JNS

CLINICAL ARTICLE

The clinical spectrum of hydrocephalus in adults: report of the first 517 patients of the Adult Hydrocephalus Clinical Research Network registry

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OBJECTIVE The authors describe the demographics and clinical characteristics of the first 517 patients enrolled in the Adult Hydrocephalus Clinical Research Network (AHCRN) during its first 2 years.

METHODS Adults ≥ 18 years were nonconsecutively enrolled in a registry at 6 centers. Four categories of adult hydrocephalus were defined: transition (treated before age 18 years), unrecognized congenital (congenital pattern, not treated before age 18 years), acquired (secondary to known risk factors, treated or untreated), and suspected idiopathic normal pressure hydrocephalus (iNPH) (≥ age 65 years, not previously treated). Data include etiology, symptoms, examination findings, neuropsychology screening, comorbidities, treatment, complications, and outcomes. Standard evaluations were administered to all patients by trained examiners, including the Montreal Cognitive Assessment, the Symbol Digit Modalities Test, the Beck Depression Inventory–II, the Overactive Bladder Questionnaire Short Form symptom bother, the 10-Meter Walk Test, the Boon iNPH gait scale, the Lawton Activities of Daily Living/Instrumental Activities of Daily Living (ADL/IADL) questionnaire, the iNPH grading scale, and the modified Rankin Scale.

RESULTS Overall, 517 individuals were enrolled. Age ranged from 18.1 to 90.7 years, with patients in the transition group (32.7 ± 10.0 years) being the youngest and those in the suspected iNPH group (76.5 ± 5.2 years) being the oldest. The proportion of patients in each group was as follows: 16.6% transition, 26.5% unrecognized congenital, 18.2% acquired, and 38.7% suspected iNPH. Excluding the 86 patients in the transition group, who all had received treatment, 79.4% of adults in the remaining 3 groups had not been treated at the time of enrollment. Patients in the suspected iNPH group had the poorest performance in cognitive evaluations, and those in the unrecognized congenital group had the best performance. The same pattern was seen in the Lawton ADL/IADL scores. Gait velocity was lowest in patients in the suspected iNPH group. Categories that had the most comorbidities (suspected iNPH) or etiologies of hydrocephalus that directly cause neurological injury (transition, acquired) had greater degrees of impairment compared to unrecognized congenital, which had the fewest comorbidities or etiologies associated with neurological injury.

ABBREVIATIONS ADL/IADL = Activities of Daily Living/Instrumental Activities of Daily Living; AHCRN = Adult Hydrocephalus Clinical Research Network; BDI-II = Beck Depression Inventory–II; HCRN = Hydrocephalus Clinical Research Network; iNPH = idiopathic normal pressure hydrocephalus; iNPHGS = iNPH grading scale; MoCA = Montreal Cognitive Assessment; mRS = modified Rankin Scale; OAB-q = Overactive Bladder Questionnaire; SDMT = Symbol Digit Modalities Test; SiNPH = suspected iNPH.

SUBMITTED December 31, 2018. **ACCEPTED** February 25, 2019.
INCLUDE WHEN CITING Published online May 24, 2019; DOI: 10.3171/2019.2.JNS183538.

CONCLUSIONS The clinical spectrum of hydrocephalus in adults comprises more than iNPH or acquired hydrocephalus. Only 39% of patients had suspected iNPH, whereas 43% had childhood onset (i.e., those in the transition and unrecognized congenital groups). The severity of symptoms and impairment was worsened when the etiology of the hydrocephalus or complications of treatment caused additional neurological injury or when multiple comorbidities were present. However, more than half of patients in the transition, unrecognized congenital, and acquired hydrocephalus groups had minimal or no impairment. Excluding the transition group, nearly 80% of patients in the AHCRN registry were untreated at the time of enrollment. A future goal for the AHCRN is to determine whether patients with unrecognized congenital and acquired hydrocephalus need treatment and which patients in the suspected iNPH cohort actually have possible hydrocephalus and should undergo further diagnostic testing. Future prospective research is needed in the diagnosis, treatment, outcomes, quality of life, and macroeconomics of all categories of adult hydrocephalus.

https://thejns.org/doi/abs/10.3171/2019.2.JNS183538

KEYWORDS hydrocephalus; idiopathic normal pressure hydrocephalus; transition; disability; registry

Hydrocephalus can affect patients at any age or any stage of life. The demographics and etiologies of hydrocephalus in children are well known;[8,27] however, the characteristics of the adult population have not been well described. Much of the literature focuses on idiopathic normal pressure hydrocephalus (iNPH) and less on acquired hydrocephalus, the transition population, or adults with congenital hydrocephalus that is not recognized or treated before the age of 18 years.

The care for the adult hydrocephalus population is fragmented. Few academic medical centers have programs dedicated to the care of these patients.[30] Consequently, most are cared for by neurosurgeons and neurologists who are familiar with hydrocephalus but may not have the clinical expertise necessary to care for the full spectrum of adults with hydrocephalus.

The Adult Hydrocephalus Clinical Research Network (AHCRN) was founded in 2014, modeled after the Hydrocephalus Clinical Research Network (HCRN), which has focused its research on issues vital to the safe and successful treatment of children with hydrocephalus (http://www.hcrn.org). The AHCRN and HCRN receive financial support from the Hydrocephalus Association, the largest patient-advocacy organization in the US for persons with hydrocephalus and their families. The first project of the AHCRN is a patient registry in which adults with all types of hydrocephalus are seen and evaluated with a standard set of examination methods.

The purpose of the present study was to describe the demographics and characteristics of the first 517 patients enrolled at the 6 centers that were in the AHCRN in its first 2 years. Patients in the registry are followed longitudinally; however, this report only describes their characteristics at the time of enrollment.

Methods

AHCRN Structure

The AHCRN was founded for the purpose of increasing awareness and understanding of adult hydrocephalus, accelerating research, and improving treatments for adults with hydrocephalus (http://www.ahcrn.org/about-ahcrn/). During the period of enrollment for the patients reported in this study, the AHCRN participating centers (and primary investigators) included the following: Cleveland Clinic (M.G.L., S.J.N.), Sinai Hospital of Baltimore (M.A.W.), University of British Columbia (T.J.Z.), University of Calgary (M.G.H.), University of Washington (M.A.W.), and Weill Cornell (N.R.). The Data Coordinating Center is at the University of Utah (R.H.).

