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Characterization of lower urinary tract symptoms in patients with idiopathic normal pressure hydrocephalus

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AIMS: The purpose of this study was to evaluate lower urinary tract symptoms (LUTS) in idiopathic normal pressure hydrocephalus (iNPH).

METHODS: Patients with new-onset iNPH were prospectively evaluated for LUTS via detailed history and physical, and administration of questionnaires from the International Consultation on Incontinence to assess incontinence (ICIq-UI), overactive bladder (ICIq-OAB), and quality of life (ICIq-LUTqol), as well as the American Urological Association Symptom Score bother scale. All patients with moderate-to-severe LUTS were offered urodynamic testing. Sub-analysis was performed based on gender, medical comorbidities, and age.

RESULTS: Fifty-five consecutive patients with iNPH completed the initial evaluation and surveys. Total urinary incontinence score was mild to moderate (8.71 ± 0.64 ; 0–21 scale) with 90.9% experiencing leakage and 74.5% reporting urge incontinence. The most common OAB symptom was nocturia (2.2 ± 0.14 ; 0–4 scale) with urge incontinence the most bothersome (3.71 ± 0.44 ; 0–10 scale). Quality-of-life impact was moderate (4.47 ± 0.4 ; 0–10 scale) and American Urological Association Symptom Score bother scale was 2.89 ± 0.22 (0–6 scale). Urodynamics testing revealed 100% detrusor overactivity and mean bladder capacity of 200 mL. Several differences were identified based on gender, medical comorbidities, and age.

CONCLUSIONS: Patients with iNPH present with mild-moderate incontinence of which nocturia is the most common symptom, urge incontinence the most bothersome, with 100% of patients having detrusor overactivity. Younger patients experienced greater bother related to LUTS. To our knowledge, this is the only prospective evaluation of urinary symptoms in patients with new-onset iNPH.

KEYWORDS

hydrocephalus, lower urinary tract symptoms, NPH, urodynamics

1 | INTRODUCTION

Normal pressure hydrocephalus (NPH) is a neurologic condition characterized by the triad of gait disturbances, dementia, and urinary incontinence. It is typically a geriatric

condition, with average onset in the eight to ninth decades. The prevalence increases with age, and approximately 6% of individuals 80 years and older will develop or be diagnosed with idiopathic normal pressure hydrocephalus (iNPH).¹ The diagnosis is made when patients meet standardized criteria based on evaluation of clinical symptoms, and are found to have enlarged lateral ventricles on cross-sectional imaging. Since the initial description of NPH by Hakim and Adams in

Dr. David Ginsberg led the peer-review process as the Associate Editor responsible for the paper.

1965,² many studies have been published with a primary focus on gait disturbances and dementia. However, little work has been performed to characterize the lower urinary tract symptoms (LUTS) in NPH. Urinary incontinence is prevalent in patients with NPH,^{3,4} and may be a significant source of bother for patients and caregivers.

NPH can be idiopathic (iNPH) or occur secondarily after stroke or other central nervous system insults. In patients with iNPH, urinary incontinence may not be as common as in secondary NPH, and may be more of a late finding.^{4,5} It has also been suggested (though not well studied) that increased urinary frequency and urgency precede urinary incontinence in iNPH and are more common presenting symptoms than frank incontinence,^{3,6} and that urinary symptoms may reflect detrusor overactivity diagnosed urodynamically.^{6,7} Study of LUTS is important in iNPH because LUTS can impact overall patient functional status,⁸ and even morbidity and mortality.^{9,10}

The mainstay of treatment for iNPH is with ventriculoperitoneal (VP) shunting.¹¹ Using this surgical method, a shunt is placed from the lateral ventricles and tunneled subcutaneously into the peritoneal cavity. With some of the newer shunts, the pressure gradient can be controlled remotely in order to improve symptoms.¹² Unfortunately, due to the advanced age and frail nature of most patients presenting with iNPH, complications from VP shunting can be quite high.^{13,14} Therefore, careful selection and counseling of patients with iNPH regarding expected changes in LUTS following surgical intervention is an important goal. The purpose of this investigation was to prospectively characterize LUTS in new-onset iNPH.

