Intracranial Pressure Monitoring as an Early Predictor of Third Ventriculostomy Outcome

Dissertation for Masters in Medicine (Neurosurgery)

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To my family and teachers for their inspiration

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Declaration

The material contained herein is original work and is not being submitted for another degree or to another institution. This work has not been published prior to registration for the MMed (Neurosurgery) degree.

Abbreviations and Glossary of Terms

CBF: Cerebral Blood Flow

CCHU: Cure Children's Hospital for Uganda

CLD: Continuous Lumbar Drainage

CNS: Central Nervous System

CSF: Cerebrospinal Fluid

CT: Computed Tomography

DTPA: Diethylenetriamine Pentaacetic Acid

EVD: External Ventricular Drain

ETV: Endoscopic Third Ventriculostomy

ETVSS: Endoscopic Third Ventriculostomy Success Score

Hg: Mercury

ICP: Intracranial Pressure

ICU: Intensive Care Unit

LP: Lumbar Puncture

MCA: Middle Cerebral Artery

mFV: Mean Flow Velocity

MMC: Myelomeningocele

MRI: Magnetic Resonance Image

NPV: Negative Predictive Value

PI: Pulsatility Index

PPV: Positive Predictive Value

ROC: Receiver Operator Curve

SAS: Sub-arachnoid Space

VPS: Ventriculoperitoneal Shunt

VRI: Ventriculostomy Related Infection

Area Under Receiver Operator Curve (AUROC) - The performance of a diagnostic variable can be quantified by calculating the area under the ROC curve (AUROC). The ideal test would have an AUROC of 1, whereas a random guess would have an AUROC of 0.5 [6]

Elastance is the inversion of compliance, with the latter being the buffering capacity of the cerebrospinal compartment with increase in CSF volume.[61]

Fisher's exact test is a statistical significance test that is used in the analysis of 2x2 tables where there are small sample sizes. It is used to examine the significance of association between two types of categorical data.[62]

Hosmer–Lemeshow test is a commonly used test for assessing the goodness of fit of a model and allows for any number of explanatory variables.[7]

Part A: Study Protocol

Application for Approval: Research Protocol

Principle Investigator: David Roytowski

Supervisor: Prof. P Semple (Primary), Dr. L Padayachy (Secondary)

Statistician: Mr. H Carrara

Study Title:

Intracranial Pressure Monitoring as an Early Predictor of Third Ventriculostomy Outcome

Background:

Hydrocephalus is a common neurosurgical condition that results from the accumulation of cerebrospinal fluid (CSF) within the ventricular system of the brain, due to disruption of the balance between CSF production and absorption.

Hydrocephalus has been described as communicating (a production/absorption imbalance) or non-communicating (an obstruction within the CSF pathways). The mainstay of treatment for non-communicating hydrocephalus has been the creation of an artificial outflow pathway – the ventriculo-peritoneal shunt (VPS).
While shunts have possibly been *the* most instrumental neurosurgical intervention in saving patients lives, they are fraught with problems and complications.

An elegant alternative to the VPS is the endoscopic third ventriculostomy (ETV) – a 'key-hole' neurosurgical procedure that creates an alternate CSF passage and reabsorption pathway, without the introduction of foreign body materials to the patient, thus, eliminating many of the complications associated with shunting.

ETVs are generally not indicated for patients with communicating hydrocephalus. In the event of ETV failure, early recognition is necessary to prevent the potentially fatal consequences of raised intracranial pressure.

Study Objective:

This study aims to determine i) if early intracranial pressure monitoring (via a transduced external ventricular drain) can predict ETV outcome, ii) the value of intraoperative assessment in predicting ETV outcome, iii) usefulness of CSF analysis to predict ETV success and iv) the complication rate (including sepsis) the study population.

Methodology

The data was collected from folders and radiological studies (CT/MRI Scans) of patients admitted to the Neurosurgical ICU/High Care following ETV intervention from 2006 until 2011.

The ICU data and subsequent follow up data from patient notes will be reviewed to determine the success or failure of the ETV.

Patient inclusion criteria for ETV were those that demonstrated a non-communicating/ tri-ventricular pattern of hydrocephalus or had evidence of VPS dysfunction and a radiographic picture that suggested the condition would be amenable to ETV.

Standard Groote Schuur Hospital pre-surgical informed consent was attained in all cases.

Patients would be ineligible for ETV if ventricular anatomy was distorted or there was evidence of intercurrent bacterial infection.

Patients that underwent an ETV were admitted to the D13 ICU/High Care. Intracranial pressure (ICP) was monitored via an external ventricular drain (EVD), which was transduced for approximately 72 hours. Raised ICP (>25 mmHg) for a sustained period – was managed by CSF release via the EVD or by lumbar puncture. Repeated episodes of raised ICP despite CSF release would result in the patient receiving a VPS.

Patient care followed best practice guidelines and all patients were treated on the merits of their condition.

Study Design:

Retrospective review

Study Size:

~ 60

Data Collected:

Variable	Type		Variable	Type
No	Numerical		Repeat ETV?	Binary
Patient	Alpha-numerical		Evidence of EVD related Sepsis	Binary
GSH NO	Numerical		Complications	Alpha-numerical
Age	Numerical		ETV Fn at D/C	Binary
Gender	Binary		ETV Fn at F/U	Binary
Pathology	Alpha-numerical		ETV Fn at 6/12 F/U	Binary
Aetiology	Categorised		Post Op Scan ETV FN?	Binary
Max ICP	Numerical		CSF App	Categorised
Mean ICP	Numerical		Poly	Numerical
CSF Release	Categorised		Lymp	Numerical
Release Type	Categorised		RBC	Numerical
Monitoring Duration	Categorised		Bact	Binary
D1 ICP	Numerical		Culture	Binary
D2 ICP	Numerical		Additional comments	Alpha-numerical
D3 ICP	Numerical		ETV Date	Date
Intraop Findings	Categorised			

Questions to be answered:

Primary

- Predictive quality of Monitoring? (i.e., does a monitoring outcome that is positive equate to F/U and 6mo F/U ETV function?)
- Predictive quality of intraoperative assessment on ETV function at F/U and 6mo F/U
- Predictive quality of CSF picture on ETV function at F/U and 6mo F/U

Secondary

- What is the rate of EVD related sepsis?
- Is there a Age, Gender, Aetiology, CSF release, Previous ETV correlation to successful ETV at F/U and 6mo F/U

Part B: Literature Review

Objectives of Literature Review

A comprehensive literature review was performed to ascertain the current body of knowledge regarding the treatment of hydrocephalus, in particular by performing an endoscopic third ventriculostomy (ETV). The key focus of the literature review was to examine the means and modalities presently employed to predict success of the ETV procedure. The primary search engines employed were pubmed, medline and google scholar. The searches were not time bounded and included published article upto and including May 2011.

Hydrocephalus

Hydrocephalus is a disease that has been described since the times of Hippocrates, with its name originating from the Greek meaning "water" "head". Since the early 1900s, hydrocephalus has been described as either, "communicating" or "non-communicating" (or "obstructive"). This is supported by the physiological theory that cerebrospinal fluid (CSF) is generated by the choroid plexus, has uninterrupted passage in the subarachnoid space (SAS) and is reabsorbed by the arachnoid granulations. Dandy outlined this physiology in his experiments on animals with injection of dye into the ventricular system that was later recovered in a spinal tap.[51] This theory has subsequently been questioned since recent evidence exists that indicate that the major CSF absorption occurs in the capillaries of the central nervous systems (CNS) and not the pacchionian granulations.[29]

The contemporary definition of Hydrocephalus has taken into consideration the ventricular system size; Rekate suggested in 2008 that 'hydrocephalus is an active distention of the ventricular system of the brain resulting from inadequate passage of cerebrospinal fluid from its point of production within the cerebral ventricles to its point of absorption into the systemic circulation."[52] Importantly, the definition does not make mention of the intracranial pressure, although an elevated intracranial pressure (ICP) often exists.

The classification of hydrocephalus has been as complicated as reaching a consensus on its definition. A classification should be able to identify the pathology as well as be useful in delineating management. Currently a view is held that apart from overproduction of CSF (as in a Choroid plexus tumour) all forms of Hydrocephalus can be considered "obstructive", at some point in the CSF passage.[52]

Ventriculomegaly results when the normal CSF absorptive mechanisms are overwhelmed, with a concomitant increase in intracranial pressure. Three main mechanisms have been described for the disequilibrium resulting in hydrocephalus; increased CSF production, increased outflow resistance, and increased dural sinus pressure.[57] An alternative theory is that increased pulsatility of the brain during systole, due to disruption of Monroe-Kelly homeostasis, causes an increased transmantle pressure gradient and ventriculomegaly.[29]

The recent classification proposed by Rekate, seeks to highlight the site of obstruction, likely pathology and indicated management. [52]

Table1: Proposed Classification of Hydrocephalus[52]

Site of Obstruction	Pathology	Treatment
None	Choroid plexus papilloma	Removal
Foramen of Monro	Tumour, congenital anomaly, post-shunt ventricular asymmetry	Tumour removal, septum pellucidotomy, ventricle shunt
Aqueduct of Sylvius	Congenital lesion, tumour secondary to extraventricular obstruction	ETV, ventricular shunt
Outlets of fourth ventricle	Chronic meningitis, Chiari II malformation	ETV, ventricular shunt
Basal cisterns	Meningitis, post subarachnoid haemorrhage	ETV, ventricular shunt, spinal thecal shunt
Arachnoid granulations	Haemorrhage or infection in infancy	Ventricle or thecal shunt
Venous outflow	Skull base anomalies, congenital heart disease	Ventricle or thecal shunt, treatment of vascular anomaly (if possible)

Such a classification system may be of value in determining which patients may benefit from an endoscopic third ventriculostomy (ETV).

