Pediatric hydrocephalus: systematic literature review and evidence-based guidelines. Part 10: Change in ventricle size as a measurement of effective treatment of hydrocephalus

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Object. The objective of this systematic review is to answer the following question: Does ventricle size after treatment have a predictive value in determining the effectiveness of surgical intervention in pediatric hydrocephalus?

Methods. The US National Library of Medicine PubMed/MEDLINE database and the Cochrane Database of Systematic Reviews were searched using MeSH headings and key words relevant to change in ventricle size after surgical intervention for hydrocephalus in children. An evidentiary table was assembled summarizing the studies and the quality of evidence (Classes I–III).

Results. Six articles satisfied inclusion criteria for the evidentiary tables for this part of the guidelines. All were Class III retrospective studies.

Conclusions. RECOMMENDATION: There is insufficient evidence to recommend a specific change in ventricle size as a measurement of the effective treatment of hydrocephalus and as a measurement of the timing and effectiveness of treatments including ventriculoperitoneal shunts and third ventriculostomies. STRENGTH OF RECOMMENDATION: Level III, unclear clinical certainty.

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KEY WORDS • hydrocephalus • ventricle size • evidence-based guidelines • practice guidelines

THE decision to treat hydrocephalus with an external shunt or endoscopic third ventriculostomy (ETV) is based on a variety of factors. The determination of successful outcome rests on a multitude of clinical and imaging correlates. Imaging indicators that have been examined include ventricle size, presence of a flow void in the ETV site, amount of CSF over the cerebral hemispheres, and the degree of periventricular edema. The objective of this particular systematic review is to answer the question: Does ventricle size after treatment have a predictive value for effectiveness of surgical intervention in pediatric hydrocephalus?

Ventricle size before and after intervention is a readily available measurement that has been used to assess success or failure of treatment. Particular attention has been given to changes in ventricle size after ETV.^{6,18,23}

Correlation with neurodevelopmental sequelae as well as correlation with other imaging parameters, such as presence of flow voids after ETV, have been suggested as indications of successful interventions.^{2,10,13,25} The evaluation of the effectiveness of treatment has therefore been limited because developmental outcomes are most applicable in infants and younger children and flow voids observed on MR images are applicable only to ETV treatment. This review, therefore, focuses on ventricle size as a tool, albeit a limited one, in the evaluation of the effectiveness of treatment. Ventricle size is an outcome that could be used to assess patients of all ages as well as both forms of intervention—the ventriculoperitoneal (VP) shunt and the ETV. The purpose of this evidence-based review is to critically examine data from the literature pertaining to change of ventricle size as a predictor of the success of surgical intervention.

Methods

We searched the US National Library of Medicine (PubMed/MEDLINE) and the Cochrane Database of

Abbreviations used in this paper: AANS = American Association of Neurological Surgeons; CNS = Congress of Neurological Surgeons; CPC = choroid plexus cauterization; ETV = endoscopic third ventriculostomy; FOR = frontal and occipital horn ratio; VP = ventriculoperitoneal.

Systematic Reviews for the period January 1966 through March 2012 using strategies listed below. The inclusion and exclusion criteria adhered to the protocol outlined in the methods section, Part 1, of these evidence-based guidelines.⁸

Search Terms

PubMed/MEDLINE

1. "Cerebrospinal Fluid Shunts"[MeSH] AND "Hydrocephalus"[Majr:noexp]
 2. 1 AND ("Magnetic Resonance Imaging"[MeSH] OR "Tomography, X-Ray Computed"[MeSH] OR "Ultrasonography"[MeSH] OR imaging[tiab])
 3. 2 AND ("ventricular size"[TIAB] OR "ventricular dilation"[tiab] OR ventricle[tiab] OR ventricles[tiab])
 4. Limit to Child (0–18 years)
 5. Limit to English and Humans
 6. Limit 3 to Child (0–18 years)
 7. Limit to English and Humans
- Number = 81