Hydrocephalus Categories

Four categories of adult hydrocephalus were defined: 1) transition—patients who were treated for hydrocephalus of any etiology before the age of 18 years; 2) unrecognized congenital—patients with imaging features, or enlarged head circumference, or both, determined to be consistent with congenital hydrocephalus but who were not recognized or treated before the age of 18 years; 3) acquired—patients with hydrocephalus secondary to known risk factors (e.g., subarachnoid hemorrhage, brain tumor), whether treated or untreated; and 4) suspected iNPH (SiNPH)—patients age ≥ 65 years referred for the evaluation of iNPH who had not previously received surgical treatment.

Inclusion Criteria and Registry Enrollment

The registry was IRB approved at all centers. Signed consent was obtained from all individuals or their legally authorized representatives. Inclusion criteria were age 18 years or older and either 1) the diagnosis or clinical suspicion of hydrocephalus and an imaging study with an Evans ratio ≥ 0.3, or 2) except for the SiNPH group, the patient had been previously treated with surgery for hydrocephalus. Patients were enrolled prospectively; however, not all patients seen at each center could be enrolled. Due to the amount of effort required for enrollment, evaluation, and data entry, and for follow-up, the AHCRN primary investigators intentionally chose to enroll fewer patients so that a complete data set would be available for each patient, rather than risk a larger enrollment with incomplete data that would be less accurate. The approach to enrollment varied among centers. For example, some attempted to enroll all eligible patients seen on specific clinic days, while others approached eligible patients consecutively on a given day until an enrollment goal was reached. Aside from the inclusion and exclusion criteria, no other prescreening of patients was performed.

Registry Features

The registry includes entry criteria, demographics, hydrocephalus category and etiology, medical history,

comorbidities, medications, symptoms, examination findings, previous and current surgical procedures (shunt or endoscopic third ventriculostomy), and imaging studies.

Standard evaluations were administered to all subjects. To ensure consistency of the testing, all examiners were trained and required to demonstrate competency for the administration and interpretation of the evaluations. Upon enrollment, the following were administered: Lawton Activities of Daily Living/Instrumental Activities of Daily Living (ADL/IADL) questionnaire, iNPH grading scale (iNPHGS), modified Rankin Scale (mRS), and Overactive Bladder Questionnaire (OAB-q) Short Form symptom bother.[6,13,17,24] Gait evaluations included 10-Meter Walk Test (time, number of steps for 10 m and for a 180-degree turn) and the Boon iNPH gait scale.[3] The core neuropsychology battery included the Montreal Cognitive Assessment (MoCA), the Symbol Digit Modalities Test (SDMT), and the Beck Depression Inventory–II (BDI-II).[2,21,23,26,28]

Other information collected, but not reported here, includes complications of treatment, the shunt configuration (ventriculoperitoneal, ventriculoatrial, ventriculopleural), the make and model of the shunt valve components when known, and the setting of programmable shunts.

Statistical Analysis

This analysis was treated as descriptive, with exploratory pairwise comparisons among the 4 categories of hydrocephalus. Binary and unordered categorical factors were compared between categories using the Pearson chi-square test; the Fisher's exact test was used when factors were rare. The Mantel-Haenszel version of the chi-square test was used for ordered categorical factors (education level). We used t-tests to compare continuous factors between categories, except for scores with highly skewed distributions (Lawton ADL/IADL total, Boon gait scale, and OAB-q Short Form symptom bother scores), which were compared using the rank-based Mann-Whitney U-test. Mean values are presented ± SD.

Results

All results are reported at the time of enrollment. Between November 19, 2014, and February 1, 2017, 517 individuals were enrolled. The consent rate was 99.6%. Table 1 contains demographic information stratified by hydrocephalus category and for the entire registry. Age at enrollment, also shown in Fig. 2 (specifically, see Fig. 2D), ranged from 18.1 to 90.7 years, with patients in the transition group (mean 32.7 ± 10.0 years) younger than those in all other groups and patients in the SiNPH group (mean 76.5 ± 5.2 years) older than those in all other groups. With regard to sex, 42% were female and 58% were male. More than 90% the patients were white, while 5.0% were Asian and 1.7% were black.

Hydrocephalus Category

Table 1 contains the hydrocephalus category for the entire registry and by center. For the entire registry, the proportion of patients was 16.6% in the transition category, 26.5% in the unrecognized congenital category, 18.2% in the acquired category, and 38.7% in the SiNPH category. Variability in the proportion of categories among centers is seen. Notably, two centers saw very few or no transition and unrecognized congenital patients, whereas all other centers enrolled patients in all categories.

Hydrocephalus Etiology

Tables 2–4 contain the etiologies of hydrocephalus by category. The etiologies differ among the 4 categories. By definition, the SiNPH etiology is idiopathic, and only the presence or absence of DESH (disproportionately enlarged subarachnoid space hydrocephalus) was recorded, and was present in only 35% (70/200).[12]

Treatment Status

Table 5 contains the treatment status by category and for the entire registry. By definition, all patients in the transition group had been treated, whereas none in the SiNPH group had been treated. Overall, approximately one-third of patients had received treatment prior to the time of enrollment, meaning that two-thirds had not received treatment.

Symptoms and Examination Findings

Cognitive and Psychological Evaluation

Figure 1A shows the MoCA scores. Compared to all other categories, patients with SiNPH had the lowest mean score (20.6 ± 5.1), and patients with unrecognized congenital hydrocephalus had the highest mean score (25.3 ± 3.1). Figure 1B shows the SDMT scores. Similarly, patients with SiNPH had the lowest mean score (23.4 ± 10.8) compared to all other categories. Figure 1C shows the BDI-II scores. No significant difference was seen in the mean or median scores across categories.

Gait and Mobility Evaluation

The mean velocity for the 10-Meter Walk is shown in Fig. 1D. Gait velocity was not measured for patients who were unable to walk. As expected, velocity is significantly slower in patients in the SiNPH group (0.77 ± 0.33 m/sec) compared to all other categories. Gait was also assessed by the Boon gait score, which was developed for people with iNPH, shown in Fig. 1E.[3] Lower scores are better. The Boon gait score was not recorded for patients who were permanently unable to walk, such as those with spina bifida or spinal cord injury. The SiNPH group had the highest score (mean 9.3 ± 6.8)—i.e., the worst gait—compared to all other groups, and the unrecognized congenital group had the lowest score (mean 2.8 ± 5.6) compared to all other groups.

