

Use of the International Prostate Symptom Score in men with Multiple Sclerosis

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ABSTRACT

Objective : Men with multiple sclerosis (MS) tend to present with urinary symptoms potentially translating to significant findings on urodynamics (UDS). We sought to assess the reliability and prognostic value of the International Prostate Symptom Score (IPSS) and Quality of Life (QoL) in patients with MS.

Methods : A prospective study between July 2014 and August 2016 included 40 consecutive men with MS and lower urinary tract symptoms (LUTs) referred for video UDS. All participants completed the IPSS and QoL assessments. Results were compared and correlated to UDS parameters.

Results : Mean ($\pm$ SD) age, IPSS, and QoL were 53.7 ± 13.5 years, 16.7 ± 8.9 and 4.1 ± 1.4 , respectively. The most common presenting symptom and UDS finding were urinary frequency (79%) and detrusor overactivity (68%). 72% had moderate-severe symptoms base on the IPSS. Reduced bladder compliance on UDS was associated with intermittency and straining answers on IPSS ($p = 0.02$ and $p = 0.03$). QoL did not predict UDS parameters.

Conclusion : QoL and total IPSS scores are likely insufficient for MS and LUTs patient assessment due to the variability of UDS findings. However, in these patients, IPSS storage

symptom questions had significant correlation with UDS. Furthermore, presenting symptoms in MS & LUTs did not correlate with UDS findings. Therefore, in patients with MS and LUTs, UDS must be performed for adequate disease assessment.

Keywords : IPSS, Multiple Sclerosis, Urodynamics, Validation

INTRODUCTION

Urinary symptoms in multiple sclerosis (MS) are severely underdiagnosed in both men and women with a prevalence of 86% and 88%, respectively [1,2]. Those with urinary symptoms reported significantly worse health-related quality of life (QoL)[3]. A large portion of people with MS have worsening urodynamics (UDS) findings on follow-up with minimal symptom changes therefore disease progression may go undetected [4]. The current American Urological Association (AUA) guideline recommend annual focused history, physical exam, and symptom assessment in the surveillance of patients with neurogenic lower urinary tract dysfunction (NLUTD). Additionally, depending on the patient's risk category, defined by their initial UDS, upper tract imaging may be recommended [5]. UDS are recommended only when there are changes in signs or symptoms or new complications or upper tract or renal function deterioration [5]. However, these changes may be subclinical or mild and may represent more significant findings on UDS [4]. Relying on laboratory changes, which typically represent late disease stages, may delay treatment and lead to irreversible damages [6].

MS is often a delayed diagnosis particularly in men and has a higher prevalence in females which make the characterization of urinary symptoms in this specific cohort even more difficult [1,7,8]. International Prostate Symptom Score (IPSS) and QoL are part of the symptom assessment in NLUTD patients. In this study, we aimed to assess the reliability of QoL and IPSS in predicting UDS changes in men with MS.

PATIENTS AND METHODS

After obtaining IRB approval (1601016896), we performed a prospective study of men with MS who failed conservative therapy including behavioral modification, and pharmacotherapy for the treatment of lower urinary tract symptoms (LUTs) at a tertiary medical center between July 2014 and August 2016. All men with the diagnosis of MS who underwent UDSs were

included in the study. Exclusion criteria included culture-proven urinary tract infections, use of medication for benign prostatic hyperplasia (BPH) or overactive bladder (OAB) such as α -blockers, anti-cholinergics⁴ or β -agonists, and histories of genitourinary surgery or malignancies. Complete medical history and physical examination were reviewed. All participants completed the IPSS and QoL assessments. UDS, uroflowmetry and post void residual (PVR) examinations were also performed according to the Good Urodynamics Practice [9]. All UDS diagnoses were made in accordance with International Continence Society (ICS) standards [10]. Mean and standard deviation ($\pm$ standard deviation [SD]) were used for numerical data while frequency and percentage for non-numerical data. Analysis of variance (ANOVA) was used to compare means of several studied group. Correlation analysis (using Pearson's and Spearman's rho method) assessed the strength of association between two quantitative variables. Multivariate logistic regression analysis was done to test for the significant independent predictors of abnormal urodynamic, and linear model was used to test for the significant independent predictors of the UDS findings. The probability/significance value (p value) ≥ 0.05 is not statistically significant and < 0.05 is statistically significant. All statistical analysis was performed using R software (Version 3.44).