Management of Hydrocephalus

Patients with hydrocephalus may present with nausea, vomiting and headaches; the triad hallmark of raised intracranial pressure. Headaches are typically frontal, but may involve the whole head, predominantly occurring in the early morning and often exacerbated by recumbancy. Some relief is gained from analgesia. In the child whose skull sutures have yet to fuse, the head circumference grows and many of the symptoms and signs of raised ICP may not be as obvious as in adults. Similarly, the presence of papilloedema is observed more commonly in the adult with hydrocephalus.[57]

The mainstay of investigation is a computed tomogram (CT) scan of the brain; which typically reveals ventriculomegaly, evidence of extraventricular fluid shift and loss of the surface sulcal CSF spaces. The aetiology of the hydrocephalus may also be determined, (e.g., posterior fossa lesion.) The CT scan allows for the assessment of the suitability and safety of lumbar CSF sampling. For further radiographic evaluation a Magnetic Resonance Image (MRI) scan will aid in defining lesions more accurately. Infective aetiology may be proven with use of lumbar puncture and CSF analysis. Similarily, an air-encephalogram may be useful in determining the communicating nature of the hydrocephalus.[22]

Since antiquity the treatment of hydrocephalus has involved a surgical intervention, and this currently remains standard practice. Hippocrates first described trephination and decompression for the treatment of this condition. Dandy is credited with attempting amongst the first ‘internal bypasses’, termed third ventriculostomy. These were undertaken via open craniotomies or using cystoscopes. The success rates were generally not high, and alternative interventions were sought.[27]

The 1950's saw the development of plastic and silicone tubing that allowed for the development of the valved shunt. CSF was diverted from the ventricular system to an alternative absorptive cavity. CSF shunting with modern materials is the standard treatment for hydrocephalus today.[51]

The value of ventriculoperitoneal shunts (VPS) is well established. However, complications from their use are common, and particularly so for children. The incidence of insertion for new VPS in the United States is 5.5 per 100,000 per year, with children representing one-third of cases.[68] Multiple causes exist for shunt malfunction, including obstruction, infection, disconnection, mechanical breakage and over-drainage, with lower socio-economic status being an independent risk factor for shunt dysfunction.[68] The failure rate is noted to be the highest in the first year after insertion, with 40% at year one and 50% before the second year.[13] Overall, between 45% – 59% of all patients will require a shunt revision.[68]

Given the high complication rate associated with VPS, an alternative CSF diversion strategy that does not require mechanical implantable materials is desirable. The advantages of rendering a patient shunt free have been widely propagated. It has been suggested that the Endoscopic Third Ventriculostomy (ETV) should be the first line therapy in non-communicating hydrocephalus, with advocates arguing for its use in cases of communicating hydrocephalus as well.[11] [27]Warf e al. recommend that ETV should be first-line therapy for hydrocephalus in the developing world.[66]

The complications associated with ETV are predominantly the intraoperative risks, which are higher than those of routine VPS placement.[27] The initial risks, however, need to be balanced against the long term complications of shunt placement.

Garton et al. undertook a cost effectiveness analysis of ETV where they compared a matched cohort of children undergoing an ETV or CSF shunt placement for hydrocephalus. This analysis compared the effect of the two therapies by taking into consideration the resource use and an effectiveness measure (days free of hydrocephalus treatment) for each group. Their results indicate that the ETV group enjoyed slightly higher days free of treatment, yet the intervention was not significantly less costly.[26] ETVs, as anticipated, required substantially higher initial resource use while shunt complications consumed resources at a later point.

Endoscopic Third Ventriculostomy (ETV)

ETV involves the creation of a direct communication through the floor of the third ventricle and the subarachnoid spaces of the interpeduncular cistern. This allows for the bypassing of an obstruction at the level of the aqueduct or the fourth ventricle. The primary indication for ETV is symptomatic obstructive hydrocephalus.

Mixter performed the first ETV using an ureteroscope in 1923.[27] The procedure did not become popular until improvements in lighting, optics and a reduction in the size of the apparatus. Improved technology has resulted in endoscopes that can be attached to powerful light sources, high definition cameras and recording equipment. Both rigid and flexible endoscopes are available, with multiple ports that facilitate the introduction of tools to perform tasks such as cautery, fenestration, ablation and biopsy.

Preoperative planning

Preoperative planning requires the use of imaging; in addition to CT scan a T2-weighted midline sagittal MRI scan is helpful in evaluating the third ventricular floor anatomy and appropriateness of an ETV procedure.[13] Pre-pontine space and basilar artery anatomy can also be assessed. CINE MRI sequences are sometimes used to evaluate CSF flow and site of blockage.[59, 65] van Lindert et al. have described the minimal information that ought to be derived from imaging studies before undertaking an ETV.

Table 2: Required information prior to performing an ETV [65]

Required information for ETV
• Shape of skull • Form and size of ventricles • Position and size of the foramen of Monro • Position and size of the interthalamic adhesion • Mamillary bodies • Dorsum Sellae and relationship to floor of the third ventricle • Slope of the floor of the third ventricle • Width of the prepontine cistern • Basilar artery and relationship to the floor of the third ventricle • Presence of space occupying lesion • Presence of membrane in ventricular system and prepontine cistern • Presence of anatomical variation

The ideal patient for an ETV has radiological imaging showing lateral and third ventricles which are enlarged and a fourth ventricle which is relatively normal – so called triventricular hydrocephalus.

Procedure

The patient is positioned supine, with the head in a neutral position. A burrhole is made anterior to the coronal suture in the mid-pupillary line, usually on the right-hand side. Consideration must be made for anatomical variation. The entry point is intended to be an extension of the line from the foramen of Monro to the interpeduncular cistern. This allows for the correct trajectory for insertion of a rigid endoscope.[17] Following durotomy and cortesectomy, a brain needle is passed, CSF delivered and sample collected. Taking note of the depth that the needle is passed before fluid returns and the pressure under which the fluid is expelled. A 0 or 30-degree endoscope is passed under visualization into the frontal horn of the right lateral ventricle. The foramen of Monro is often visualized upon entry into the ventricle. The head of the caudate is situated laterally and the septum pellucidum is located medially. The choroid plexus of the lateral ventricle projects forward into the foramen, then turns posteriorly to lie under the roof of the third ventricle. The vein of septum pellucidum, located anteromedially, joins the thalamostriate vein, located posterolaterally, at the posterior rim of the foramen of Monro. The endoscope is passed through the formen of Monro into the Third Ventricle. The floor of the Third Ventricle should enter the visual field.

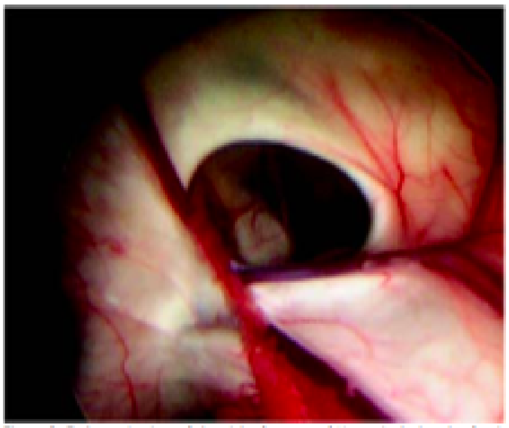

Figure 1: Endoscopic view of the foramen of Monro, also visible fornix, choroids plexus, head of caudate and thalamostriate vein.[17]

The floor is often thin due to long-standing raised intracranial pressure, allowing for visualization of the underlying anatomy, including the Basilar artery. Sometimes the floor may be opaque and thickened, or the CSF turbid, making visualization of the underlying anatomy more difficult.

A stoma is created in the midline of the floor of the Third Ventricle, anterior to the Basilar Artery into the interpeduncular cistern. Generally the stoma is created with a blunt instrument (often the tip of the cautery stylet or balloon catheter), but techniques utilizing forceps, wires and laser have been described.[17] A St Rose (figure 8) balloon is advanced through the fenestration and inflated with 0.6ml of air to dilate the stoma. One should assess whether Lilequist's membrane (an arachnoid condensation traversing the upper dorsum sellae to anterior edge of mammillary bodies [29]) remains intact, as this too would need to be fenestrated to allow for CSF passage to the SAS. Warmed Ringer's solution is routinely used as irrigation fluid to clear minor haemorrhage and prevent the ventricular system from decompressing.[64] If infusion pumps are used, the infusion rate is maintained at under 15ml/minute.[35]

Flow of CSF through the stoma, and pulsation of the floor of the third ventricle suggests a successful procedure. The endoscope is then removed, followed by a watertight dural closure, layered scalp wound closure and an external ventricular drain (EVD) is left in situ. Placement of an EVD is not universally undertaken, but is common practice in our institution.

Complications of ETV

Complications from ETV range from 0% to 15%, with a 1% mortality rate.[17 55] Intraoperative complications include; minor hemorrhage from the endoscope tract that usually abate spontaneously or after irrigation, or more rarely hemorrhage from the perforating branches may require endoscopic coagulation. Bradycardia can develop - this is thought to be a result of disturbance to the hypothalamic nuclei located in the floor of the third ventricle. Normal cardiac rhythm usually commences after removal of balloon compression.[18] Early postoperative complications include CSF leak, ventriculitis and stomal closure. Kombogiorgas and Sgouros have found that CSF leak was adversely associated with ETV success. [40]The development of basilar tip traumatic pseudoaneurysms may warrant endovascular or microsurgical attention. Restenosis is the most frequent late complication.[18, 55] Seizure incidence following ETV is approximately 1%. [14]Hypothalamic and fornix injury results from endoscope movement and may present with endocrine deficits and short-term memory loss. [3, 55] The entity late rapid deterioration after ETV is estimated to occur between 1% – 2% of ETVs and is usually fatal. [15]

Postoperative period

Patients are assessed clinically for signs of raised ICP suggestive of ETV failure; many institutions routinely place external ventricular drains to directly monitor intracranial pressure.