Cochrane Database

1. MeSH descriptor Child
2. MeSH descriptor Infant
3. MeSH descriptor Hydrocephalus
4. MeSH descriptor Cerebrospinal Fluid Shunts
5. (MeSH descriptor Magnetic Resonance Imaging) or (MeSH descriptor Ultrasonography) or (MeSH descriptor Tomography, X-Ray Computed) or imaging
6. (1 or 2) and 3 and 4 and 5
7. 3 and 4 and 5

Search Strategy

An evidentiary table was constructed to facilitate data review and analysis by the Pediatric Hydrocephalus Systematic Review and Evidence-Based Guidelines Task Force.

For each article included in the evidentiary table, the study type, summary findings, and major conclusions were recorded, and a preliminary data class was assigned. The Task Force met to discuss the ranking of the evidence and the classification of data. Recommendations then were made based on the strength of the data in the evidentiary table. In these discussions, if a disagreement was encountered among members, a blinded vote was held and a consensus or majority opinion was reached.

Search Results

A total of 81 abstracts were screened and 18 full-text articles listed in the databases were retrieved for review (Fig. 1). The selection for review was based on the determination of evidence data relevant to the question of the effect of treatment on ventricle size. An examination of the reference lists of these 18 full-text articles yielded 4 additional articles that warranted full-text review. All 22 articles were read and reviewed in detail by the full Task Force. Sixteen articles were excluded based on predefined criteria, which are described in Part 1⁸ of the Guidelines. Six articles satisfied the inclusion criteria and form the basis for the evidentiary tables in this recommendation.

Results

The 6 articles that met the inclusion criteria and were selected for final review were all Class III retrospective studies (Table 1).

In 2000, Kulkarni et al.¹⁸ published the results of a retrospective, blinded observational study of a group of 29 children who had undergone ETV and whose ventricle size was assessed by 4 independent observers using the FOR (frontal and occipital horn ratio) both preoperatively and postoperatively (Table 1). Postoperatively, the mean reduction in ventricle size was 7% in cases that were deemed treatment failures (8 patients in whom symptoms either recurred or never resolved) and 16% in cases that were clinically successful (21 patients)—a result that was statistically significant ($p = 0.03$, t -test). The authors concluded that ventricle size appeared to be somewhat reduced in both groups of patients; however, the reduction was significantly greater among the clinically successful cases. The authors also assessed imaging correlates; they found that the presence of a flow void seemed to correlate with clinical success and its absence with clinical failure. The most significant limitation in this study is its retrospective nature. Surgeon bias, the linear measurement of ventricle size, and the variation in time when postoperative imaging was conducted were confounding factors.

In another retrospective study, published in 2009, Warf et al.²⁴ described neurocognitive outcomes and ventricle volumes in infants with myelomeningoceles and hydrocephalus (Table 1). The same method was used to compare ventricle size in 55 children treated by ETV with choroid plexus cauterization (CPC), 19 children who received a VP shunt, and another 19 children who required no intervention. The mean FOR was similar among groups, with no significant difference between the untreated group and either the VP shunt or ETV with CPC group before treatment. The groups also were compared for neurocognitive outcomes, and no significant difference was identified. The FOR did not correlate with neurocognitive performance. Bias existed with respect to the VP shunt group because most patients had already experienced ETV with CPC failure. This is another non-randomized study with the potential for strong confounding factors within treatment groups. A valid conclusion was that stable mild-to-moderate ventriculomegaly alone should not trigger intervention in an asymptomatic infant with a myelomeningocele.

Another Class III single-center retrospective study in the myelomeningocele population was published by Chakraborty et al.⁴ in 2008 (Table 1). These authors studied 28 patients who were selected from a group of 54 who satisfied the determined inclusion criteria. Overall, using a stringent shunt placement policy, about half (51.9%) of their patients required a VP shunt. The authors suggest that a more critical evaluation and tolerance of ventriculomegaly may decrease the need for shunt placement and will reduce shunt dependency in children with myelomeningocele, without worsening outcome.