2 | MATERIALS AND METHODS

Our work was supported by a grant from the American Geriatrics Association, and was performed after approval from the Virginia Commonwealth University Institutional Review Board. Patients presenting to a specialized iNPH clinic and who reported any LUTS were prospectively enrolled in this study. All patients signed informed consent prior to being enrolled. Relkin et al.⁵ previously outlined strict criteria for the diagnosis of Probable, Possible, or Unlikely iNPH. All patients enrolled in this study were evaluated by a dedicated team of neurosurgeons and neuroscientists, and were diagnosed with Probable iNPH based on established criteria, including information on onset and duration of symptoms, gait testing, memory testing, the presence of urinary incontinence, brain imaging, and spinal infusion testing.^{5,15,16} As such, 100% of our patient population had the classic triad of gait disturbances, cognitive impairment, and urinary symptoms. Patients who met criteria for new-onset iNPH were included and are the subject of the current investigation.

All patients were seen by a single attending neuro-urologist who performed a standardized history and physical examination. Recorded data included demographics (age and gender), medical comorbidities, and prior treatments for LUTS and incontinence. Patients were administered a series of validated surveys to assess the type, severity, and quality-of-life (QOL) impact of LUTS. The surveys included three from the International Consultation on Incontinence Questionnaire (ICIQ) including the Urinary Incontinence Short Form (ICIQ-UI) to assess the type and severity of incontinence, the overactive bladder (OAB) questionnaire (ICIQ-OAB) to assess the type and severity of OAB symptoms, and LUTS QOL questionnaire (ICIQ-LUTSqol) to assess the QOL impact from LUTS. In addition, all patients were administered the American Urological Association Symptom Score (AUA-SS) bother question. All surveys were administered directly by the attending neurourologist with assistance from care providers if patients had limited cognitive abilities. LUTS were compared among groups with respect to gender, medical comorbidities, and age. All patients with new-onset iNPH reporting moderate-severe LUTS or bother from LUTS (AUA-SS ≥ 3) were offered urodynamic testing to be performed prior to any treatments for incontinence or surgical interventions for iNPH.

Data were analyzed with assistance from a professional statistician using SPSS software and are reported as means with standard errors. Comparisons between groups were made using student's *t*-tests or Fisher's Exact tests (two-tailed) with $P < 0.05$ considered significant.

3 | RESULTS

One hundred fifty-one patients were initially evaluated, including nine patients with probable iNPH. Thirty-four of the 93 patients with probable iNPH had been treated with VP shunting prior to their initial urologic evaluation, and were excluded from the current study. Another four patients were excluded due to incomplete evaluation or information, withdrawal from the study, or death. Fifty-five consecutive patients met criteria for new-onset iNPH and were included for evaluation (Supplemental Fig. S1). Thirty-eight men (69%) and 17 women (31%) were evaluated, with a mean age of 77 ± 0.7 years (range 68–86 years). In total, 82% of patients were found to have significant comorbidities (84% of men and 76% of women). Significant comorbidities were considered diabetes (DM), coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD), hypertension (HTN), cancer, seizures, depression, Parkinson's disease, and Alzheimer's disease. A detailed breakdown of patient comorbidities is shown in Table 1. There was no statistically significant difference between men and women in terms of age at the time of enrollment, or medical comorbidities.

TABLE 1 Patient information

	Total	Male	Female	P-value
Average age (years)	77 ± 0.7	76 ± 1.1	78 ± 1.2	0.228
N (%)	55 (100)	38 (69)	17 (31)	
DM	11 (20.0)	8 (21.1)	3 (17.6)	1.000
CAD	12 (21.8)	10 (26.3)	2 (11.8)	0.304
COPD	0 (0)	0 (0)	0 (0)	1.000
HTN	26 (47.3)	16 (42.1)	10 (58.8)	0.381
Cancer	12 (21.8)	9 (23.7)	3 (17.6)	0.735
Seizures	2 (3.6)	1 (2.6)	1 (5.9)	0.527
Depression	12 (21.8)	7 (18.4)	5 (29.4)	0.482
Parkinson's	4 (7.3)	4 (10.5)	0 (0)	0.299
Alzheimer's	11 (20.0)	7 (18.4)	4 (23.5)	0.722
BPH/prostate cancer	7 (12.7)	7 (18.4)	NA	NA

DM, diabetes mellitus; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; HTN, hypertension; BPH, benign prostatic hyperplasia.

