Hydrocephalus Clinical Research Network

- The Impact of Neuropsychiatric Symptoms in Perceived Quality of Life in Patients With Progressive Supranuclear Palsy
- Complications of ventriculoperitoneal shunting: Is there further need of more evidence-based approach to care?
- Surgeon perceptions and utilization of evidence-based medicine
- Ventriculitis characteristics and outcomes (VELCRO): an international retrospective cohort study
- Neurophysiology of Atypical Parkinsonian Syndromes: A Study Group Position Paper
- Complex shunt system comparison: an observational study by the Hydrocephalus Clinical Research Network
- Risk factors and influence on neurodevelopmental outcomes of neonatal seizures in very low birth weight infants based on nationwide cohort
- Radiological Predictors of Cognitive Impairment in Paediatric Brain Tumours Using Multiparametric Magnetic Resonance Imaging: A Review of Current Practice, Challenges and Future Directions

http://hcrn.org

The Hydrocephalus Clinical Research Network (HCRN) grew out of the frustration of parents and doctors struggling to save children from a sentence of life-long disability. This multi-site collaboration will overcome the obstacles that have stymied previous research efforts: too few patients to study in any one hospital, uncoordinated research, and under-staffed studies.

This is an exciting opportunity to make a positive impact in treating this condition.

This prospectus provides highlights of the business plan and five-year funding requirements. Our goal is to raise $4,000,000 for the first five years of operations. We've already secured over 37.5% of this goal from private philanthropy, and hospital surgery departments. But we still need others to step up and fill the gap to make sure the research progresses. Every dollar invested supports efforts to improve treatments and outcomes for kids suffering from hydrocephalus.

Our vision is that, in 5 to 10 years, doctors will use HCRN research-based evidence to improve the diagnosis, treatment and outcomes of hydrocephalus patients and that these patients will live longer, more trouble-free lives than they do at present. Over that same timeframe, we envision greater attention and financial resources directed toward hydrocephalus research and treatment.

The Problem: Lack of Research.

While shunts have been life-saving, they have also created the illusion of a cure.

This illusion has delayed research. In addition, not enough hydrocephalus patients are seen in any one hospital, which makes it harder to collect the volume of study participants needed to answer important scientific questions. These realities have two unfortunate, and interrelated, consequences. First, there is no standard of care. Practices for diagnosing and treating hydrocephalus vary, often dramatically, from hospital to hospital and even from specialist to specialist. Second, the body of medical and practical research about the condition is fragmented and inconclusive, which makes it harder for practitioners to improve patients' outcomes.

Hydrocephalus research is clearly needed. A recent paper by an HCRN researcher, Dr. Tamara Simon, found that, for each year investigated in her study (1997, 2000, 2003), there were 38,200-39,900

admissions, 391,000-433,000 hospital days, and total hospital charges of $1.4-2.0 billion for pediatric hydrocephalus. These are just in the inpatient costs alone! One might expect that, given the immense economic and social costs of the condition, federal research dollars would be directed toward solving this medical riddle. Sadly, this is not the case. There were only five active NIH grants totaling $3.2M from 2000-2005 specifically for studying hydrocephalus. In essence, the condition is being ignored at a national research level. This climate has made it even more difficult to attract researchers and increase the scientific base of knowledge.

National advocacy groups like the Hydrocephalus Association and others are to be commended for trying to draw greater attention to the problem. However, the lack of a coordinated research effort has forestalled a deeper understanding of what we can do, and do quickly, to make a dramatic improvement on the outcomes and lives of these kids. That is where the HCRN steps in.

Imagine pediatricians, neurosurgeons, nurses and therapists equipped with scientific evidence of treatments that critically improve the long term outcomes of kids suffering from hydrocephalus. Imagine that promising techniques can be quickly, ethically, and safely studied by the world’s leading hydrocephalus researchers using larger patient populations. Imagine that medical providers, equipped with this new knowledge, make shunt surgery-related infections a thing of the past. Or that premature infants with brain hemorrhages will not automatically develop hydrocephalus, as virtually all now do, but instead may live normal, healthy lives.

Imagine research that shows ways of reducing the suffering of kids and their families. This is the goal of the HCRN.

Studies

2016

Kulkarni et al., report prospective, multicenter results from the Hydrocephalus Clinical Research Network (HCRN) to provide the most accurate determination of morbidity, complication incidence, and efficacy of ETV in children and to determine if intraoperative predictors of ETV success add substantially to preoperative predictors.

All children undergoing a first ETV (without choroid plexus cauterization) at 1 of 7 HCRN centers up to June 2013 were included in the study and followed up for a minimum of 18 months. Data, including detailed intraoperative data, were prospectively collected as part of the HCRN's Core Data Project and included details of patient characteristics, ETV failure (need for repeat hydrocephalus surgery), and, in a subset of patients, postoperative complications up to the time of discharge.