In a study by St. George et al., limited by its small number of subjects, the authors examined 13 patients with multiple diagnoses who had undergone ETV (Table 1).²³

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Fig. 1. Flowchart showing the process involved in identifying relevant literature.

The comparison of preoperative and postoperative ventricular volume was confined to patients in this treatment group. The authors found postoperative measurements of ventricular volume to be lower than measurements obtained preoperatively but higher than normalized values for patient ages and sexes. The pattern of change in ventricle size varied between a large ventricular volume group, which demonstrated a significant decrease at the 3- to 6-month postoperative time point, and a small volume group, in which there was a much less steep reduction in ventricle size in the first 3–6 months. After that time period, the volume appeared to stabilize or fall slightly.

Two additional papers reported that ventricle size was not necessarily a predictor of outcome (Table 1). These 2 studies looked at ETV alone and found that in both infants and older children, reduction in ventricle size was not necessary to have a clinically effective treatment of hydrocephalus. Like the previously cited studies, these studies were retrospective, and both enrolled a small number of patients (Buxton et al.: $n = 27$; Kim et al.: $n = 29$ in whom neuroimaging studies were available).^{2,16}

Excluded Evidence

The evidence reviewed was predominantly Class III. Those papers not used in the analysis were excluded for multiple reasons including the following: reports combining adult and pediatric patient populations without reporting pediatric patients separately;^{3,7,9–11,15} a review of other studies;²⁰ and a technical report.²¹ Jain et al.¹⁴ reported the effect of valve design on repeated operation, not on effectiveness of treatment. Another paper described how to measure ventricles.¹⁹ Kombogiorgas et al.¹⁷ confined their evaluation to the question of ventricle size predicting the need for shunting after tumor resection in patients with posterior fossa tumors. The large study by Shankaran and

colleagues²² looked at the impact of ventriculomegaly on outcome, without expressly addressing the shunt status of the patients and was thus excluded. One article could not be retrieved for full-text review and was therefore excluded.¹ The paper by Horbar et al.¹² did not meet inclusion criteria due to enrollment of fewer than 10 patients. One by Choudhury⁵ was excluded because it did not report ventricle size as an outcome of interest and therefore did not report data to answer the clinical questions addressed in this section. Goumnerova and Frim¹⁰ reported a study including adults and children, but did not analyze the pediatric patients separately.

Conclusions

RECOMMENDATION: There is insufficient evidence to recommend a specific change in ventricle size as a measurement of effective treatment of hydrocephalus and as a measurement of the timing and effectiveness of treatments including ventriculoperitoneal shunts and third ventriculostomies. **STRENGTH OF RECOMMENDATION:** Level III, unclear clinical certainty.

The purpose of hydrocephalus treatment is to return the CSF and/or pressure within the brain of an affected infant or child to as normal a condition as possible. Resources to effect these changes are currently limited primarily to the use of a ventriculoperitoneal (VP) shunt or endoscopic third ventriculostomy (ETV). Intracranial pressure and its effect on brain function cannot easily be measured, and thus an alternate way of judging treatment effectiveness is necessary. The size of ventricles revealed by a number of imaging modalities, including ultrasonography, CT, and MR imaging, is frequently used as a measure of the effectiveness of intervention. Our evaluation of the evidence reveals that reliance on ventricle size

