±28) µl as reported in Schroeder et al.[15]. The explanation is probably that the opening of the ETV stoma is significantly larger in size than in the aqueduct and the floor is usually very thin. So, the low resistance provided by the ventriculostomy allows increased CSF flow[14].

There was highly significant correlation as regard the clinical results and greater stroke volumes at the ventriculostomy which was a positive forecaster of promising results [16].

Patients with worsen clinical results had the lower stroke volume values in comparison to the high stroke volume values in patients with total and partial clinical improvement with statistically significant values, but we did not found any significant volumetric differences between the patients which totally improved and partially improved patients with insignificant value and this in agreement with Bargalló et al.[11].

In the current study, during the second follow up period, 20% of patients showed low CSF flow values (mean absolute stroke volume 20 µl) below the control group values, in spite some of them presented with minor symptoms such as somnolence or nausea which was difficult to clinically diagnose ETV insufficiency until they progressed after that during close clinical follow up. The variance in the spectrum of symptoms and signs during follow ups made it difficult to be a predictive utility alone, in particular, with chronic patients due to permanent neurological deficit[17] for whom we used the CSF flowmetric data to support the clinical assessment and decision making.

ROC curves by utilizing the flowmetric values evaluated that stroke volume is a better test than the other variables to expect the ventriculostomy patency in the postoperative researches[17].

In this study, we analyzed the collected volumetric data using ROC curve and found that the absolute stroke volume when becomes more than 85µl indicating successful ETV outcome, while if the stroke volume less than 85µL, further clinical and radiologic follow up is necessary to determine the efficiency of ventriculostomy as this group of patients are usually associated with high failure rate. The sensibility and specificity of such procedure to detect cases whom enhanced were 84.3% and 81.7%, correspondingly while Bargalló et al.[11] determined the value of 75µL as a cutoff value with sensitivity and specificity of 76.7% and 87.5%, respectively.

The higher CSF flow above the cutoff value may help to prevent occlusion of the ETV stoma. Such report is reinforced by monitoring the cases presented by closure of an ETV when the Liliequist membrane was inadequately opened. The arachnoid membrane decreased the flow via the ventriculostomy, and the decreased CSF flow leads to ventriculostomy closure[14].

Although some patients may show adequate qualitative and quantitative data of flow through the ventriculostomy above the cutoff values, they display symptoms and signs of clinical deterioration and this is explained as inefficient ETV due to basal cisterns obstruction and considered communicating hydrocephalus which was observed by Di et al. [18], which was not reported in our study.

In conclusion, Evaluation of the ETV flow using cine MRI provides reliable information about the hydrodynamics of flow. ETV restores the physiological pulsatile bidirectional wave-form of CSF flow similar to the waveform in normal aqueduct, in spite of high flow signal intensity of ventriculostomy over the aqueduct due to the higher ventriculostomy stroke volume.

Conflict of interest

Authors declare that, there was no conflicts of interest.

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