Urinary Symptoms

The OAB-q Short Form symptom bother scores are shown in Fig. 1F.[6] Lower scores are better. As expected, patients with SiNPH had the highest score (29.9 ± 24.1) compared to all other categories. Perhaps unexpectedly, patients in the transition category had the lowest score (12.2 ± 19.2); however, the influence on the score of urinary conduits, intermittent catheterization, or chronic catheterization, as are often used for patients with spina bifida or myelomeningocele, was not recorded.

TABLE 1. Demographic information and highest education level at the time of enrollment by category and enrollment at each of the 6 study sites by category

Variable	Transition (n = 86)	Unrecognized Congenital (n = 137)	Acquired (n = 94)	Suspected iNPH (n = 200)	Overall (n = 517)
Sex					
Statistical significance	A*, SiNPH***	SiNPH*	T*	T***, UC*	
Female	50 (58.1%)	63 (46.0%)	40 (42.6%)	65 (32.5%)	218 (42.2%)
Race					
Statistical significance	UC*, A*	T*, A*	T*, UC*, SiNPH**	A**	
White	79 (91.9%)	126 (92.0%)	78 (83.0%)	185 (92.5%)	468 (90.5%)
Asian	1 (1.2%)	7 (5.1%)	11 (11.7%)	7 (3.5%)	26 (5.0%)
Black	2 (2.3%)	0 (0.0%)	2 (2.1%)	5 (2.5%)	9 (1.7%)
Other	3 (3.5%)	0 (0.0%)	2 (2.1%)	0 (0.0%)	5 (1.0%)
Missing	1 (1.2%)	4 (2.9%)	1 (1.1%)	3 (1.5%)	9 (1.7%)
Age					
Statistical significance	UC***, A***, SiNPH***	T***, SiNPH***	T***, SiNPH***	T***, UC***, A***	
Age at consent, years	32.7 ± 10.0	54.3 ± 14.2	57.3 ± 16.9	76.5 ± 5.2	59.8 ± 19.3
Age range, years	18.1–62.0	19.9–80.9	20.1–90.7	64.9–87.6	18.1–90.7
Highest education level					
Statistical significance	UC***, A***, SiNPH***	T***	T***	T***	
Less than high school	11 (12.8%)	9 (6.6%)	3 (3.2%)	20 (10.0%)	43 (8.3%)
High school/GED	41 (47.7%)	26 (19.0%)	18 (19.1%)	49 (24.5%)	134 (25.9%)
2-year college	11 (12.8%)	38 (27.7%)	9 (9.6%)	31 (15.5%)	89 (17.2%)
Bachelor's degree	9 (10.5%)	32 (23.4%)	19 (20.2%)	33 (16.5%)	93 (18.0%)
Master's/professional degree	0 (0.0%)	12 (8.8%)	13 (13.8%)	36 (18.0%)	61 (11.8%)
Missing	14 (16.3%)	20 (14.6%)	32 (34.0%)	31 (15.5%)	97 (18.8%)
Enrollment by study site (category %)					
Cleveland Clinic	4 (4.7%)	5 (5.8%)	17 (19.8%)	60 (69.8%)	86
Sinai Hospital of Baltimore	3 (9.4%)	12 (37.5%)	5 (15.6%)	12 (37.5%)	32
University of British Columbia	21 (23.1%)	15 (16.5%)	32 (35.2%)	23 (25.3%)	91
University of Calgary	31 (14.2%)	97 (44.5%)	19 (8.7%)	71 (32.6%)	218
University of Washington	27 (42.9%)	8 (12.7%)	17 (27.0%)	11 (17.5%)	63
Weill Cornell	0 (0%)	0 (0%)	4 (14.8%)	23 (85.2%)	27
Total enrolled in the registry	86 (16.6%)	137 (26.5%)	94 (18.2%)	200 (38.7%)	517

Values are presented as the number (%) of patients or as the mean ± SD and range.
*p < 0.05, ** p < 0.01, ***p < 0.001 for pairwise comparisons by t-test (age) or appropriate chi-square test (all other variables). Each comparison is denoted by a code, where T = transition, UC = unrecognized congenital, A = acquired, and SiNPH = suspected iNPH. For example, T** denotes that p < 0.01 comparing distributions of a factor with patients in the transition category.

Outcome Scales

The Lawton ADL/IADL total score, iNPHGS total score, and mRS score are shown in Fig. 2A–C. Lower scores reflect better function for each of these scales. For the Lawton ADL/IADL score, compared to all other categories, unrecognized congenital patients had the lowest mean score (2.2 ± 3.4), and SiNPH patients had the highest mean score (7.4 ± 7.2). For the iNPHGS and the mRS, unrecognized congenital patients again had the lowest mean scores (iNPHGS score 2.3 ± 2.3; mRS score 1.2 ± 1.1) compared to all other groups, and SiNPH patients had mean scores (iNPHGS score 5.6 ± 2.4; mRS score 2.5 ± 1.1) higher than patients in the transition and unrecognized congenital groups but not the acquired group.

Comorbidities

Table 6 lists the comorbidities. Patients in the unrecognized congenital group were most likely to have no comorbidities (40.9%) compared to those in the SiNPH group (15.5%; p < 0.001). The role of comorbidities complicating the assessment and treatment of SiNPH has been previously described.[18] The prevalence of all cardiovascular risk factors was highest in the SiNPH group, with the exception of stroke, which was highest in the acquired group, but not significantly different from that in the SiNPH group. The acquired category included many patients with hydrocephalus secondary to stroke or brain hemorrhage. Similarly, cervical or lumbar spinal stenosis was highest in SiNPH, which probably represents the higher incidence

TABLE 2. Hydrocephalus etiologies for the transition category containing 86 patients

Etiology	No. of Patients (%)
Myelomeningocele	29 (33.7%)
Aqueductal stenosis	13 (15.1%)
IVH of prematurity	8 (9.3%)
Postinfectious	6 (7.0%)
ICH w/ IVH except prematurity	4 (4.7%)
Craniosynostosis	4 (4.7%)
Posterior fossa tumor	4 (4.7%)
Subarachnoid hemorrhage	2 (2.3%)
Midbrain tumor or lesion	2 (2.3%)
Arachnoid cyst	1 (1.2%)
Dandy Walker	1 (1.2%)
Supratentorial tumor	1 (1.2%)
Encephalocele	1 (1.2%)
Other	3 (3.5%)
Unknown	15 (17.4%)

ICH = intracerebral hematoma; IVH = intraventricular hemorrhage.

of these disorders in the elderly population. Epilepsy was most common in the transition and acquired groups, probably reflecting the coexisting brain injury seen in both these groups. Only 1% of SiNPH patients had epilepsy, which was lower than the 2.3% rate in presurgical patients and 4.5% rate in shunt-treated patients reported from the Swedish Hydrocephalus Quality Registry.[16]

Discussion

This is the first report of a large, multicenter cohort of patients with all categories of adult hydrocephalus who were enrolled prospectively and assessed using the same standard evaluations performed by trained examiners. Because all the study sites are academic specialty centers and because the registry enrollment includes only a portion of all patients seen, the results and trends identified may or may not reflect the broader population of adult hydrocephalus in the US and Canada; however, the results yield important insight into the similarities, differences, and needs across all 4 adult hydrocephalus categories.