The ICIq-UI Short Form was utilized to evaluate urinary incontinence. Total urinary incontinence score was mild to moderate (8.71 ± 0.64 ; 0–21 scale) with 90.9% experiencing leakage and 74.5% reporting urge incontinence (Figs. 1A and 2A). The ICIq-OAB questionnaire was used to evaluate OAB symptoms, and the most common symptom was two times/night nocturia (2.2 ± 0.14 ; 0–4 scale), with urge incontinence the most bothersome (3.71 ± 0.44 ; 0–10 scale) (Figs. 1B and 2B). The ICIq-LUTSqol form was used to evaluate the impact of urinary symptoms on QOL. This survey addressed impact of LUTS on physical activities (questions 3–6), social activities (questions 7–11), and emotional state (questions 12–16, 21). Questions 17–20 addressed degree of urinary leakage and question 22 evaluated overall impact on QOL (Figs. 1C and 2C). This global QOL question showed moderate QOL impact (4.47 ± 0.4 ; 0–10 scale) which was similar to the AUA-SS bother score (2.89 ± 0.22 ; 0–6 scale) (Fig. 2D).

There were several statistically significant differences in survey results between men and women. Fifty-nine percent of women reported stress incontinence with cough or sneeze versus 8% of men ($P = 0.0001$) based on the ICIq-UI Short Form. Women reported significantly more urge incontinence, than men. Women reported more often having to wear pads to stay dry than men, and women reported significantly more bother from having to wear pads than men. Overall, women reported more urinary leakage than men. There was no statistically significant difference in the amount of bother with respect to urinary leakage (not shown) (Table 2).

Twenty-eight patients (51%) reported two or more comorbidities. Questionnaire responses from these patients were compared to those with fewer than two comorbidities. There was no significant difference in answers between the two groups in response to the ICIq-UI Short Form or ICIq-OAB questionnaires (not shown). However, patients with two or more comorbidities reported a greater impact of