RESULTS

We identified 40 consecutive men with MS with mean (SD) age of 54.8 ± 13.5 years diagnosed with LUTs for at least 6 months (Table 1). Mean IPSS and QoL were 16.7 ± 8.9 and 4.1 ± 1.4 , respectively. MS subtypes were available for 24 (60%) men. The majority (54%) had relapsing-remitting MS (RRMS) and (48.5%) were diagnosed with MS 11-20 years ago. The most common symptoms were urinary frequency (60%), urgency (50%), nocturia (35%), and incomplete emptying (28%) (Table 2). The most prevalent UDS findings were detrusor overactivity (68%), bladder outlet obstruction (40%), and detrusor underactivity (38%) (Table 3). Age, body mass index (BMI), MS subtypes, disease durations, and presenting chief complaints were not predictors of UDS findings. The majority (72%) had moderate-severe symptoms base on the IPSS categories. This group was also younger compared to the mild group (mean age of 51.0 years vs 65.1 years, respectively). Men with moderate-severe symptoms had a lower mean volume of first sensation compared to those with mild symptoms (158 vs 282.5 mL, $p = 0.016$) (Table 4). No further statistical significance was identified comparing urodynamic parameters and symptom severity groups. Comparing IPSS and urodynamics parameters, decreased bladder compliance on UDS was associated with intermittency and straining questions on the IPSS questionnaire ($p =$

0.02 and $p = 0.03$, respectively) (Table 5). Straining was also associated with volume of first urge ($p = 0.01$), volume of severe urge ($p = <0.001$), volume at capacity ($p = 0.01$) and PVR ($p = 0.04$). Weak stream on the IPSS was also associated with low peak pressure on uroflow ($p = 0.02$). Additionally, no significant correlation was seen with QoL and UDS parameters.

Table 1 : Demographics of cohort of patients with MS

Demographics	Patients (N=40)
Age (years)	53.7 ± 13.5
Range	(23-86)
BMI	24.7 ± 7.7
Race	
Caucasian (N)	32 (66.6%)
Non-Caucasian(N)	6 (12.5%)
Declined to answer (N)	10 (20.1%)
Disease Type	24 patients
Primary-Progressive (PPMS)	5 (20.8%)
Secondary-Progressive (SPMS)	6 (25%)
Relapsing-Remitting (RRMS)	13 (54.2%)
Disease Duration	33 patients
1-10 years	7 (21.2%)
11-20 years	16 (48.5%)
21-30 years	7 (21.2%)
31+ years	3 (9.1%)
Ambulatory Status	43 Patients
Ambulatory	21 (43.8%)
Uses Cane/Scooter	9 (18.8%)
Wheelchair bound	13 (27.1%)

BMI = Body Mass Index

Table 2 : Chief Complaints of MS Patients

Chief Complaint (N=40)	N (%)
Frequency	24 (60%)
Urgency	20 (50%)
Nocturia	14 (35%)
Incomplete emptying	11 (28%)
Incontinence	9 (23%)
Hesitancy	9 (23%)
Retention	6 (15%)
Slow stream	5 (13%)
Intermittency	1 (3%)
Pain	1 (3%)

Table 3 : Urodynamic Characterization of MS Patients

Urodynamic Diagnosis (N=40)	N (%)
Detrusor Overactivity	27 (67.5%)
Bladder Outlet Obstruction	16 (40%)
Detrusor Underactivity	15 (37.5%)
Detrusor-external sphincter dyssnergia (DESD)	12 (30%)
Small capacity	10 (25%)
Pseudodyssynergia	7 (17.5%)
Impaired sensation	6 (15%)
Vesico-ureteral reflux	3 (7.5%)
Stress Urinary incontinence	3 (7.5%)
Intrinsic Sphincter Deficiency	1 (2.5%)

Table 4 : Urodynamic Parameters of MS Patients Stratified by Symptom Severity on IPSS

Urodynamic Parameters	Mild (N = 11)	Moderate (N = 11)	Severe (N = 18)	p-value
Volume of First Sensation (mL)	282.5±167.3	210.6±99.3	158±68.7	0.02
Volume of First Urge (mL)	373.5±244.7	318.4±134.3	239.5±90.9	0.09
Volume of Severe Urge (mL)	486.2±290.8	372.6±234.8	346.3±181.4	0.28
Volume at Capacity (mL)	558.2±397.5	436.1±211	383.4±214.5	0.26
Compliance	14.7±15	17.4±16.9	16.8±17.6	0.92
Uroflow				
Qmax (mL/sec)	4.3±4.8	12.5±15.5	6.0±5.7	0.10
Peak Pressure (mm H2O)	50.3±17.3	47.5±16.9	48.5±25.8	0.95
Post void residual PVR (mL)	399.7±391.1	185.9±172.2	228.7±201.3	0.13