TABLE 3. Hydrocephalus etiologies for the unrecognized congenital category containing 137 patients

Etiology	No. of Patients (%)
Aqueductal stenosis	67 (48.9%)
Aqueductal pattern	24 (17.5%)
Arachnoid cyst	6 (4.4%)
Midbrain tectal lesion	1 (0.7%)
Other	1 (0.7%)
Classic classification	
Noncommunicating	75 (54.7%)
Communicating	55 (40.1%)
Unknown	7 (5.1%)

TABLE 4. Hydrocephalus etiologies for the acquired category of hydrocephalus containing 94 patients

Etiology	Total No. (%)	Subtotal No. (%)
Brain tumor	30 (31.9%)	
Benign		23/30 (76.7%)
Malignant		7/30 (23.3%)
Intraventricular adhesion or web or colloid cyst	14 (14.9%)	
Nontraumatic SAH	12 (12.8%)	
Head trauma	10 (10.6%)	
Other masses or vascular anomalies	8 (8.5%)	
Meningitis/ventriculitis	6 (6.4%)	
Bacterial		4/6 (66.7%)
Unknown		2/6 (33.3%)
Craniotomy or suboccipital (not TBI)	5 (5.3%)	
Nontraumatic ICH	3 (3.2%)	
Cerebellar hemorrhage or infarction	3 (3.2%)	
Brain abscess	1 (1.1%)	
Chronic SDH	1 (1.1%)	
Other	11 (11.7%)	
Encephalitis of unknown etiology		3/11 (27.3%)
Idiopathic		2/11 (18.2%)
Acquired obstructive, compensated		1/11 (9.1%)
Aqueductal stenosis		1/11 (9.1%)
CNS vasculitis		1/11 (9.1%)
Postirradiation atrophy		1/11 (9.1%)
Cerebral ischemia due to small vessel disease		1/11 (9.1%)
Neurodegeneration/possible Alzheimer dementia		1/11 (9.1%)

SAH = subarachnoid hemorrhage; SDH = subdural hematoma; TBI = traumatic brain injury.

The results demonstrate that the adult hydrocephalus population consists of more than iNPH and acquired hydrocephalus. While 39% of patients had SiNPH, 43% had hydrocephalus that arose in childhood (transition, unrecognized congenital). The clinical profiles of adults and young adults with previously treated or untreated hydrocephalus from childhood have not previously been explored in such a large multicenter cohort.

Transition

The transition category includes patients with significant impairment and comorbidities, as well as patients who are normal. This range reflects the known patterns in pediatric hydrocephalus, in which the initial injury or disease process (i.e., etiology) that results in hydrocephalus for many patients also can cause neurological impairment directly. For example, 25.6% of transition patients had epilepsy, which adversely influences quality of life measures

TABLE 5. Treatment status at the time of enrollment for all categories and for all categories excluding the transition category

Treatment	Hydrocephalus Category				Overall (n = 517)	Overall, Excluding Transition (n = 431)
	Transition (n = 86)	Unrecognized Congenital (n = 137)	Acquired (n = 94)	Suspected iNPH (n = 200)		
Shunt	82 (95.3%)	29 (21.2%)	28 (29.8%)	0 (0.0%)	139 (26.9%)	57 (13.2%)
ETV	12 (14.0%)	28 (20.4%)	12 (12.8%)	0 (0.0%)	52 (10.1%)	40 (9.3%)
Any treatment	86 (100%)	51 (37.2%)	38 (40.4%)	0 (0.0%)	175 (33.9%)	89 (20.6%)

ETV = endoscopic third ventriculostomy.

in pediatric hydrocephalus.[15] The highest educational level attained by patients in the transition category (Table 1) was significantly lower than all other groups, which probably reflects intellectual developmental delay as a result of the etiology of the hydrocephalus or its treatment-related complications. The adverse effect of hydrocephalus on educational attainment has been demonstrated in young adults with spina bifida in the Netherlands, as only 50% of those with hydrocephalus completed regular secondary education, compared to 92% of those without hydrocephalus.[1]

Unrecognized Congenital

Those in the unrecognized congenital group had the best scores for function and the fewest comorbidities, reflecting the fact that many were normal adults with incidentally discovered hydrocephalus who were asymptomatic or minimally symptomatic. As a rule, the etiologies of hydrocephalus in this category (e.g., those with aqueductal stenosis or idiopathic communicating hydrocephalus) were "simpler" or more benign than the etiologies in the transitional category. Thus, any neurological impairment arose mainly from the hydrocephalus, especially for those patients who were untreated.

Notably, 63% of unrecognized congenital patients were untreated. An important unanswered question is whether asymptomatic patients should be managed conservatively and monitored longitudinally until the emergence of symptoms, or if they should undergo diagnostic testing (e.g., intracranial pressure [ICP] monitoring) to determine whether craniospinal compliance is impaired and surgery is indicated. Some of the AHCRN centers have these patients undergo formal neuropsychological testing to establish a baseline for future comparison, as cognitive impairment can be an early symptom of decompensating hydrocephalus in this population.[5,11,22] Equipoise exists among clinicians with respect to the need to treat or not treat asymptomatic hydrocephalus, and a prospective trial with appropriate controls, precautions, and outcome measures is warranted.

The fact that many of the unrecognized congenital adults are asymptomatic and are presumed to have had asymptomatic untreated hydrocephalus when they were children raises the question of whether a more conservative approach to the decision for shunt surgery for children with asymptomatic hydrocephalus could be considered, or, in the care of children with treated hydrocephalus, whether a greater degree of ventricular enlargement could be tolerated. The challenge is that for hydrocephalus in childhood, it currently is not possible to predict whether the long-term outcomes of conservative management would be better than the long-term outcomes of early treatment and its potential complications. The HCRN is currently evaluating the impact of ventricular size on neurocognitive outcome in children (ClinicalTrials.gov identifier: NCT01797627).