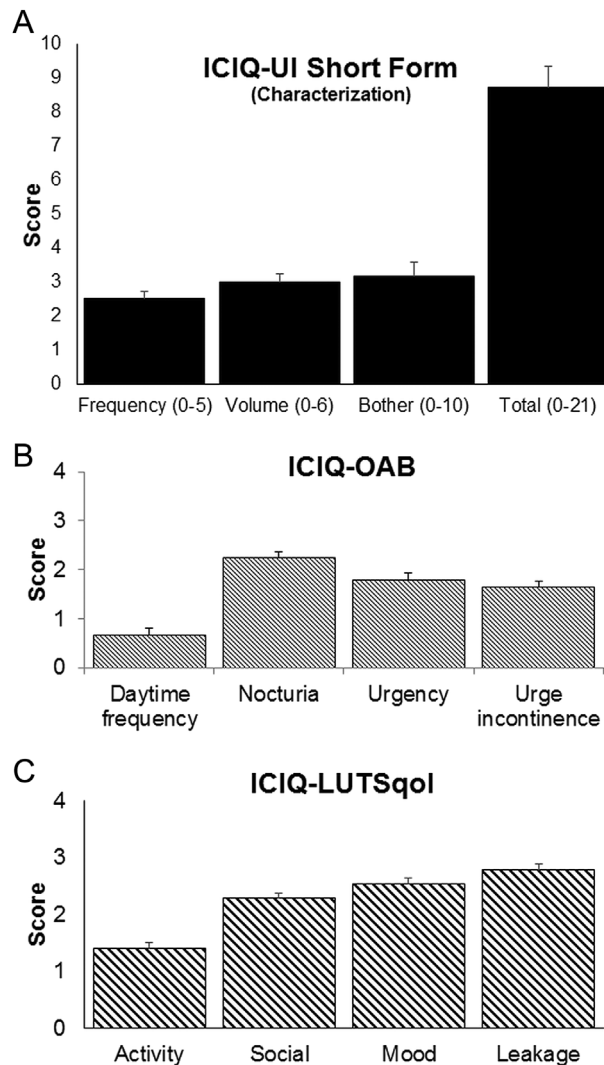


FIGURE 1 Symptom evaluation by questionnaire. (A) ICIq-UI Short Form assessment of leakage frequency, volume, bother, and total score. (B) ICIq-OAB Questionnaire assessing symptoms of daytime frequency, nocturia, urgency, and urge incontinence. (C) ICIq-LUTSqol Questionnaire assessing quality-of-life impact of LUTS on physical activities, social activities/relationships, and mood, as well as impact from urinary leakage

LUTS on several domains including physical activities and emotional state. In addition, there were differences in individual questions within each domain, including work and daily activities, relationships, depression, and self-image. Though there was no difference in overall impact from volume of urinary leakage, patients with greater than two comorbidities reported more bother from having to change clothing when wet due to urinary symptoms (Table 2). No other questions showed a significant difference. There was no difference between groups in response to overall QOL (ICIq-LUTsqol #22, 3.00 ± 0.60 vs. 4.11 ± 0.54 , $P = 0.173$), or in response to the AUA-SS bother score (2.46 ± 0.27 vs. 3.29 ± 0.32 , $P = 0.057$).

Patients were also evaluated based on age. Groups were divided into patients greater than or equal to the cohort's mean