TABLE 1: Ventricle size: summary of evidence*

Authors & Year	Study Description	Data Class, Quality, & Reasons	Conclusion
Chakraborty et al., 2008	Single-center, 10-yr retrospective review of pts w/ MMC, excluding pts in whom primary closure was performed elsewhere. Shunt placed for symptomatic hydrocephalus, severe hydrocephalus, or progression of ventriculomegaly after closure. 54 cases included; shunt required in 28 (52%). Evaluated shunt insertion, complications, & clinical outcomes.	Class III Single center, retrospective, single cohort. "Increasing ventriculomegaly assessed by a neuroradiologist w/ the neurosurgeon. No specific imaging measurement was used to define hydrocephalus."	Shunt insertion rates in pts w/ MMC lower than previously published results (& similar to those of in utero closure) when allowing mild ventriculomegaly.
Kim et al., 2000	32 children w/ ETV. Mean follow-up: 19 mos. Postprocedural neuroimaging studies available in 29 pts. Outcomes: good in 21 pts & poor in 8 pts. Ventricle size, edema, widening of sub-arachnoid space, surgical changes in 3rd ventricle examined. Floor cine-MR findings studied btwn the 2 outcome groups.	Class III Retrospective study.	Good outcomes group: In 11 of 16 pts there was a decrease in ventricle size 1 mo postop. In 5 of 16 pts only minimal changes were observed. Ventricle size tended to decrease w/ time. Changes in ventricle size could not predict surgical outcome completely alone. No correlation.
St. George et al., 2004	Single-center, 13 consecutive pts w/ hydrocephalus undergoing ETV studied. MR images were reviewed, & ventricle vol calculated. Preop vol 207 cm ³ , 1 wk 120 cm ³ , 3 mos 104 cm ³ , 6 mos 119 cm ³ , 12 mos 146 cm ³ , 24 mos 185 cm ³ (skewed because they did not have many 24-mo follow-ups, so it was overly influenced by increases in 13 pts who originally had large ventricles). Decrease in size was more rapid in those pts. w/ larger ventricles.	Class III Single center, no comparison group. Did not compare use of volumetric evaluation in pts receiving shunts.	Pts w/ moderate ventriculomegaly had a less steep decrease in ventricle size in the first 6 mos after ETV than pts w/ large preop ventricles. Steady-state vols were larger than normal.
Warf et al., 2009	93 pts, spina bifida. Assessment of development & ventricle size. 55 pts underwent ETV w/ CPC; 19 pts received VP shunts; 19 received no Tx.	Class III Retrospective study. Nonrandomized, noncontrolled.	No Tx group showed better development than treated group. There was better receptive communication in the ETV w/ CPC group than in the VP shunt group (p = 0.02). No difference in ventricle vol between the ETV w/ CPC & VP shunt groups.
Buxton et al., 1998	Outcomes & reasons for failure in ETVs performed in children <1 yr old: 27 total pts. Postop ventricle size & flow through stoma documented. Comparison was performed between successes & failures (21 pts, 77% of procedures).	Class III Retrospective review of prospectively acquired data.	Postop ventricle size was not an indicator of success or failure. Size does not matter.
Kulkarni et al., 2000	Retrospective study of FOR (measure of ventricle size) change post-ETV in comparing successes & failures.	Class III Retrospective case series. Images evaluated by 4 observers, 2 blinded & 2 unblinded, looking at ventricle size, flow void, periventricular edema, & CSF in subarachnoid space. Comparison w/ 2-tailed t-test	ETV failures: mean postop reduction in ventricle size was 7%. ETV clinical successes: mean postop reduction in ventricle size was 16% (reduction significantly greater). Decreased FOR in all pts. Slightly more in the successful cases, but not when compared to normal ventricles. (Ventricles do not return to normal even after successful ETV.)

* MMC = myelomeningocele; pts = patients; Tx = treatment.

alone, as a demonstration of treatment effectiveness, is not supported by the available evidence. Unfortunately, there are no other direct methods currently in general use.

Certainly, developmental progress is worth monitoring, but this is more difficult to accomplish for routine post-surgical evaluations.

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This systematic review and evidence-based guideline demonstrates that the objective measurement of ventricle size by simple methods such as the frontal and occipital horn ratio (FOR) has not proven to be a reliable benchmark of effectiveness. Clinical outcome ascertained by the neurosurgeon and team is still the most accepted and useful evaluation, surpassing other more “objective” standards.

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