Assessment of success may be difficult to prove, as ventricular size does not readily decrease, despite a functional ETV and symptom resolution in many cases. The definition of successful ETV varies in the literature, but mostly involves the avoidance of a subsequent surgical procedure for definitive CSF diversion or death related to hydrocephalus within six months of the procedure.[36] Failure of ETV appears to be more common early post procedure, (i.e., within six months) than late. This is thought to be as a result of the patient's CSF physiology being unfavourable for ETV.[21]

Nevertheless, success rates for ETV are between 60% to 90%, with a plateau between 60% - 75% in the long term.[17336] Higher ETV success rates are observed for hydrocephalus as a result of aqueduct stenosis than for post-infectious, post-hemorrhagic, meningomyelocoele and VPS failures.[41] A repeat ETV following stomal closure has a success rate of up to 50%. Commonly associated risk factors for failure include history of CSF infection, previous VPS and age under six months.[36] Age is the strongest independent predictor of ETV success, with age under six months the lowest ETV predicted success.[36] If failure occurs, there is a cumulative probability of 90% that the failure declares itself during the first 16 days after surgery.[54]

Intracranial pressure monitoring can be achieved by transduction of an indwelling external ventricular drain (EVD) that is placed at operation, or via a dedicated ICP monitor probe. Advantages of the EVD include the ability to perform CSF removal and sampling (allowing for a measure of safety should the stoma occlude acutely), with a distinct disadvantage being the concern for ventriculostomy related infections (VRI). The risk of ventriculomeningitis associated with ICP monitoring via an EVD ranges between 0% to 22%.[46]

Much debate exists in the literature with respect to prophylactic catheter changes. Mayhall et al reported a reduced rate of infection in patients in whom the ventricular catherter was routinely changed after five days. [47] Recent metanalysis have proven no increased risk of infection beyond five days, and recommend against prophylactic changes. [30] Dedicated ICP monitoring has a negligible risk of the development of meningitis, irrespective of whether the probe is placed intraparenchymally or via a subarachnoid bolt. Drainage of CSF from the ventricular catheter is also not associated with a higher incidence of ventriculitis.[47]

Early ETV failure may be as a result of failure of CSF absorption rather than closure of the stoma. The clinical course immediately post ETV is highly variable with many patients experiencing short periods of intracranial hypertension. The interval between the creation of the stoma and the opening of the basal cisterns (closed due to raised ICP) has been termed the 'adaptation period'. [31] The transient periods of raised pressure have often led practitioners to believe that the ETV had failed, and an alternative CSF diversion would be required. A number of hypotheses exist to explain the 'adaptation period'; the chronic compression exerted on the basal cisterns from long-term raised ICP can cause a delay in the opening of the SAS [5] Alternatively, previously masked communicating hydrocephalus may now limit the resorption capacity for CSF.[5, 56]

Postoperative imaging of ETV shows wide variability in the change in ventricular size. In general, should the ventricles decrease in size following ETV, this provides some evidence that the procedure has been successful. [53] In successful ETVs it has been noted that the ventricular size appears to decrease but will not reach normal equivalents.[42] Often the third ventricle demonstrates a larger reduction in size than the lateral ventricles which differs between acute and chronic hydrocephalus. [42] The clinical significance of this ongoing ventriculomegaly is unknown, although some have suggested that the ETV has resulted in a compensatory communicating hydrocephalus.[58] Ventricular size assessment should be considered a useful adjunct to the post-operative clinical assessment of patients, with rapid decrease in ventricular size not precluding the possibility of delayed ETV failure.

Given the challenges with early radiological assessment and uncertainty of ETV failure or ‘adaptation period’, some authors have proposed the use of continuous lumbar drainage (CLD) following ETV. The proposed mechanism is based on the premise that absorption problems following ETV are temporary; many ETVs would be ‘successful’, if a safe strategy is used to facilitate this absorption. The lumbar drain is thought to have physiological advantages over an EVD, including encouraging flow across the stoma, washing out debris, blood and protein load. However, it is advocated that the CLD be utilized in conjunction with ICP monitor.[49]

Prediction of Endoscopic Third Ventriculostomy Outcome

ETV success has been defined as not requiring a ventriculo-peritoneal shunt in the long term.[3, 9, 37] The success rates quoted in the literature are between 60% - 90%. [3, 17] No technique has been shown to adequately demonstrate patentcy of the SAS – a vital factor in predicting positive ETV outcome.[50] Given the uncertainty of an ETV being successful a number of modalities and techniques have been devised to predict the likelihood of ETV success.

Intraoperative impression

The use of clinical, aetiological and radiological data is utilised to make an assessment of the suitability of an ETV for the treatment of hydrocephalus, and inherent in this assessment, the prediction of success. During an ETV, the surgeon typically would take note of the size and position of the stoma created, thickness of the third ventricular floor, presence of adhesions, presence of intraventricular haemorrhage and CSF flow through the stoma. Zohdi et al. have suggested the “whirl sign”, a downward flow of CSF through the stoma could predict ETV success.[69]

Kombogiorgas et al. in their series of ETVs assessed the following: i) relative stomal size, ii) intraoperative haemorrhage, iii) thick/ double third ventricular floor, iv) presence of adhesions, v) CSF flow through stoma, vi) aetiology of hydrocephalus, vii) shunt presence, viii) CSF infection or haemorrhage and x) previous ETV. Their study did not demonstrate a correlation between adhesions, thickened floor and ETV success, but did suggest an association of success to patients without previous shunts, and stoma size. CSF leaks were strongly associated with failure. [40]

Greenfield et al, sought to devise a simple intraoperative assessment criteria to allow surgeons to predict ETV success without the need for postoperative monitoring and imaging. A scoring system that included age of patient (<2 years), neonatal IVH history, meningitis history or VPS infection, each contributed to a maximal preoperative score of 2. The intraoperative assessment involved, three categories Anatomy, Subarachnoid Space and CSF movement, each contributing one point.

Table 3: Intraoperative Scoring Criteria [28]

Unusual Anatomy	Subarachnoid Space	Stoma
Intraventricular scaring	Presence of scaring	Stomal CSF movement
Intraventricular synechiae	Presence of adhesions	
Leptomeningeal tumor dissemination		

A maximal score of five, would be tallied at the end of the procedure, Grade 0 patients have 95% ETV success rate, while patients with at least a Grade 3 have 100% failure rate.[28] As the authors of the above analysis acknowledge, defining "reproducible objective measurements of features including CSF pulsation, subarachnoid scaring and anatomical variance" is difficult.

The literature appears to be divided regarding the predictive power of the intraoperative impression during ETV; hence recommendations calling for further blinded prospective trials to be undertaken.[16]

Hydrostatic Pressure Testing

The mobility and pulsatility of the floor of the third ventricle after stoma creation is thought to be an indication of procedure success. Kamel et al, undertook a simple investigation to assess the mobility and flow through a newly created stoma. Once a stoma was created the irrigating solution was set at 30cm above the external auditory meatus and the valve opened for 10 seconds, all ports on the endoscope were closed. The floor of the third ventricle ballooning downward would accompany good flow through the stoma. Once the irrigation was stopped and ports opened, reverse flow would cause an upward displacement of the floor. These outcomes would score a positive hydrostatic test. The authors report a test sensitivity 95.24%, specificity 66.67%, positive predictive value 86.96% and negative predictive value 85.7%. Their sample had an ETV success rate of 70%, which was significantly higher in patients with a positive hydrostatic test ($p < 0.05$). The hypothesis for a mobile floor correlating with a successful ETV is i) a mobile floor represents a dilated third ventricle with a pressure differential between the third ventricle and the subarachnoid space, and ii) good flow through the stoma i.e., functional stoma.[37] The hydrostatic test does not provide insight into the absorptive capacity of the subarachnoid space, hence late failures may be accounted for by this group.

Intracranial Pressure Monitoring

Many authors have suggested that an accurate assessment of the function of the ETV stoma and subsequent ‘opening up’ of the subarachnoid reabsorptive pathways can be deduced from ICP measurement. [23, 27, 31] The most reliable means of detecting recurrent hydrocephalus following ETV is through formal ICP monitoring.[1] The principle purpose of ICP monitoring is to ascertain if there is development of the ‘adaptation period’, where previously compressed basal cisterns begin to allow the passage of CSF for convexity absorption. Commonly, intracranial pressure is monitored via ventricular ICP probes or transduced through closed external ventricular drains.[5, 10, 50] More recently studies have described the use of telemetric ICP monitoring systems following ETV.[67] The claimed benefits being longer term pressure monitoring and little restriction on patient mobilization.