Acquired

The results for patients with acquired hydrocephalus seem consistent with conventional wisdom, as many have significant neurological impairment that is a result of the injury or process that resulted in ventricular enlargement. In this respect, the acquired hydrocephalus category is similar to that of the transition category. However, 40% of patients in the acquired category had been treated, whereas 60% had not. The overriding question for the untreated patients is whether the ventriculomegaly is due to hydrocephalus (i.e., impaired CSF circulation or resorption) as opposed to tissue loss from the underlying causes. Evaluation of the need for shunt surgery is often challenging, as the underlying cause may have created permanent neurological injury responsible in whole or in part for the patient's symptoms and impairment. Further research on methods to determine the need for hydrocephalus treatment, as well as on the incremental gains of such treatment on patient outcomes, is warranted.

Suspected iNPH

The results in the suspected iNPH group should be interpreted cautiously. Patients were eligible for enrollment if they had been referred for evaluation of iNPH and had an Evans ratio above 0.3. No other clinical criteria were required, and none of the patients had been treated. Thus, this category contains not only patients with signs and symptoms of possible iNPH but also asymptomatic patients and patients with other disorders responsible for their symptoms (e.g., vascular or degenerative dementia, cervical or lumbar stenosis, or multifactorial disease). Therefore, this group reflects the range of patients referred for expert evaluation to exclude other causes of their symptoms before initiating invasive diagnostic testing for possible iNPH, as recommended in the international and the Japanese guidelines for iNPH.[19,20] The experience with diagnostic tests, treatment, and outcomes of iNPH from the AHCRN registry will be reported separately.

Outcome Scores

The Lawton ADL/IADL scale, iNPHGS, and mRS, when compared within each of the 4 hydrocephalus cat-

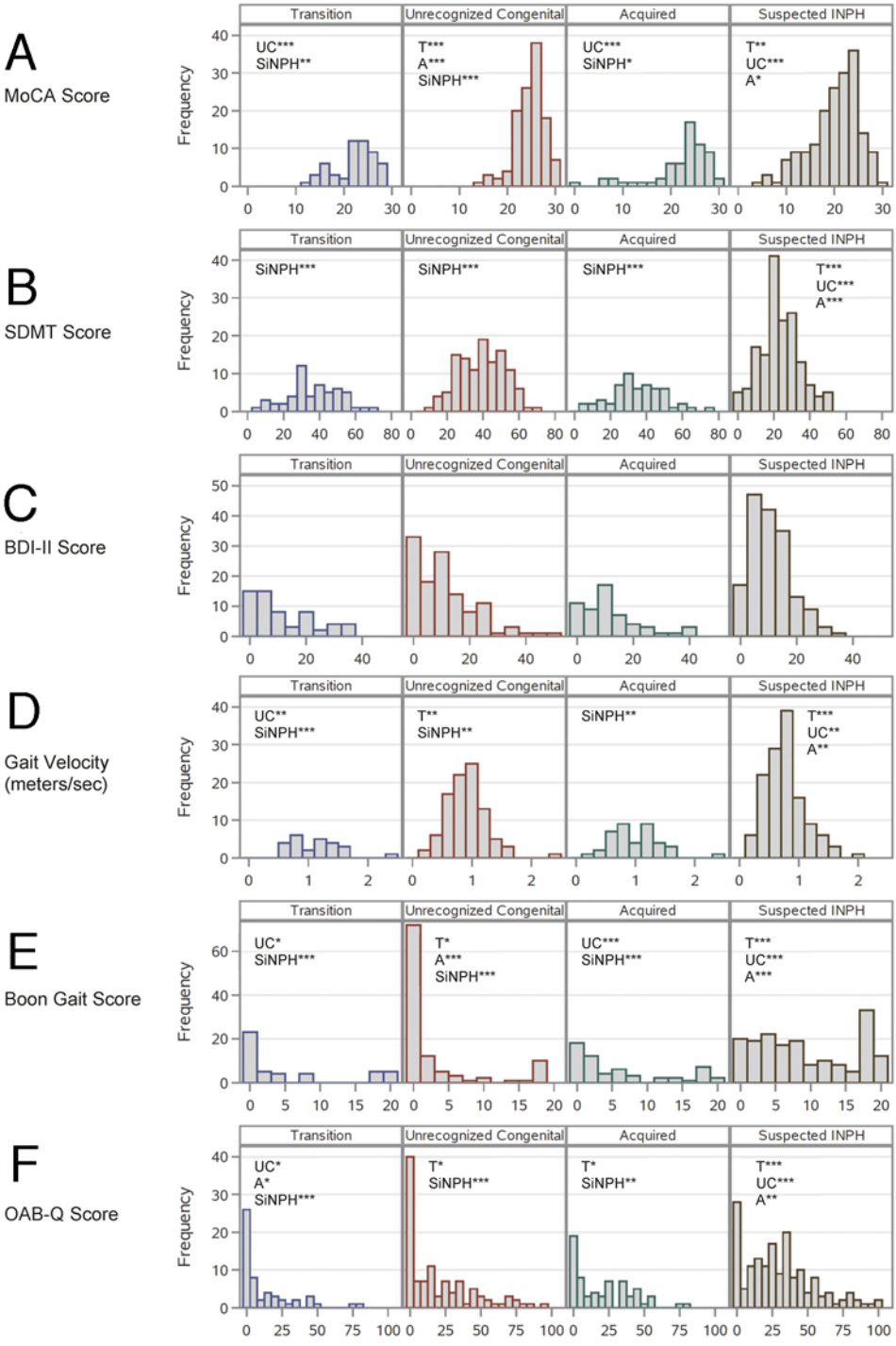

FIG. 1. Cognitive, depression, gait, and bladder screening results for all adult hydrocephalus categories. **A:** MoCA scores: range 0–30; cutoff score ≥ 26 for the normal elderly population. **B:** SDMT scores: number of correct responses; normal population scores range from 33.31 (SD 9.02) to 69.91 (SD 12.64). Performance is sensitive to age and education. **C:** BDI-II scores: score of 0–13 is the minimal range, 14–19 is mild, 20–28 is moderate, and 29–63 is severe. **D:** 10-Meter Walk Test velocity in meters/second. **E:** Boon iNPH gait scale scores: range 0–20; normal elderly control group scores range from 3 to 10. The mean score is 5.8 ± 1.9. **F:** OAB-q Short Form symptom bother scores: range 0–100; control group score is 9.8 ± 11.7. *$p < 0.05$, ** $p < 0.01$, ***$p < 0.001$ for pairwise comparisons by t-test or Mann-Whitney U-test. Each comparison is denoted by a code, where T = transition, UC = unrecognized congenital, A = acquired, and SiNPH = suspected iNPH. For example, T** denotes that $p < 0.01$ comparing distributions of a factor with patients in the transition category. Figure is available in color online only.