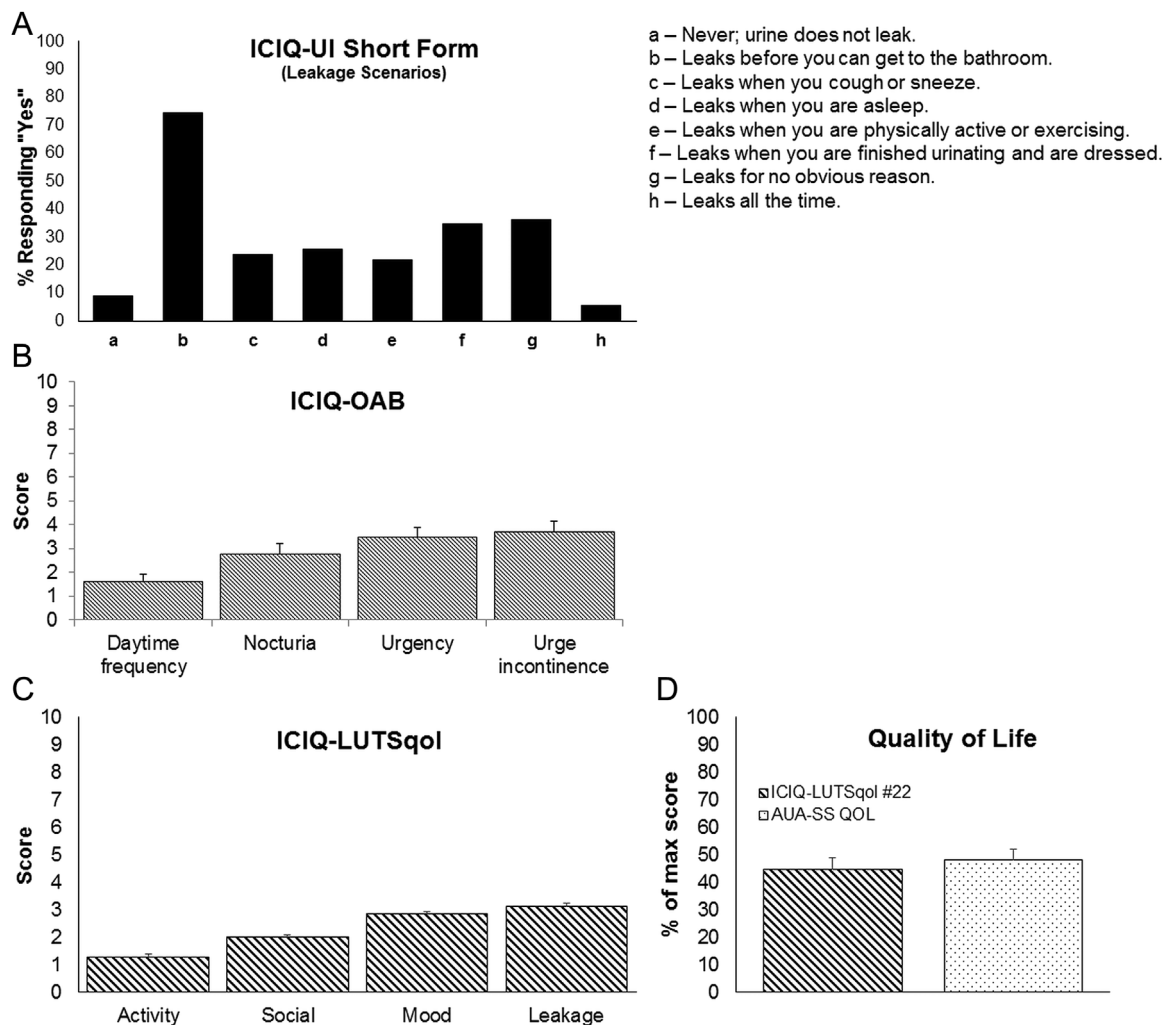


FIGURE 2 Bother associated with urinary symptoms. (A) ICIQ-UI Short Form categorizing specific scenarios during which leakage occurs. (B) ICIQ-OAB Questionnaire assessing associated bother from daytime frequency, nocturia, urgency, and urge incontinence. (C) ICIQ-LUTSqol Questionnaire assessing associated bother from LUTS on physical activities, social activities/relationships, and mood, as well as impact from urinary leakage. (D) ICIQ-LUTSqol impact score (Question #22, 0–10 scale), and the AUA-SS (0–6 scale). Scores are plotted as percentage of total scale in order to compare responses

age of 77 ($N = 30$), or younger than the mean age ($N = 25$). There was no significant difference between groups in response to the ICIQ-UI Short Form total score (8.00 ± 0.89 vs. 9.56 ± 0.91 respectively, $P = 0.23$), or individual questions (not shown). However, the younger age group reported more urinary urgency than the older age group. There were no differences between groups in response to any of the ICIQ-LUTSqol questionnaire items (not shown). In addition, the younger age group reported significantly greater impact of urinary symptoms on QOL (Table 2).

Urodynamics testing was offered to patients reporting moderate-to-severe symptoms or bother. Urodynamics was performed in 19 patients (35%) prior to any interventions for urinary symptoms or iNPH. One hundred percent of patients tested were found to have detrusor overactivity with 78.9% having detrusor overactivity-associated incontinence (DOI), and 10.5% of patients with urodynamic stress incontinence (USI). Additional urodynamic results are shown in Table 3.

4 | DISCUSSION

iNPH consists of the classic triad of gait disturbance, dementia, and urinary incontinence. Most studies have focused on the dementia and gait disturbance manifestations of this condition, with little attention paid to urinary symptoms. To our knowledge, this is the first prospective study to provide a detailed characterization of the type, severity, QOL impact, and urodynamic assessment of LUTS in patients with new-onset iNPH prior to treatment.

This study revealed that 91% of patients reported some degree of urinary incontinence, which occurred on average of once/day, consisted of a small-to-moderate volume, and caused a mild-to-moderate interference with everyday life. In terms of OAB symptoms, 74.5% of patients with new-onset iNPH reported experiencing urge incontinence. The most common OAB symptom was nocturia, and the most bothersome OAB symptom was urinary urge incontinence.