Repana et al demonstrated that, following ETV, up to 50% of their patients have transient ICP rises which were responsive to CSF removal. They also noted that variable ICP patterns occurred among groups of patients. Raised ICP episodes are clustered within the first two days postoperatively. Patients presenting with shunt malfunction or intraventricular lesions tended to develop the most severe intracranial hypertension following ETV. ICP monitoring in such patients is recommended by this group. However, Rapana was unable to assign predictive value to the different postoperative ICP patterns.[50]

Four groups were identified, each with their own ICP characteristics:

Table 4: ICP Pattern Characteristics[50]

	Aqueduct Stenosis	**Shunt Malfunction**	**Ventricular Lesions**	**Extrinsic Aqueductal Compression**
ICP Characteristics	• Rasied ICP concentrated within the first two postoperative days • Small amount of CSF removal required to restore normal pressures	• Raised ICP lasted upto fourth postoperative day • Frequent CSF withdrawals necessary – having less effect on ICP	• Raised ICP in the three days following ETV • Very frequent CSF withdrawals required	• No symptomatic raised ICP • No requirement for CSF withdrawal

Rapana et al concluded, "no relationship could be established between post operative ICP course and late outcome."

Cinalli et al recorded ICP in 64 children following ETV for an average of seven days and further described the ICP trend patterns post ETV into four categories.

Table 5: ICP Trend Patterns Post ETV[10]

Progressive Decrease	**Stable**	**Progressive Increase**	**Secondary Rise**
• Daily average ICP dropped constantly after the third post-operative day	• ICP remained within a 3mm Hg range throughout monitoring period	• Ongoing rise in ICP throughout the monitoring period	• After an initial decrease the daily average ICP rose constantly from the third postoperative day

The higher incidence of "Secondary Rise" and "Progressive Increase" patterns in the Failed ETV group compared with the Successful ETV group is statistically significant. (P = 0.01) This suggests that there is some predictive quality to these ICP Trend Patterns. However, the authors make note that high ICP in the first postoperative days (with or without symptoms and signs of raised ICP) may not be related to failure of the ETV, but rather a transient phase.[10]

Table 6: ICP Trend Patterns Relating to ETV Success [10]

ICP Trend Patterns	**Successful ETV**	**Failed ETV**
Progressive Decrease	27 (56%)	2 (15%)
Stable	7 (15%)	0 (0%)
Progressive Increase	0 (0%)	3 (23%)
Secondary Rise	14 (29%)	8 (62%)
Total	48 patients	13 patients

Cinalli et al. go on to conclude that a cycle of one to three lumber punctures should be performed before deciding that ETV has failed and that shunting is required.

Currently, it is not clear that ICP pressure patterns are useful in differentiating between the ‘adaptation period’ transient intracranial hypertension and future failure of ETV.

Scoring Systems

Strong and independent predictors of ETV success include age, aetiology, and presence of previous shunt.[41] Age, appears to be the strongest predictor, infants younger than six months having the lowest predicted ETV success. Kulkarni et al. developed an ETV Success Score (ETVSS) that approximates the probability of successful ETV. (Table 7) Later work by Kulkarni et al. has shown that favourable ETVSS scores (>=80) predict ETV failure rate being lower than that of shunt failure, and patients with less favourable scores (ETVSS <= 70) have ETV failure risk initially higher than shunt risk, but lowering between 3-6 months after surgery.[43]

ETV Success Score = Age Score + Aetiology Score + Previous Shunt Score ≈ Percentage probability of ETV success

Table 7: ETVSS Scoring Criteria [41]

Score	**Age**	**Aetiology**	**Previous Shunt**
0	< 1 month	Post-infectious	Previous Shunt
10	1 month to < 6 months		No Previous Shunt
20		MMC Intraventricular Haemorrhage Non-Tectal Tumour	
30	6 months to 1 year	Aqueductal Stenosis Tectal Tumour Other	
40	1 year to 10 years		
50	> 10 years		

The scoring system has been criticized by colleagues, as representing what is already known. By definition patients with high ETVSS are older than 1 year, likely to carry the diagnosis of aqueducal stenosis or a tectal glioma. Infants under one year are unable to have high ETVSS.[12]

An alternative scoring system was developed at Cure Children's Hospital for Uganda (CCHU), the ETV Success Score, with ranges from 0 (least likely to succeed) to 9 (most likely to succeed). (Table 8)

Table 8: CCHU ETV Success Score Criteria [66]

		Score
Age	< 6 Months	0
	6 Month – 1 year	1
	1 year or older	3
Aetiology	Other	0
	Post-infectious	1
	Myelomeningocoele	2
Choroid Plexus Cauterization	None	0
	Partial /Unilateral	2
	Complete / Bilateral	4

Although the Hosmer-Lemeshow statistic was not significant when validating the model, the CCHU ETV Success Score was able to stratify into high, moderate and low chance of ETV success.[66] The authors noted that early success of ETV forecasts a high chance of long-term success. In their series successful ETV at 6 months was associated with a 3-year success rate of 95%.[66] One must, however, consider the differences in the Ugandan hydrocephalus population before applying the CCHU ETV Success Score in other geographies.

Kehler and colleagues proposed another attempt at a semi-quantitative predictive system. Criteria measured include; i) extent of the bulge of floor of the third ventricle,

ii) presence of visualized CSF pathway obstruction at MRI imaging and iii) the progression of clinical symptoms. Five grades are assigned; retrospective analysis showed that ETV success (or failure) was correctly predicted in 40% (Grade 3), 58% (Grade 4) and 95% (Grade 5).[38]

No scoring or grading system appears to have the predictive quality that would give operators full confidence around the future success of the ETV.

Cine phase-contrast MRI

Conventional spin-echo MRI has been utilized to demonstrate a CSF flow void at the anterior/inferior border of the third ventricle following ETV. The flow void in the T2 weighted images caused by rapid turbulent flow, indicate a functioning ventriculostomy. Absence of the void does not preclude a functional ETV, and interference from basilar artery pulsation may affect interpretation.[33] Quantitative cine phase-contrast MRI allow for time-resolved measurement of flow via anatomic structures; arteries, veins and CSF spaces. The cine format is sufficient for measuring patency – it is, however, subjective.[45] Measuring velocities at multiple sites provides additional physiologic and prognostic information.[45] Velocity encoded images are obtained by acquiring an imaging parallel to the floor of the third ventricle that focuses on the ventriculostomy. Velocity encoding is usually set at between 10 – 20 cm/sec and applied in three orthogonal directions. Axial analysis allows for quantitative CSF flow dynamics to be studied, while a mid-sagittal analysis provides good qualitative assessment. [2]

During CSF diastole, CSF moves in a caudocranial direction (termed positive velocity), in CSF systole, flow is craniocaudal (negative velocity). The CSF stroke volume is the net CSF volume inflow and outflow during cardiac cycle.[2]

Flow across the ventriculostomy and the flow rate measurement has become an outcome measure in and of itself – with success of ETV assessed with flow MR studies. Active pulsatile flow is seen as confirmation of ventriculostomy function.[59] Fukuhara et al conclude that a cine PR MR image studying flow of CSF is highly reliable for detecting ETV obstruction and patency. Minor flow in the third ventricle should be considered an early sign of obstruction.[25] In 85%-100% of clinically improved patients, there is evidence of flow through the ETV site.[42] However, even in clinical failures patency of the ETV has been shown, up to 50% in some series.[9] Stivaros et al. in a pilot study of thirteen patients proved that an ETV induces changes in brain volume and cerebral blood flow (CBF). However, they also note that there is no literature support of changes in CBF and improved clinical outcome.[59]

Bargallo et al concluded that stroke volume quantification is a good indicator of ETV function and that overall flow magnitude (systolic stroke volume + net diastolic stroke volume) was the most effective variable determining which patients would improve after surgery. (Values >75mm^3 showed a sensitivity 76.7%, specificity 87.5%)[2]

With regard to long term follow up, Faggin et al, have concluded that Cine phase-contrast MRI “has a high capacity to detect a flow defect through a ventriculostomy, raising the suspicion of ETV failure.”[19] The data presented remains insufficient to conclude that cine MRI is useful to reveal ETV malfunction in an asymptomatic population.

Radioisotope Cisternography

Under normal metabolic conditions, radioisotope tracer injected into the subarachnoid space passes up to the basal cisterns within 1 hour, sylvian fissure by 2 to 6 hours and over the convexities by 12 to 24 hours.[48] Radionucleotide cerebrospinal fluid scintigraphy (RCFS), is said to have the advantage over CT and MRI scans by being able to differentiate between communicating and non-communicating hydrocephalus.[21] Diethylenetriamine pentaacetic acid (DTPA), a radioisotope, degrades from 4 to 6 hours, with minimal remaining after 48 hours. The DTPA counts are obtained by a gamma camera and a C48:C5 ratio is calculated. Normal adult C48:C5 ratio is less than 0.35.[48] In their study, Nishiyama et al. showed images obtained at 5 hours demonstrated a higher radioisotope activity in the ventricles at 6 months compared to 1 week post-ETV. 48-hour images revealed decreased persistent radio-isotope at the convexities from 1 week to 6 months after ETV.[48] The literature reveals that some authors suggest cisternography should be performed prior to ventriculostomy, ensuring that CSF absorption mechanisms are intact, however this does not appear to be common practice nor practical.[34]

Intraoperative ventriculo-stomographic evaluation

Intraoperative ventriculo-stomography (IOVSG) is a technique that allows the confirmation of adequacy of the endoscopic procedure during surgery. The infiltration of radio-opaque contrast (commonly iohexol – due to its limited neurotoxic effects) via a working channel of an endoscope into the ventricular system is assessed with the aid of an image intensifier. Typically images are acquired at 1, 3, and 5-minute intervals, tracing the flow of contrast into the SAS. Husain et al define stoma functionality as good (rapid transit, <1 minute), fair (transit 1 – 3 minutes) or poor (retention of contrast in cisternal spaces > 3 minutes). Patients with poor functionality would be planned for VPS.[32] The authors suggest the use of this technique to assess obstruction site, CSF dynamics and functional status of ETV.[32]

Outflow resistance and elastance

A Swedish study[61] undertook to assess the correlation between clinical outcome after ETV and resistance to outflow of CSF and elastance. These parameters can be measured by bolus injection, constant flow rate infusion or constant pressure infusion. The day prior to ETV, an EVD catheter is placed into the ventricle, connected to a pressure transducer, and the burrhole then closed with silicone plug and tisseel. Infusion tests are conducted with dedicated software to analyse the ICP response. The intraventricular Outflow resistance (R_{out}) and elastance can be calculated. After several hours of data collection, an ETV is performed. After the ETV, R_{out} was decreased as compared with the values of the two preoperative compartments. The decrease of R_{out} correlated with the clinical improvement of the patients. The decrease in R_{out} might reflect the increased area of CSF absorption in both the SAS and the ventricles. Preoperative elastance correlated positively with clinical improvement, but elastance was unchanged after ETV. The preoperative values of R_{out}-SAS and R_{out}-IV *do not* predict patient outcome after ETV in adults with hydrocephalus due to aqueduct stenosis.[61] Hence, it appears that R_{out} and elastance are insufficient measures to predict success of ETV.