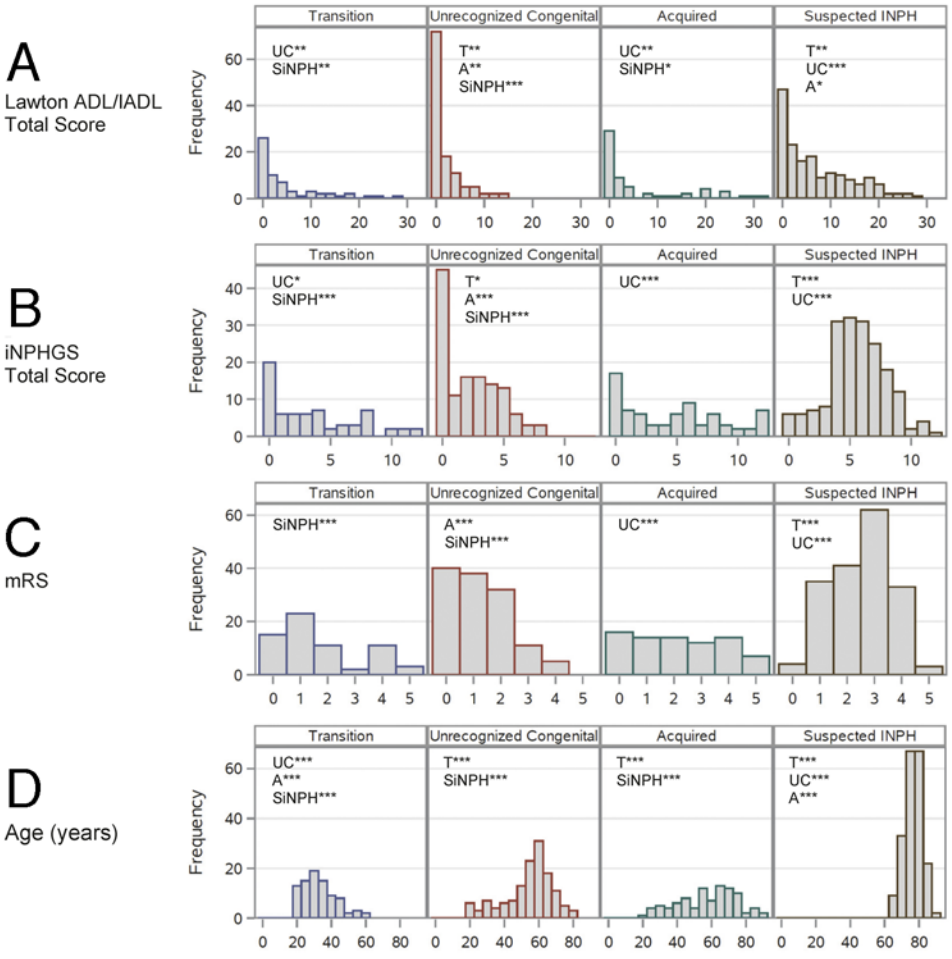

FIG. 2. Functional and outcome scales and age distribution for all adult hydrocephalus categories. **A:** Lawton ADL/IADL total score: range 0–32. With self-rating scores, < 5 suggests functional independence. **B:** iNPHGS total score: range 0–12, with 0 indicating no symptoms. **C:** mRS scores: range 0–6, with 0 indicating no symptoms. **D:** Age in years. *p < 0.05, ** p < 0.01, ***p < 0.001 for pairwise comparisons by t-test or Mann-Whitney U-test. Each comparison is denoted by a code, where T = transition, UC = unrecognized congenital, A = acquired, and SiNPH = suspected iNPH. For example, T** denotes that p < 0.01 comparing distributions of a factor with patients in the transition category. Figure is available in color online only.

egories in Fig. 2, show that overall the unrecognized congenital category has the best scores and that the SiNPH category has the worst scores. The shape of the mRS score distribution, compared to that of the Lawton ADL/IADL, appears to obscure the presence of high-functioning individuals in all 4 categories. For SiNPH, the shape of the iNPHGS score distribution, compared to that of the Lawton ADL/IADL, similarly hides high-functioning patients. These differing distribution patterns suggest potential shortcomings in using the mRS or iNPHGS to measure function in adults with hydrocephalus.

Treatment Status

Excluding the 86 patients in the transition category, who were all treated, nearly 80% of adults in the remaining 3 categories had not been treated (Table 5). Therefore, a primary role for adult hydrocephalus centers is to determine whether patients with ventriculomegaly require treatment. For patients with SiNPH, the international and Japanese guidelines provide the basis for reviewing the differential diagnosis and performing tests that demonstrate either a response to CSF drainage or an abnormal CSF resorptive capacity to determine if shunt surgery is indicated.[19,20,25] For the patients who fall into the acquired or unrecognized congenital categories of hydrocephalus, no guidelines exist; however, ICP monitoring,[5,9,22] CSF outflow resistance,[9] or response to CSF drainage[5] have all been used. The need for detailed evaluation of the differential diagnosis of presenting symptoms and the evaluation of pathophysiological markers of hydrocephalus highlights the importance for neurologists and neurosurgeons to collaborate in the care of these patients.