TABLE 2 Significant differences in LUTS by gender, medical comorbidities, and age

Questions		Men (N = 38)	Women (N = 17)	P-value
ICIQ-OAB				
Effect	ICIQ-OAB: 6a	1.39 ± 0.16	2.18 ± 0.15	0.005
Bother	ICIQ-OAB: 6b	3.13 ± 0.54	5.00 ± 0.66	0.049
ICIQ-LUTSqol				
Leakage				
Effect	ICIQ-LUTSqol: 17a	1.61 ± 0.18	3.06 ± 0.33	0.0001
	ICIQ-LUTSqol: 17a-20a	1.70 ± 0.10	2.15 ± 0.16	0.020
Bother	ICIQ-LUTSqol: 17b	0.84 ± 0.40	3.59 ± 1.00	0.003
		≥2CM (N = 28)	<2CM (N = 27)	
ICIQ-LUTSqol				
Physical activities				
Effect	ICIQ-LUTSqol: 4a	1.68 ± 0.18	1.19 ± 0.11	0.023
	ICIQ-LUTSqol: 3a-6a	1.62 ± 0.17	1.21 ± 0.09	0.042
Bother	ICIQ-LUTSqol: 4b	2.54 ± 0.63	0.48 ± 0.29	0.005
	ICIQ-LUTSqol: 3b-6b	1.91 ± 0.54	0.65 ± 0.30	0.047
Social activities				
Effect	ICIQ-LUTSqol: 9a	1.8 ± 0.25	1.11 ± 0.08	0.019
Bother	ICIQ-LUTSqol: 9b	2.3 ± 0.72	0.32 ± 0.23	0.013
Emotional state				
Effect	ICIQ-LUTSqol: 12a	1.71 ± 0.20	1.15 ± 0.07	0.010
	ICIQ-LUTSqol: 14a	1.61 ± 0.20	1.11 ± 0.06	0.020
	ICIQ-LUTSqol: 12-16,21a	1.77 ± 0.17	1.40 ± 0.06	0.046
Bother	ICIQ-LUTSqol: 12b	2.32 ± 0.62	0.74 ± 0.36	0.033
	ICIQ-LUTSqol: 14b	2.21 ± 0.67	0.41 ± 0.23	0.015
Leakage				
Bother	ICIQ-LUTSqol: 19a	4.04 ± 0.64	2.11 ± 0.52	0.023
		<77 yrs (N = 25)	≥77 yrs (N = 30)	
ICIQ-OAB				
Effect	ICIQ-OAB: 5a	2.16 ± 0.19	1.5 ± 0.18	0.014
AUA-SS		3.64 ± 0.31	2.24 ± 0.25	0.0009

CM, comorbidities; yrs, years.

This aligns with prior smaller studies, which reported detrusor overactivity in iNPH patients in 63–100%.^{9,17,18} Urinary urgency is thought to precede urge incontinence in the progression of iNPH.⁶ This is significant considering the combination of early age of onset and mild symptoms/early diagnosis are the best prognostic factors in terms of response to shunt surgery.¹⁹

In our study, patients also reported that LUTS had only a mild-to-moderate QOL impact. This stands in contrast to QOL impact from gait and memory impairment, which can be quite profound in this population. In the classic study by P. M. Black in 1980, 90% of patients had memory impairment, 85% had gait disturbances, but only 55% had incontinence. Only 50% of their patients had the classic triad of dementia, gait disturbances, and urinary incontinence. In that study, 54% of patients with urinary incontinence, and 42% of patients without incontinence had improvement in activity level

following shunting, confirming that surgical management of iNPH may improve overall activity, regardless of the presence of urinary symptoms.²⁰

Responses were also compared based on gender, comorbidities, and age. Women reported significantly more stress incontinence, urge incontinence, and pad use. This may reflect the higher prevalence of stress incontinence in this population.²¹ Patients with two or more medical comorbidities reported that urinary symptoms had a greater impact on physical activities and emotional state than patients with fewer comorbidities. This is consistent with other studies showing that comorbidities can profoundly impact QOL, especially in older adults.^{22–24} Interestingly, patients who were younger than the mean age of 77 reported greater impact from LUTS on physical activity, and significantly worse overall impact of LUTS on QOL. This may reflect a more generalized acceptance of LUTS in very elderly patients²⁵ or