Transcranial Doppler Sonography

Transcranial Doppler sonography (TCD) has been developed to detect the changes in cerebral blood flow velocities. It is a non-invasive, risk-free, easily repeatable technique that can be performed at the patient's bedside. A TCD is measured transtemporally with an ultrasonic transducer over the middle cerebral artery (MCA). The mean flow velocity (mFV) is assessed from the resulting graphic trace. Pulsatility Index (PI) is a derived value from the difference in the flow velocity divided by the mFV.

Pulsatility Index = (Peak Systolic Velocity – End Diastolic Velocity)/Mean Flow Velocity

Bellner et al. showed in their study of eighty-one patients that there is a strong correlation (correlation coefficient 0.938) between ICP and PI.[4] Further more, preliminary data, from a study by Vajda et al. suggested that the PI is a useful non-invasive tool for determining the patency of fenestration following ETV in the early follow-up period.[63] They conclude that the TCD-defined PI is "a very sensitive diagnostic tool in the follow-up patients who required a 3rd ventriculostomy." Results showed a decrease in the PI immediately following ETV and on the fifth post-operative day in all patients with a functioning stoma. However, their study has been criticized for the short post-op period of analysis (five days). Nevertheless, TCD in conjunction with a clinical assessment may well prove to be a useful non-invasive method to evaluate stoma patency.

Table 9: Summary of Pertinent Literature Review

Modality		Author	Publication Date	Study Design	Sample Size	Population	Findings / Conclusions
Non Invasive	Scoring Systems	Kulkarni	2009	Multi-center retrospective cohort	618	Children	ETVSS devised that can identify children likely to have successful ETV
		Kulkarni	2010	Multi-center cohort	489 ETV 720 VPS	Children	Risk of ETV failure is progressively lower than risk of VPS failure with increasing time from surgery. ETVSS stratifies patient risk
		Warf	2010	Prospective cohort study	979	Children	CCHU ETVSS predicts chance of ETV success in children with hydrocephalus in sub-Saharan Africa
	Cine PC-MRI	Lev	1995	Prospective-control study	6/12	Adults Children	Velocity ratio between pontine cistern and spinal cord can help determine functional status of third ventriculostomy. Pulsation from basilar artery may interfere with interpretation.
		Fukuhara	1999	Prospective study	11	Adults Children	Cine PC MR imaging is reliable for detecting patency of third ventriculostomy. Minor flow should be considered an early sign of obstruction
		Cinalli	1999	Retrospective study	213	Children	Midline sagittal T_2 weighted MR with CINE PC MR provide reliable tool for diagnosis of aqueductal

							stenosis and stoma follow-up evaluation
		Kulkarni	2000	Prospective study	29	Children	Ventricular size reduces in successful and failed ETV. Reduction significantly greater in success. Flow void correlates with clinical success.
		Bargallo	2005	Prospective study	38	Adults Children	Quantification of stroke volume at ventriculostomy is a good indicator of ETV functional status. High stroke volume is a positive predictor of ETV success
		Stivaros	2009	Prospective study	13	Adults	ETV induces changes in brain volume and CBF
		Faggin	2011	Retrospective study	84	Children	Intraoperative observation of thickened arachnoid and decreasing flow on routine Cine MR are significant risks for deterioration. Cine MR has high capacity to detect flow defect
	Transcranial Doppler Ultrasonography	Vajda	1999	Prospective study	22	Adults Children	PI useful in evaluating patency of fenestration in early follow up of Post-ETV patients
		Bellner	2004	Prospective study	81	Adults Children	Strong correlation between PI and ICP demonstrated, independent of type of intracranial pathology
Invasive	Intraoperative Impression	Komborgiogas	2006	Retrospective review of videos of ETV	33	Children	No correlation between pre-pontine adhesions, double or thickened third ventricle floor and ETV success. Stoma size may correlate with success. CSF leak assoc. with

Invasive	Intraoperative Impression	Komborgiogas	2006	Retrospective review of videos of ETV	33	Children	No correlation between pre-pontine adhesions, double or thickened third ventricle floor and ETV success. Stoma size may correlate with success. CSF leak assoc. with failure
		Greenfield	2008	Prospective study	109	Adults Children	Intraoperative assessment more reliable than post ETV MRI and EVD monitoring. Grading scale useful adjunct to reducing unnecessary tests
	Hydrostatic Test	Kamel	2005	Prospective study	30	Adults Children	Positive test confirms adequate flow through stoma. Stoma mobility important predictor of ETV success.
	Radioisotope Cisternography (RC)	Nishiyama	2003	Prospective study	15	Adults Children	CSF dynamics convert from shunt dependant to shunt independent state within 1 week. Absorptive capacity through SAS my show improvements for several months post-ETV
		Jaksche	1986	Retrospective & Literature study	79	Undisclosed	Only cases with open cisterns should be considered for RC. Mortality 1%, Neurological deficit 5% following procedure
	Intraoperative Ventriculo-	Husain	2010	Prospective study	17	Adults Children	IOVSG is simple and safe, confirms adequacy of ETV during procedure. Facilitates further management.
	Outflow Resista	Tisell	2002	Propspective study	15	Adults	Resistance could not predict ETV outcome. Reduction in resistance

	ICP Monitoring	Frim	1997	Case study	1	Adult	Reduction in ICP post ETV documented after initial period of acclimation
		Bellotti	2001	Prospective study	10	Adults	Postoperative ICP monitoring provides useful information to determine correct stoma functioning in early postoperative period
		Rapana	2004	Prospective study	26	Adults	Unable to assign predictive value to different postoperative ICP patterns. Patients with VPS malfunction and intraventricular mass lesions show higher propensity to develop raised ICP post-ETV
		Cinalli	2006	Prospective	64	Children	High ICP early post-ETV probably related to slow permeation of SAS. Lumbar puncture probably decreases CSF outflow resistance. Cycle 1 – 3 LP should be performed before ETV assumed to have failed

Part C: Manuscript

Abstract

Objectives: Endocscopic third ventriculostomy (ETV) is a routinely utilized alternative to ventriculoperitoneal shunt (VPS) in obstructive hydrocephalus. We attempt to determine the usefulness of the surgeon's intraoperative impression and early postoperative period intracranial pressure monitoring that may help guide clinicians in predicting the functional outcome of ETV.

Methods: The patients who underwent ETV between 2006 and 2011 were retrospectively reviewed. The sample included sixty-three patients, 23 female and 40 male, between the ages of 13 and 69. In each case the surgeon's intraoperative impression, cerebrospinal fluid (CSF) samplings and post-operative intracranial pressure (ICP) monitoring (via transduced external ventricular drain for seventy-two hours) was recorded and evaluated in light of functional outcome of ETV at discharge and early followup. (1-2 months)

Results: ICP monitoring predicted initial function of the ETV in 51 cases (80.9%) and in 12 cases (19%) suggested ETV failure. Monitoring has a positive predictive value (PPV) of 76.3% and a negative predictive value (NPV) of 100%. While the surgeon's intraoperative impression of future function has a PPV of 76.5%, and NPV of 76.9%. CSF sampling has a much poorer predictive quality owing to the wide confidence interval and a PPV of 63.6% and NPV 38.2%. In our series the evidence of sepsis as a result of EVD was found to be 11.67%.

Conclusions: ETV is a valuable means of treating obstructive hydrocephalus. By considering the surgeon's intraoperative impression and post-operative ICP monitoring course some of the uncertainty around its functional outcome can be

overcome. The surgeon's impression and the ICP monitoring offer approximately the same predictive quality for ETV outcome.

Key Words

Endoscopic third ventriculostomy (ETV), Hydrocephalus, Outcome ETV, Intracranial pressure (ICP) monitoring

Introduction

Endoscopic third ventriculostomy (ETV) is increasingly employed as the first-line treatment for non-communicating hydrocephalus.[10, 15, 17, 44, 63, 66] The procedures high success rate and limited complications make it an attractive option. [3, 15, 24, 36, 43, 55, 61] However determining if the procedure is likely to be successful can be difficult.[9] Many approaches to this problem have been sought; none yet providing adequate predictive quality for routine practice.[37, 65] Radiological studies of ventricle size are recognized to be inadequate to infer ETV success, MRI assessment of flow across the ETV stoma has been demonstrated to be present in clinically proven failures.[2, 19, 21, 25, 29, 42, 45, 53, 59] Invasive ventriculographic studies have a role to play but are not without complication and are cumbersome when compared to what is otherwise an elegant procedure.[32] Non-invasive testing with transcranial dopplers shows promise; but insufficient study exists to consider it for routine clinical application.[61, 63] Intracranial pressure monitoring remains an acknowledged means of determining ETV function and a proxy to inferring sub-arachnoid space (SAS) absorptive function.[5, 10, 50, 67] This study has been undertaken primarily to assess value of post-ETV ICP monitoring in predicting the early outcome of ETV. In parallel, the surgeon's intraoperative impression on the future function of ETV is evaluated and compared to the postoperative ICP monitoring results. Cerebrospinal fluid (CSF) sampled at the time of ETV is also evaluated for its predictive quality on future ETV function.