Influence of Etiology and Comorbidities

As seen especially in the transition and acquired categories, etiologies of hydrocephalus that directly cause neurological injury tend to result in more impairment compared to etiologies that result only in hydrocephalus,

TABLE 6. Comorbidities for all categories

Comorbidity	Transition (n = 86)	Unrecognized Congenital (n = 137)	Acquired (n = 94)	Suspected iNPH (n = 200)	Overall (n = 517)
Cancer	6 (7.0%)	10 (7.3%)	14 (14.9%)	45 (22.5%)	75 (14.5%)
Statistical significance, pairwise comparison	SiNPH**	SiNPH***		T**, UC***	
Coronary artery disease	4 (4.7%)	5 (3.6%)	8 (8.5%)	49 (24.5%)	66 (12.8%)
Statistical significance, pairwise comparison	SiNPH***	SiNPH***	SiNPH**	T***, UC***, A**	
Diabetes	6 (7.0%)	13 (9.5%)	10 (10.6%)	43 (21.5%)	72 (13.9%)
Statistical significance, pairwise comparison	SiNPH**	SiNPH**	SiNPH*	T**, UC**, A*	
Epilepsy/seizures	22 (25.6%)	3 (2.2%)	12 (12.8%)	2 (1.0%)	39 (7.5%)
Statistical significance, pairwise comparison	UC***, A*, SiNPH***	T***, A**	T*, UC**, SiNPH***	T***, A***	
Hypertension	7 (8.1%)	38 (27.7%)	29 (30.9%)	111 (55.5%)	185 (35.8%)
Statistical significance, pairwise comparison	UC***, A***, SiNPH***	T***, SiNPH***	T***, SiNPH***	T***, UC***, A***	
Major psychiatric disorder	11 (12.8%)	22 (16.1%)	11 (11.7%)	8 (4.0%)	52 (10.1%)
Statistical significance, pairwise comparison	SiNPH**	SiNPH***	SiNPH*	T**, UC***, A*	
Musculoskeletal disease	11 (12.8%)	5 (3.6%)	3 (3.2%)	4 (2.0%)	23 (4.4%)
Statistical significance, pairwise comparison	UC*, A*, SiNPH***	T*	T*	T***	
Obesity (BMI >30)	15 (17.4%)	19 (13.9%)	12 (12.8%)	16 (8.0%)	62 (12.0%)
Statistical significance, pairwise comparison	SiNPH*			T*	
Orthopedic problems	11 (12.8%)	11 (8.0%)	10 (10.6%)	25 (12.5%)	57 (11.0%)
Parkinson's	0 (0.0%)	1 (0.7%)	2 (2.1%)	8 (4.0%)	11 (2.1%)
Primary urologic disorders	11 (12.8%)	4 (2.9%)	2 (2.1%)	12 (6.0%)	29 (5.6%)
Statistical significance, pairwise comparison	UC**, A**	T**	T**		
Sleep disorders	11 (12.8%)	14 (10.2%)	8 (8.5%)	21 (10.5%)	54 (10.4%)
Spine (not including stenosis)	24 (27.9%)	6 (4.4%)	5 (5.3%)	10 (5.0%)	45 (8.7%)
Statistical significance, pairwise comparison	UC***, A***, SiNPH***	T***	T***	T***	
Spinal stenosis (cervical, lumbar)	3 (3.5%)	1 (0.7%)	3 (3.2%)	29 (14.5%)	36 (7.0%)
Statistical significance, pairwise comparison	SiNPH**	SiNPH***	SiNPH**	T**, UC***, A**	
Stroke	4 (4.7%)	3 (2.2%)	11 (11.7%)	13 (6.5%)	31 (6.0%)
Statistical significance, pairwise comparison		A**	UC**		
Vestibular disorder	1 (1.2%)	2 (1.5%)	0 (0.0%)	3 (1.5%)	6 (1.2%)
No comorbidities	29 (33.7%)	56 (40.9%)	29 (30.9%)	31 (15.5%)	145 (28.0%)
Statistical significance, pairwise comparison	SiNPH***	SiNPH***	SiNPH**	T***, UC***, A**	

Values are presented as the number (%) of patients.
*p < 0.05, **p < 0.01, ***p < 0.001, pairwise comparisons by appropriate chi-square test. Each comparison is denoted by a code, where T = transition, UC = unrecognized congenital, A = acquired, and SiNPH = suspected iNPH. For example, T** denotes that p < 0.01 comparing distributions of a factor with patients in the transition category.

such as aqueductal stenosis or idiopathic communicating hydrocephalus. Patients with more comorbidities, such as epilepsy or shunt complications in the transition group, or stroke and vascular risk factors in the acquired and SiNPH groups, tend to have greater degrees of impairment than patients with fewer comorbidities, especially in the unrecognized congenital group.

Impairment and Disability

Significant degrees of impairment and disability are seen in all 4 categories of adult hydrocephalus. Generally, the same types of impairment (cognitive, urinary control, gait and mobility, and IADL) occur, although with differences in the frequency and severity of each type of impairment across categories. Thus, the population of adults with hydrocephalus needs frequent access to healthcare services. Their impairments may prevent many of the patients from participating in adult education (community college, university, or vocational training) or being gainfully employed. Furthermore, the families of these patients often carry significant responsibilities and burdens. For example, the parents of young adults in the transition group frequently provide care until the patients are middle-aged and the parents are elderly. For patients in the acquired, unrecognized congenital, or SiNPH categories, caregiver responsibilities often fall to their spouses, and in the SiNPH category, caregivers are often their grown children. Thus, secondary effects of hydrocephalus on families are exerted, often with a social or employment impact, as is recognized in Alzheimer dementia.[4,10]

Although the impact of impairment in the cohort is significant, the results also reveal that more than half of

patients have minimal or no impairment in all categories except for SiNPH, based on a total Lawton ADL/IADL score of 0–2 (Fig. 2). Approximately 55% of transition, 75% of unrecognized congenital, and 55% of acquired hydrocephalus patients have minimal or no impairment, a clinical finding that plays a significant role in treatment decisions.

Population Health Needs

Few organized adult hydrocephalus centers exist in the US and Canada.[30] Thus, the population's health needs are often met by primary physicians, as well as by neurosurgeons or neurologists in community practice or in academic medical centers where no formal program exists. Many patients and families, through their calls to the Hydrocephalus Association, express their desire to be seen at centers that focus on hydrocephalus. Many of the AHCRN centers provide healthcare services for patients longitudinally with the goals of optimizing the care of those with hydrocephalus and helping to determine whether new symptoms are related to hydrocephalus or to other causes. While it is easy to speculate that specialized care has a beneficial effect on patient outcomes, as well as healthcare expenditures, such data do not yet exist, and this concept should be evaluated in future research. Regardless, the need for more centers to provide care for the full spectrum of adults with hydrocephalus exists, especially considering that hydrocephalus is the third most common of 10 conditions that require essential neurosurgical care, constituting 7% of all patients across the lifespan worldwide, more than brain tumor (5%) or vascular anomalies (2.2%).[7]

Under-Representation of Black Patients

Only 1.7% of patients who were enrolled in the AHCRN registry are black compared to 12.7% of the US population who are black/African American (https://censusreporter.org/data/table/?table=B02001&geo_ids=01000US&primary_geo_id=01000US). While none of the study sites had screening or enrollment practices that would be expected to result in enrollment bias, and we suspect the under-representation is due to referral patterns to the AHCRN centers, we cannot reach any firm conclusions retrospectively. The AHCRN is exploring outreach efforts to increase referral of racial and ethnic minority patients to its centers.