TABLE 3 Urodynamic findings and diagnoses

Sensation	FS (mL)	FD (mL)	SD (mL)	BC (mL)
Mean	77 ± 12.9	123 ± 18.1	178 ± 36.0	202 ± 30.8
Sample (N)	13	15	13	19
Voiding function	Qmax (mL/s)	pDetQmax (cmH ₂ O)	Voided volume (mL)	PVR (mL)
Mean	7 ± 1.0	64 ± 9.1	115 ± 19.1	88 ± 31.8
Sample (N)	18	17	19	19
Detrusor function	Compliance (mL/cmH ₂ O)	1st IDC volume (mL)	Peak IDC pressure (cmH ₂ O)	
Mean	45 ± 9.9	164 ± 26.1	83 ± 9.9	
Sample (N)	18	19	18	
	N	%		
Normal	0	0.0		
Detrusor overactivity	19	100.0		
Acontractile detrusor	0	0.0		
Urethral function				
Normal	7	38.9		
Bladder outlet obstruction	9	50.0		
Incompetent urethral closure mechanism	2	11.1		
Incontinence				
No	0	0.0		
Yes	19	100.0		
Incontinence type				
DOI	15	78.9		
USI	2	10.5		
Both	2	10.5		

FS, first sensation; FD, first desire; SD, strong desire; BC, bladder capacity; IDC, involuntary detrusor contraction; PVR, post-void residual; DOI, detrusor overactivity incontinence; USI, urodynamic stress incontinence.

the overall decline in participation in activities in this age group.

Our finding of 100% DO in patients with new-onset iNPH is consistent with findings by Sakakibara et al.⁶ reporting 95.2% of patients having DO, but higher than a reported rate of 45.6% in a study by Campos-Juanatey et al.¹⁷ The common finding of DO across multiple studies may reflect an altered neurologic pathway in patients with iNPH. Our mean bladder capacity was low at 202 mL, which is also similar to findings by Sakakibara et al.⁶ and Campos-Juanatey et al.¹⁷

Limitations of this study are the use of surveys instead of more objective measures of LUTS (pad tests and void diaries). We administered pad tests and void diaries to all patients; however, response rates and compliance with pad collection and diaries were poor and did not offer evaluable data. This may reflect the very advanced age of the population coupled with varying degrees of cognitive impairment and the fact that many patients came from long distances to this highly specialized multi-disciplinary clinic. In addition, we did not offer urodynamic testing except to patients who reported at least moderate bother from LUTS based on AUA-SS bother scale due to ethical concerns about invasivity and potential complications in this extremely high-risk

cohort. Finally, we did not present results in patients in this group who were followed and ultimately were treated with VP shunting. Our preliminary data have shown a significant improvement in urinary symptoms across multiple domains following shunting, possibly due, in part, to restoration of blood flow to the bilateral mid-cingulate cortex and other cerebral micturition centers as recently demonstrated by Sakakibara et al.²⁶ However, this is beyond the scope of the current investigation and is the subject of our next study.

5 | CONCLUSIONS

This study presents, to our knowledge, the first prospective characterization of LUTS in patients with new-onset iNPH using validated surveys and urodynamics testing. The results demonstrate that LUTS are highly prevalent, but bother is much less significant as compared to bother from gait disturbances and memory impairment. Indeed, the results of this study suggest that patients with iNPH who report LUTS as the most impactful symptom in the NPH triad (gait disturbances, memory impairment, and incontinence) should

be counseled that iNPH treatment may not improve their LUTS. This is because the typical iNPH patient has only mild-to-moderate bother and QOL impact from their LUTS.

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POTENTIAL CONFLICTS OF INTEREST

Nothing to disclose.

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SUPPORTING INFORMATION

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