Clinical Materials and Methods

Patient Population

Sixty-three patients aged between thirteen and sixty-seven years who underwent ETV for hydrocephalus between January 2005 and July 2011 were studied. The mean age of the studied population was 41.28 years, comprising 23 females (36.5%) and 40 males (63.49%).

The range of pathology is displayed in Table 1 below:

Table 1: Sample Population Aetiology

Aetiology of Hydrocephalus	**Number**	**Percentage**
Congenital	4	6%
Haemorrhage	4	6%
Infective – Bacterial	5	8%
Infective – Tuberculous	8	13%
Infective – NOS	6	10%
Tumour – Posterior Fossa	23	37%
Tumour – Supratentorial	3	5%
Other[1]	10	16%
Total	63	100%

[1] Other includes conditions where aetiology is unknown (n=5) with VPS dysfunction (n=2), Ventriculo-atrial shunt dysfunction (n=1), previous ETV (n=2)

For fifty-seven patients (90.5%) the studied procedure was their index ETV, and in 10 patients (9.5%) the procedure was a repeat ETV. Patients were followed up at the Neurosurgical outpatients department between one and three months post-discharge. Follow up rate were generally poor, (Table 2)

Table 2: Patient Follow Up

Data at Follow Up	**Follow Up**
Died	6 (9.5%)
Data available	50 (79.4%)
Lost to follow up	7 (11.1%)

Patient Evaluation and Therapy

Patients were all admitted under Neurosurgical care to a single tertiary hospital that is a referral center for a population of approximately 10 millions people[2]. Hydrocephalus was diagnosed in all patients by Computed Tomography and/or Magnetic Resonance scans. In many patients there were symptoms or signs of raised ICP. Cine phase MRI is not common practice in our institution, and was not performed.

The decision to perform an ETV was taken upon review of the radiology by consensus among the consultant staff of the Neurosurgical unit. Depending on the urgency, the patients were prepared for surgical procedure for the same day or next elective slate. In our series, multiple surgeons performed the ETVs, with the senior consultant present in the majority of cases.

[2] Census 2001, Stats SA. Western Cape 4524336, Eastern Cape 6436763

Equipment utilized and procedure method

A 6mm rigid endoscope and stack (Storz and co., Tuttlingen, Germany) was used for all cases. A burrhole was created in the mid-pupillary line anterior to the coronal suture and an ETV performed via ipsilateral ventricle with perfusion of warmed Ringers solution. A CSF sample was taken prior to insertion of endoscope; care would be taken to ensure minimal loss of CSF. The endoscope was utilized to identify the foramen of Monro, through which the endocsope was advanced. Entry into the third ventricle allowed for fenestration of the floor with the aid of monopolar cautery probe or balloon catheter. The stoma was dilated by inflation of a St Rose figure of 8 balloon with 0.6ml of air. Once the stoma was created, the endoscope was advanced through to visualize the Basilar artery and pontine perforators. Care was taken to ensure that perforation through Liliequist membrane had been achieved. Haemorrhage, when it occurred, was treated by continuous wash with warmed Ringers solution. After the endoscope had been removed a standard ventriculostomy drain was placed in the lateral ventricle via the tract and secured to the scalp. A drainage bag was attached, and the system remained clamped.

Findings and surgical notes

The operator would make note of the intraventricular environment, including the clarity of the CSF, thickness of the third ventricular floor, presence of membranes (synaechiae), pulsatility of floor, flow through stoma and anatomical variations. Note would also be made of any intraoperative complications from the procedure; incorrect trajectory, tract haematomas, intraventricular bleeding and damage to intracranial structures.

Post-operative management and monitoring

All patients were then transferred to the Neurosurgical Highcare or ICU. The EVD would be connected, in an aseptic fashion, by the nursing staff to a TruWave Disposable Pressure Transducer. ([PX260], Edwards Lifesciences, Irvine, Ca.) Care was taken to avoid loss of CSF at time of connection to the transducer. The catheter remained clamped and the transducer attached to a Nihon Kohden Lifescope Bedside Monitor ([MU-651RK], Nihon Kohden Corporation, Tokyo, Japan.) The apparatus was zeroed with the transducer at the level of the tragus, and the transducer secured. Graphic trace and numerical data would be continuously displayed on the monitor with recordings manually captured every thirty minutes for the first two hours postoperatively and hourly thereafter. Intracranial pressures were displayed in millimeters mercury. Decisions were taken based on the patient’s clinical condition, ICP readings and radiology (when requested). Sustained high ICP readings (more than fifteen minutes), may have warranted CSF release, this would be performed via lumbar puncture and/or opening of the EVD.

The data collected for analysis was captured from the ICU nursing charts that reflect the ICP values as recorded by the unit’s staff. Data captured included the maximal ICP, daily ICPs (taken consistently at the same time each day) and CSF release mechanism, if undertaken.

Table 3: Duration and Number of Monitored Patients Post-ETV

Hours Monitored	Number	Percentage
48	15	23.8%
72	43	68.3%
96	4	6.3%
120	1	1.6%

In the majority of cases the monitoring was performed for 72 hours. Thereafter the EVD was removed, scalp closed in the standard fashion and the patient transferred to the general neurosurgical ward.

Results

Analysis of the data was performed utilizing Stata IC version 12.0 (StatCorp LP, College Station, TX, US), statistical software. Monitoring predicted function of the ETV in 51 cases (80.9%) and in 12 cases (19%) suggested ETV failure and these patients went on to have a VPS. When ETV function was evaluated at the initial follow up, the monitoring predictive quality resulted in a positive predictive value (PPV) of 76.3% and a negative predictive value of 100%.

Intraoperative impression was classified into positive expectation of ETV function (n=44), negative expectation (n=19) and uncertain (n=11). The intraroperative impression has a test PPV of 76.5%, and negative predictive value (NPV) of 76.9%.

CSF as a predictive test for ETV function, as anticipated, is of little value. At initial follow up the test shows a PPV of 63.6% and NPV 38.2% with wide confidence intervals.

Table 4: Predictive Tests Statistical Results

Predictive Test		Positive Predictive Value	Negative Predictive Value	Sensitivity	Specificity	ROC area (AUROC)
Monitoring		**76.3%**	**100%**	100%	57.1%	0.786
	95% CI	59.8%	75.3%	88.1%	34%	0.667
		88.6%	100%	100%	78.2%	0.894
Intra-operative Impression		**76.5%**	**76.9%**	89.7%	55.6%	0.726
	95% CI	58.8%	46.2%	72.6%	30.8%	0.595
		89.3%	95%	97.8%	78.5%	0.857
CSF		**63.6%**	**38.2%**	40%	61.9%	0.51
	95% CI	40.7%	22.2%	23.9%	38.4%	0.375
		82.8%	56.4%	57.9%	81.9%	0.644

Table 5: ETV Function at Discharge and Follow Up

ETV Function Data	Discharge	Follow Up
ETV functional	51 (81%)	29 (58%)
ETV non-functional	12 (19%)	21 (42%)
Total	63	50

Table 6: Aetiology and ETV Function at Follow Up

Aetiology of Hydrocephalus	**ETV Functional Follow Up**	
	Number	**Percentage[3]**
Congenital	1	33.3%
Haemorrhage	3	75%
Infective	10	62.5%
Tumour – Posterior Fossa	2	66.7%
Tumour – Supratentorial	5	35.7%
Other[4]	8	80%
Total	29	58%

A consequence of post-operative monitoring is the need for either a dedicated pressure transducer or a transduced external ventricular drain; concern exists about the risk of infection posed by these devices. In our study we noted an infection rate related to EVD of 11.67%. This is consistent with findings in the literature, of ventriculostomy related infections rates between 0 – 22%.[46, 47]

Patients underwent CSF release if the monitoring reflected prolonged raised ICP and/or the clinical picture suggested intracranial hypertension. 58% of patients did not require any form of CSF release, 9.7% required a single CSF release and 32% required multiple CSF subtractions.

[3] Reflects the proportion of successful ETVs out of the proportion of ETVs performed in that aetiology category

[4] Other includes conditions where aetiology is unknown (n=5) with VPS dysfunction (n=2), Ventriculo-atrial shunt dysfunction (n=1), previous ETV (n=2)

Table 7: CSF Release

CSF Release	No.	Percentage
None	36	58.1%
Single	6	9.7%
Multiple	20	32.3%

The release mechanism was via Lumbar puncture (n=9, 34.6%), EVD (n=14, 53.9%) and both Lumbar Puncture and EVD (n=3, 11.5%)

Table 8: Release Mechanism

CSF Release Mechanism	No.	Percentage
Lumbar Puncture	9	34.5%
EVD	14	53.9%
Both	3	32.3%

The monitored population who underwent CSF release were analysed to ascertain if there was a predictive quality to action of CSF release on the outcome of the ETV at follow up. Results indicate that there is little predictive quality in favour of a positive or negative predictive outcome.