Healthcare disparities were noted in an analysis of the US Medicare database for hydrocephalus in the elderly, with African Americans only 50% as likely to receive shunt surgery if they had the diagnosis of hydrocephalus.[29] While racial, ethnic, and socioeconomic healthcare disparities have been noted for other disorders requiring neurological surgery, further research into the presence and causes of disparities in the care of adults with hydrocephalus is warranted, which the AHCRN is initiating.

Limitations

The results of the AHCRN registry may not be representative of national trends or profiles because the participating centers all have programs dedicated to adult hydrocephalus and may see a higher proportion of more complex patients than seen by other physicians at their institutions or than exist in the general population. The number of patients enrolled in the registry at each study site is only a portion of all patients seen by the primary investigators, as described in the *Methods*. The results reported here represent a cross-sectional survey of adults with hydrocephalus at varying stages of the diagnosis and treatment. Longitudinal data and, specifically, response to treatment are not reported in this study.

The criteria for categorizing patients as unrecognized congenital varied among centers. Some required that the head circumference be above the 97th percentile,[5] regardless of the anatomical pattern of hydrocephalus, while other centers considered patients with aqueductal stenosis, or an "aqueductal pattern," to have congenital hydrocephalus regardless of head circumference.

Some of the evaluation instruments used in the registry were originally developed for iNPH. Thus, their validity for the transition, unrecognized congenital, and acquired categories is unproven; however, the AHCRN primary investigators believed that using consistent evaluation methods was better than using different evaluation methods for each hydrocephalus category.

The AHCRN registry database is structured so that modifications to the data elements can be made to improve on shortcomings or ambiguities identified in this report—e.g., urinary incontinence in patients with spina bifida, as well as others identified by primary investigators during periodic reviews of the data elements.

Future Research

The AHCRN registry, which had 1241 individuals as of February 12, 2019, provides an opportunity to explore additional questions relevant to the diagnosis and treatment of hydrocephalus in adults. For example, is variation among AHCRN centers in the use of diagnostic test modalities, endoscopic third ventriculostomy, and shunt systems associated with different outcomes? Are outcomes better at the AHCRN centers compared to national trends, as has been demonstrated for the HCRN for children?[14] What are the outcomes of the SiNPH category with respect to diagnostic tests, treatment decisions, and shunt surgery? The AHCRN is also a platform for clinical trials, and it currently is enrolling subjects for a blinded, placebo-controlled trial of shunt surgery in iNPH (ClinicalTrials.gov identifier: NCT03350750).

Conclusions

The clinical spectrum of hydrocephalus in adults comprises much more than iNPH or acquired hydrocephalus. Only 39% of patients in the AHCRN registry had SiNPH, whereas 43% (transition and unrecognized congenital groups) had childhood onset. The severity of symptoms and impairment is worsened when the etiology of the hydrocephalus or complications of treatment causes additional neurological injury or when multiple comorbidities are present. However, more than half of patients in the transition, unrecognized congenital, and acquired hydrocephalus categories have minimal or no impairment. Excluding patients in the transition group, nearly 80% of

patients in the AHCRN registry were untreated at the time of enrollment. A major role for adult hydrocephalus centers is to determine whether patients in the unrecognized congenital and acquired hydrocephalus categories need treatment and which patients in the SiNPH cohort actually have possible hydrocephalus and should undergo further diagnostic testing. Future prospective research in the diagnosis, treatment, outcomes, quality of life, and macroeconomics of all categories of adult hydrocephalus is needed.

Acknowledgments

We wish to express our thanks to all patients who gave their consent to be included in the registry. We wish to acknowledge the diligent efforts of the research coordinators at each of our sites and to the staff at the Data Coordinating Center at the University of Utah. We are grateful to the Hydrocephalus Association for its support of the AHCRN.

As of February 1, 2019, the AHCRN participating centers (and primary investigators) include: Cleveland Clinic (S.J.N.), Columbia University (G.M.M.), Johns Hopkins University (M.G.L., A.M.), New York University (J.H.W., J.G.), University of British Columbia (T.J.Z.), University of Calgary (M.G.H.), University of Washington (M.A.W.), and Southmead Hospital, Bristol, United Kingdom (R.J.E.). The Data Coordinating Center is at the University of Utah (R.H.).

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Disclosures

Dr. Hamilton, Dr. Moghekar, and Dr. Williams report being a member of the Medical Advisory Board for the Hydrocephalus Association. Dr. Hamilton and Dr. Williams report being a member of the Hydrocephalus Association Board of Directors. Dr. Edwards reports receiving honoraria for delivering CME-accredited lectures/courses on hydrocephalus from Johnson & Johnson, Inc., and having an ownership stake in Integra LifeSciences and in B. Braun Miethke. Dr. Hamilton reports being a consultant for Integra Canada.

The AHCRN currently receives support from Codman/Integra for a prospective clinical trial of shunt surgery in iNPH. Support was received from the Hydrocephalus Association.

Author Contributions

Conception and design: Williams, Luciano, Relkin, Katzen, Holubkov, Hamilton. Acquisition of data: Williams, Nagel, Luciano, Relkin, Zwimpfer, Katzen, Moghekar, Hamilton. Analysis and interpretation of data: all authors. Drafting the article: Williams. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Williams. Statistical analysis: Holubkov. Study supervision: Hamilton.

Supplemental Information

Online-Only Content

Supplemental material is available with the online version of the article.

Supplemental Tables A and B. https://thejns.org/doi/suppl/10.3171/2019.2.JNS183538.

Previous Presentations

Presented in abstract form at the Annual Meeting of the Congress of Neurological Surgeons, October 6–10, 2018, Houston, Texas; the International Society for Hydrocephalus and Cerebrospinal Fluid Disorders, October 19–22, 2018, Bologna, Italy; and the Annual Meeting of the American Academy of Neurology, May 4–10, 2019, Philadelphia, Pennsylvania.

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