Three hundred thirty-six eligible children underwent initial ETV, 18.8% of whom had undergone shunt placement prior to the ETV. The median age at ETV was 6.9 years (IQR 1.7-12.6), with 15.2% of the study cohort younger than 12 months of age. The most common etiologies were aqueductal stenosis (24.8%) and midbrain or tectal lesions (21.2%). Visible forniceal injury (16.6%) was more common than previously reported, whereas severe bleeding (1.8%), thalamic contusion (1.8%), venous injury (1.5%), hypothalamic contusion (1.5%), and major arterial injury (0.3%) were rare. The most common postoperative complications were CSF leak (4.4%), hyponatremia (3.9%), and pseudomeningocele (3.9%). New neurological deficit occurred in 1.5% cases, with 0.5% being permanent. One hundred forty-one patients had documented failure of their ETV requiring repeat hydrocephalus surgery during

follow-up, 117 of them during the first 6 months postprocedure. Kaplan-Meier rates of 30-day, 90-day, 6-month, 1-year, and 2-year failure-free survival were 73.7%, 66.7%, 64.8%, 61.7%, and 57.8%, respectively. According to multivariate modeling, the preoperative ETV Success Score (ETVSS) was associated with ETV success ($p < 0.001$), as was the intraoperative ability to visualize a “naked” basilar artery ($p = 0.023$).

The authors' documented experience represents the most detailed account of ETV results in North America and provides the most accurate picture to date of ETV success and complications, based on contemporaneously collected prospective data. Serious complications with ETV are low. In addition to the ETVSS, visualization of a naked basilar artery is predictive of ETV success [1)]

The Hydrocephalus Clinical Research Network (HCRN) conducted a comprehensive prospective observational study of hydrocephalus management, the aim of which was to isolate specific risk factors for shunt failure.

The study followed all first-time shunt insertions in children younger than 19 years at 6 HCRN centers. The HCRN Investigator Committee selected, a priori, 21 variables to be examined, including clinical, radiographic, and shunt design variables. Shunt failure was defined as shunt revision, subsequent endoscopic third ventriculostomy, or shunt infection. Important a priori-defined risk factors as well as those significant in univariate analyses were then tested for independence using multivariate Cox proportional hazard modeling.

A total of 1036 children underwent initial CSF shunt placement between April 2008 and December 2011. Of these, 344 patients experienced shunt failure, including 265 malfunctions and 79 infections. The mean and median length of follow-up for the entire cohort was 400 days and 264 days, respectively. The Cox model found that age younger than 6 months at first shunt placement (HR 1.6 [95% CI 1.1-2.1]), a cardiac comorbidity (HR 1.4 [95% CI 1.0-2.1]), and endoscopic placement (HR 1.9 [95% CI 1.2-2.9]) were independently associated with reduced shunt survival. The following had no independent associations with shunt survival: etiology, payer, center, valve design, valve programmability, the use of ultrasound or stereotactic guidance, and surgeon experience and volume. CONCLUSIONS This is the largest prospective study reported on children with CSF shunts for hydrocephalus. It confirms that a young age and the use of the endoscope are risk factors for first shunt failure and that valve type has no impact. A new risk factor-an existing cardiac comorbidity-was also associated with shunt failure [2)].

Dr. Jay Riva-Cambrin is an associate professor and pediatric neurosurgeon at the University of Utah and Primary Children’s Hospital. Since the MYI award, Dr. Riva-Cambrin has received tenure and is Director of the Pediatric Neurosurgery Fellowship Program at the University of Utah School of Medicine. He is also the Medical Director of the Neurotrauma Unity at Primary Children’s Hospital and is a primary investigator for the Hydrocephalus Clinical Research Network. Dr. Riva-Cambrin received a BSc in pharmacology and a MD from the University of Alberta and an MSc in clinical epidemiology from the University of Toronto.

1)

Kulkarni AV, Riva-Cambrin J, Holubkov R, Browd SR, Cochrane DD, Drake JM, Limbrick DD, Rozzelle CJ, Simon TD, Tamber MS, Wellons JC, Whitehead WE, Kestle JR; Hydrocephalus Clinical Research Network.. Endoscopic third ventriculostomy in children: prospective, multicenter results from the Hydrocephalus Clinical Research Network. J Neurosurg Pediatr. 2016 Oct;18(4):423-429. PubMed

PMID: 27258593.

2)

Riva-Cambrin J, Kestle JR, Holubkov R, Butler J, Kulkarni AV, Drake J, Whitehead WE, Wellons JC 3rd, Shannon CN, Tamber MS, Limbrick DD Jr, Rozzelle C, Browd SR, Simon TD; Hydrocephalus Clinical Research Network. Risk factors for shunt malfunction in pediatric hydrocephalus: a multicenter prospective cohort study. J Neurosurg Pediatr. 2016 Apr;17(4):382-90. doi: 10.3171/2015.6.PEDS14670. Epub 2015 Dec 4. PubMed PMID: 26636251.