Table 9: Predictive Test: CSF Release

Predictive Test		Positive Predictive Value	Negative Predictive Value	Sensitivity	Specificity	ROC area (AUROC)
CSF Release (single and multiple)		**40.9%**	**25.9%**	31%	35%	0.33
	95% CI	20.7%	11.1%	15.3%	15.4%	0.193
		63.6%	46.3%	50.8%	59.2%	0.467

The risk of EVD related sepsis was reviewed in the context of CSF release, to determine if the action of CSF removal contributed to development of sepsis. A Fisher's exact test was performed, which returned a value of 1.0, indicating that there was no correlation, in our sample, between CSF removal and EVD related sepsis. This result needs to be interpreted in light of the fact that 7 (11.67%) patients in the sample had evidence of sepsis.

A subgroup analysis was performed to determine if there was correlation between age at time of procedure and function of ETV at follow up. The data was dichotomized to patients younger and older than 40 years. This age cut off was selected, as the mean age of the sample population was 39, mode 30 and median 37 years. The prevalence ratio of 1.26 in the age category 40 years and above was not significant (p=0.348), the odds ratio of 1.74 also was not significant (p=0.342).

Similar analysis was undertaken for gender, revealing that males had a prevalence ratio of 1.35 with a p-value of 0.298 and an odds ratio of 1.97 (p=0.264). A prevalence ratio of 2.2 was noted for ETV success at follow up if CSF release was either taken on a single occasion or not performed, however, the result was not significant.

Table 10: Prevalence Ratio Analysis

Variable	Follow Up		
	No.	% Success	PR (95% CI)
Female	17	47.1%	1.0 (ref)
Male	33	63.6%	1.35 (0.77-2.39)
Age < 40	27	51.9%	1.0 (ref)
Age > 40	23	65.2%	1.26 (0.78 – 2.03)
Multiple CSF Release[5]	18	33.3%	1.0 (ref)
No Release[5]	27	74.1%	2.22 (1.11-4.41)
Single CSF Release[5]	4	75%	2.25 (0.92-5.45)
LP release[5]	8	75%	1.0 (ref)
EVD release[5]	11	18.1%	0.24 (0.09-1.09)
LP + EVD release[5]	3	33.3%	0.44 (0.09-2.14)

Furthermore, the analyses of ETV success at follow up with respect to CSF release via LP, EVD or both did not reveal a statistically significant result, but did suggest that LP were associated with a higher likelihood of ETV success.

[5] Less than the total number of patients that had CSF release are analysed in this sample due to the loss to follow up proportions

Discussion

Obstructive hydrocephalus remains the main indication for ETV, with this treatment an effective and safe alternative to VPS or other shunt procedures.[8, 21, 31] Despite the recognized advantages of ETV, success rates in most series are between 60-90%.[3, 17, 49] Failures of ETV are documented to mainly occur early[8, 26]No technique has been able to prove patency of the SAS, a vital factor in predicting postive ETV outcome.[50] Numerous methods and techniques have been proposed to evaluate the potential for successful ETV outcome. Authors have suggested the Intraoperative impression can be classified and scored.[28, 40, 69] However, reproducible, objective measurements of many of these features is extremely difficult and further blinded prospective trials have been suggested. [16] Intra-operative hydrostatic pressure testing has been shown to have a positive predictive value of 86.9%. [37] Yet, this technique probably provides little insight into late failures. Several scoring systems have been developed that consider numerous criteria including; age, aetiology, previous shunt, choroids plexus cauterization and in some instances radiographic features. [12, 38, 41, 43, 66] While age appears to have a strong correlation with success (in the paediatric population in particular), scoring systems don't have predictive quality that gives operators full confidence in future ETV success. Cine phase-contrast MRI is widely used to assess the function of an ETV stoma, however there is evidence of patency of ETV in upto 50% of failed cases.[9] Faggin et al conclude that cine phase-contrast MRI has high capacity to detect flow, and subsequently raise suspicion of ETV failure.[19] Literature review reveals that radioisotope cisternography, [20, 21, 34, 48]intraoperative ventriculo-stomography,[32] outflow resistance,[61]and transcranial doppler sonography[463] have been investigated to some degree to predict ETV success, none of which are widely used techniques. Numerous authors have suggested that measuring ICP post-ETV would provide accurate assessment of stoma function and 'opening up' of the SAS and evaluation of the 'adaptation period'. [1, 23, 27, 31]

We investigated 63 patients who underwent an ETV followed by insertion of EVD and post-operative ICP monitoring. The mean weighted duration of monitoring was 68.6 hours. We assessed a successful ETV outcome as resolution from symptoms of hydrocepalus and shunt independence. Santamarta concluded that delayed failure of ETV is rare and that there is a 90% cumulative probability that failure will declare itself during the first 16 days post surgery.[54] Given this understanding, the primary purpose of our study was to determine if ICP monitoring and subsequent response to the data provided by the monitoring had a predictive quality on the early successful outcome of the ETV. The literature is not clear on the predictive quality of ICP monitoring, nor on the value of ICP patterns post-ETV. Rapana had concluded that "no relationship could be established between the post-operative course and late outcome."[50] While Cinalli et al suggest that there is some predictive quality between certain ICP trend patterns. [10] Our results indicate that ICP monitoring has a Positive Predictive Value (PPV) of 76.3% with a 95% confidence interval 58.9% - 88.6%. The receiver operator curve area was calculated at 0.786. All patients that failed monitoring (i.e., sustained high ICPs and/or clinical signs to suggest intracranial hypertension) went on to have VPS. Hence, the negative predictive quality for this test was 100%.

Greenfield et al. in a prospective study concluded that an intraoperative assessment is more reliable than post-operative MRI and EVD pressure monitoring.[28] Our findings with respect to the surgeon's intraoperative impression revealed a PPV of 76.5% with a 95% confidence interval of 58.8% - 89.3%, almost identical to that of ICP monitoring. The Negative Predicitive Value (NPV) for the intraoperative impression was 76.9%.

To our knowledge there is no study that has evaluated the CSF attained at ETV and compared to outcome. Not surprisingly, the predictive quality of CSF analysis was poor, (PPV 63.6%, NPV 38.2%, AUROC 0.51) with wide confidence intervals. In a recent study published by Ozisik, recommendation is made for placement of lumbar drain to encourage flow across the stoma, in selected patients. [49] Our data indicated that there was no predictive quality to CSF release, irrespective of method (via LP or EVD), nor was there an increased risk of developing sepsis. However, although not statistically significant, when compared to EVD CSF release, LP are associated with a higher likelihood of success.

Methodological Limitations of the Study

Owing to its retrospective design, this study has limitations; generally the same consultant staff would make the decision of failure or success during the course of normal clinical activities. There was no design into this study to have peer review, thus surgeon bias is a consequence. In addition the data collected was from nursing chart documentation that are captured irrespective of the clinical state (or times of physiologically raised ICP), but researches would have been blinded to this fact. The single daily and maximum ICP readings could be criticized for the same reason that these events may well have been missed as they did not coincide with charting / review times. A continuous ICP capture with trend analysis could overcome this problem. However, the current limitations are not far removed from the reality on which clinical decisions are taken, and thus may be more relevant.

The lost to follow up rate of the study population, as noted previously, is thought to be due to the type of underlying pathologies, (often terminal) and the nature of the population. (lower socio-economic strata and geographically dispersed sample) Attempts to contact patients resulted in little improvement in the follow up numbers achieved, perhaps a prospective study with formal data collection and return incentives would improve follow up numbers.

Analysis methodology

We have chosen to represent the prevalence ratio for the data based on review of article by Thompson et al. that suggests that the prevalence ratio is conservative, consistent, and interpretable relative to the intrinsic relative ratio and should be used in preference to the prevalence odds ratio. [60]

Conclusion

There is presently no completely reliable means of predicting successful ETV outcome, many patients may undergo an 'adaptation period' while the SAS develops its absorptive capacity. During this time, ETV may be deemed to have failed – having EVD insitu, monitoring patients and removing CSF appears to have no detrimental effect on the rate of sepsis, provides an element of safety and reasonable predictive quality test. Both surgeons' intraoperative impression and post-operative ICP monitoring have a role to play in predicting the future functional state of ETV, interestingly the two modalities offer almost identical predictive quality with respect to a successful procedure.

Part D: Supporting documentation

References

1. Aquilina K: Routine placement of a ventricular reservoir at endoscopic third ventriculostomy. **Neurosurgery 53:**91, 2003

2. Bargallo N: Functional analysis of third ventriculostomy patency by quantification of CSF stroke volume by using cine phase-contrast MR imaging. **AJNR, American Journal of Neuroradiology 26:**2514, 2005

3. Beems T: Long-term complications and definition of failure of neuroendoscopic procedures. **Child's Nervous System 20:**868, 2004

4. Bellner J: Transcranial doppler sonography pulsatility index (PI) reflects intracranial pressure (ICP). **Surg Neurol 62:**45, 2004

5. Bellotti A: Intracranial pressure monitoring after endoscopic third ventriculostomy: An effective method to manage the 'adaptation period'. **Clin Neurol Neurosurg 103:**223, 2001

6. Bewick V: Statistics review 13: Receiver operating characteristic curves. **Critical Care 8:**508, 2004

7. Bewick V, Cheek L, Ball J: Statistics review 14: Logistic regression. **Critical Care 9:**112-118, 2005

8. Brockmeyer D: Endoscopic third ventriculostomy: An outcome analysis. **Pediatr Neurosurg 28:**236, 2000

9. Cinalli G: Failure of third ventriculostomy in the treatment of aqueductal stenosis in children. **J Neurosurg 90:**448, 1999

10. Cinalli G: Intracranial pressure monitoring and lumbar puncture after endoscopic third ventriculostomy in children. **Neurosurgery 58:**126, 2006

11. Cinalli G: The role of endoscopic third ventriculostomy in the management of shunt malfunction. **Neurosurgery 43:**1323, 1998

12. Cohen AR: Prediction, with restriction. **J Neurosurg Pediatrics 6:**307, 2010

13. Drake JM: CSF shunts 50 years on–past, present and future. **Child's Nervous System 16:**800, 2000

14. Drake JM: Endoscopic third ventriculostomy in pediatric patients: The canadian experience. **Neurosurgery 60:**881, 2007

15. Drake J: Late rapid deterioration after endoscopic third ventriculostomy: Additional cases and review of the literature. **Journal of Neurosurgery.Pediatrics 105:**118, 2006

16. Drake J, Riva Cambrin J: Can intraoperative assessment of endoscopic third ventriculostomy predict success? **Journal of Neurosurgery.Pediatrics 2:**295-6, 2008

17. Elbabaa SK: Endoscopic third ventriculostomy. **Contemporary Neurosurgery 31:**1, 2009

18. Erşahin Y: Complications of endoscopic third ventriculostomy. **Child's Nervous System 24:**943, 2008

19. Faggin R: Long-term operative failure of endoscopic third ventriculostomy in pediatric patients: The role of cine phase-contrast MR imaging. **Neurosurgical Focus 30:**1, 2011

20. Feng F: Evaluation of radionuclide cerebrospinal fluid scintigraphy as a guide in the management of patients with hydrocephalus. **Clin Imaging 33:**85, 2009

21. Feng H: Endoscopic third ventriculostomy in the management of obstructive hydrocephalus: An outcome analysis. **J Neurosurg 100:**626, 2004

22. Figaji AA: Air encephalography for hydrocephalus in the era of neuroendoscopy. **Child's Nervous System 21:**559, 2005

23. Frim DM: Telemetric intraventricular pressure measurements after third ventriculocisternostomy in a patient with noncommunicating hydrocephalus. **Neurosurgery 41:**1425, 1997

24. Fukuhara T: Risk factors for failure of endoscopic third ventriculostomy for obstructive hydrocephalus. **Neurosurgery 46:**1100, 2000

25. Fukuhara T: Third ventriculostomy patency: Comparison of findings at cine phase-contrast MR imaging and at direct exploration. **AJNR, American Journal of Neuroradiology 20:**1560, 1999

26. Garton HJL: A cost-effectiveness analysis of endoscopic third ventriculostomy. **Neurosurgery 51:**69, 2002

27. Grant JA: Third ventriculostomy: A review. **Surg Neurol 47:**210, 1997

28. Greenfield JP: Intraoperative assessment of endoscopic third ventriculostomy success. **Journal of Neurosurgery Pediatrics 2:**298, 2008

29. Greitz D: Radiological assessment of hydrocephalus: New theories and implications for therapy. **Neurosurg Rev 27:**145, 2004

30. Holloway KL: Ventriculostomy infections: The effect of monitoring duration and catheter exchange in 584 patients. **J Neurosurg 85:**419, 1996

31. Hopf NJ: Endoscopic third ventriculostomy: Outcome analysis of 100 consecutive procedures. **Neurosurgery 44:**795, 1999

32. Husain M: Intraoperative ventriculo-stomographic evaluation of endoscopic cerebrospinal fluid diversion and flow restoration procedures. **British Journal of Neurosurgery 24:**672-678, 2010

33. Jack Jr CR: Stereotactic third ventriculostomy: Assessment of patency with MR imaging. **AJNR, American Journal of Neuroradiology 10:**515, 1989

34. Jaksche H: Burr hole third ventriculo-cisternostomy. **Acta Neurochir 79:**48, 1986

35. Jallo GI: Endoscopic third ventriculostomy. **Neurosurgical Focus 19:**1, 2005

36. Kadrian D: Long-term reliability of endoscopic third ventriculostomy. **Neurosurgery 56:**1271, 2005

37. Kamel MH: Use of a simple intraoperative hydrostatic pressure test to assess the relationship between mobility of the ventricular stoma and success of third ventriculostomy. **J Neurosurg 103:**848, 2005

38. Kehler U: Outcome prediction of third ventriculostomy: A proposed hydrocephalus grading system. **Minimally Invasive Neurosurgery 49:**238-243, 2006

39. Kim SK: Surgical outcome of pediatric hydrocephalus treated by endoscopic III ventriculostomy: Prognostic factors and interpretation of postoperative neuroimaging. **Child's Nervous System 16:**161, 2000

40. Kombogiorgas D: Assessment of the influence of operative factors in the success of endoscopic third ventriculostomy in children. **Child's Nervous System 22:**1256, 2006

41. Kulkarni AV: Endoscopic third ventriculostomy in the treatment of childhood hydrocephalus. **J Pediatr 155:**254, 2009

42. Kulkarni AV: Imaging correlates of successful endoscopic third ventriculostomy. **J Neurosurg 92:**915, 2000

43. Kulkarni AV: Predicting who will benefit from endoscopic third ventriculostomy compared with shunt insertion in childhood hydrocephalus using the ETV success score. **Journal of Neurosurgery Pediatrics 6:**310, 2010

44. Kwiek SJ: Endoscopic third ventriculostomy for hydrocephalus: Early and late efficacy in relation to aetiology. **Acta Neurochir 145:**181, 2003

45. Lev S: Functional analysis of third ventriculostomy patency with phase-contrast MRI velocity measurements. **Neuroradiology 39:**175, 1997

46. Lozier AP: Ventriculostomy-related infections: A critical review of the literature. **Neurosurgery 51:**170, 2002

47. Mayhall CG: Ventriculostomy-related infections. **N Engl J Med 310:**553, 1984

48. Nishiyama K: Changes in cerebrospinal fluid hydrodynamics following endoscopic third ventriculostomy for shunt-dependent noncommunicating hydrocephalus. **J Neurosurg 98:**1027, 2003

49. Ozisik P: Continuous spinal drain following endoscopic third ventriculostomy: A proposal to change the definition of failure. **Childs Nerv Syst Online:**2011

50. Rapana A: Intracranial pressure patterns after endoscopic third ventriculostomy. preliminary experience. **Acta Neurochir 146:**1309, 2004

51. Rekate HL: A contemporary definition and classification of hydrocephalus. **Semin Pediatr Neurol 16:**9, 2009

52. Rekate HL: The definition and classification of hydrocephalus: A personal recommendation to stimulate debate. **Cerebrospinal Fluid Research** 2008

53. Santamarta D: Changes in ventricular size after endoscopic third ventriculostomy. **Acta Neurochir 150:**119, 2008

54. Santamarta D: Outcome of endoscopic third ventriculostomy. results from an unselected series with noncommunicating hydrocephalus. **Acta Neurochir 147:**377, 2005

55. Schroeder HWS: Complications of endoscopic third ventriculostomy. **J Neurosurg 96:**1032, 2002

56. Schwartz TH: Ventricular volume following third ventriculostomy. **J Neurosurg 91:**20, 1999

57. Shakeri M: A review of hydrocephalus: History, etiologies, diagnosis, and treatment. **Neurosurgery Quarterly 18:**216, 2008

58. St. George E: Changes in ventricular volume in hydrocephalic children following successful endoscopic third ventriculostomy. **Child's Nervous System 20:**834, 2004

59. Stivaros SM: Endoscopic third ventriculostomy: Predicting outcome with phase-contrast MR imaging. **Radiology 252:**825, 2009

60. Thompson ML: Prevalence odds ratio or prevalence ratio in the analysis of cross sectional data: What is to be done? **Occup Environ Med 55:**272, 1998

61. Tisell M: Elastance correlates with outcome after endoscopic third ventriculostomy in adults with hydrocephalus caused by primary aqueductal stenosis. **Neurosurgery 50:**70, 2002

62. Upton GJG: Fisher's exact test. **155:**395-402, 1992

63. Vajda Z: Transcranial doppler-determined pulsatility index in the evaluation of endoscopic third ventriculostomy (preliminary data). **Acta Neurochir 141:**247, 1999

64. van Aalst J: Acute distortion of the anatomy of the third ventricular during third ventriculostomy. **J Neurosurg 96:**597, 2002

65. van Lindert EJ: The role of different imaging modalities: Is MRI a conditio sine qua non for ETV? **Child's Nervous System 22:**1529, 2006

66. Warf BC: Endoscopic third ventriculostomy in the treatment of childhood hydrocephalus in uganda: Report of a scoring system that predicts success. **Journal of Neurosurgery Pediatrics 5:**143, 2010

67. Welschehold S: First clinical results with a new telemetric ICP monitoring system. **Neurosurgery 70:**44, 2012

68. Wu Y: Ventriculoperitoneal shunt complications in California: 1990 to 2000. **Neurosurgery 61:**557, 2007

69. Zohdi A: Variations in the site and size of third ventriculocisternostomy. **Minim Invasive Neurosurg 41:**194, 1998

Research Ethics Approval

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HREC REF: 377/2011

Dr D Roytowski
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Dear Dr Roytowski

PROJECT TITLE: INTRACRANIAL PRESSURE MONITORING FOR EARLY DETECTION OF THIRD VENTRICULOSTOMY FAILURE

Thank you for submitting your study to the HREC for review.

It is a pleasure to inform you that the Ethics Committee has **formally approved** the above-mentioned study.

Approval is granted for one year till the 15 August 2012.

Please submit a progress form, using the standardised Annual Report Form (FHS016), if the study continues beyond the approval period. Please submit a Standard Closure form (FHS010)if the study is completed within the approval period.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the REC. REF in all your correspondence.

Yours sincerely

signature removed

PROFESSOR M BLOCKMAN
CHAIRPERSON, HSF HUMAN ETHICS

Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

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Data Collection Sheet