Table 5 : Correlation between subcategories of IPSS and urodynamic parameters in male MS patients (p value)

Urodynamic Parameters	Total	Incomplete emptying	Frequency	Intermittency	Urgency	Weak stream	Straining
Volume of First Sensation (mL)	0.22 (0.09)	0.10 (0.53)	-0.17 (0.28)	0.37 (0.01)	-0.18 (0.25)	0.31 (0.04)	0.20 (0.19)
Volume of First Urge (mL)	0.23 (0.14)	-0.02 (0.92)	-0.09 (0.55)	0.24 (0.11)	-0.07 (0.65)	0.28 (0.07)	0.41 (0.01)
Volume of Severe Urge (mL)	0.34 (0.02)	0.03 (0.84)	-0.14 (0.38)	0.28 (0.06)	0.01 (0.97)	0.26 (0.09)	0.50 (<0.001)
Volume at Capacity (mL)	0.25 (0.05)	0.01 (0.96)	-0.08 (0.60)	0.26 (0.08)	0.01 (0.96)	0.17 (0.26)	0.39 (0.01)
Compliance	0.26 (0.10)	0.10 (0.49)	-0.02 (0.89)	0.33 (0.02)	-0.19 (0.22)	0.30 (0.052)	0.33 (0.03)
Uroflow							
Qmax (mL/sec)	0.07 (0.64)	-0.07 (0.64)	0.09 (0.58)	-0.10 (0.51)	0.082 (0.6)	0.06 (0.7)	0.15 (0.34)
Peak Pressure (mm H2O)	-0.25 (0.10)	-0.11 (0.46)	0.08 (0.63)	-0.27 (0.08)	0.021 (0.89)	-0.34 (0.02)	-0.28 (0.07)
Post void residual PVR (mL)	0.19 (0.20)	-0.11 (0.47)	0.07 (0.64)	0.16 (0.31)	-0.0029 (0.99)	0.2 (0.19)	0.31 (0.04)

DISCUSSION

Total IPSS scores and presenting urinary symptoms were poorly correlated with UDS findings in men with MS. However, questions pertaining to storage symptoms on IPSS were correlated with UDS findings. The most important of these UDS findings is reduced compliance, which can lead to upper tract deterioration. This was found to be correlated with questions pertaining to intermittency and straining on IPSS. No voiding-related questions were correlated with IPSS scores. Interestingly, incomplete emptying on IPSS was not correlated with PVR. Straining on the IPSS had the greatest number of significant correlations with urodynamic parameters including volume of first urge ($p = 0.01$), volume of severe urge ($p = <0.001$), volume at capacity ($p = 0.01$), compliance ($p = 0.03$), and PVR ($p = 0.04$). Thorough review of storage questions on IPSS is necessary on follow-up exams in NULTD patients and a low threshold for performing UDS is needed as presenting symptoms are not indicative of UDS findings in this population.

The validity of a questionnaire in target populations is crucial in evaluating treatment effectiveness. There are a handful of cross-validated questionnaires in the general neurogenic population such as the Expanded Disability Status Scale (EDSS), Incontinence Quality of Life (I-QOL), the Qualiveen, and the short-form (SF)-Qualiveen. Out of these, the Qualiveen and SF-Qualiveen questionnaires assessed broad urinary symptoms including incontinence and were specifically applied to individuals with MS in clinical trials [11–13]. Qualiveen was originally developed for French speaking people with spinal cord injury and was validated in English to measure urinary-specific quality of life in people with MS. However, the questionnaires recommended by the AUA guidelines, such as QoL and IPSS, have not been validated in the MS population for the evaluation of urologic symptoms nor disease progression. In fact, our study indicates that QoL and total IPSS scores are likely insufficient for MS + LUTs patient assessment due to the variability of the findings on UDS.

Different transformations of the IPSS have been seen to better characterize disease progression and are worth considering for use in select populations. Jiang et al. looked at 298 men with LUTs who underwent UDS and found the ratio of IPSS- storage (IPSS-S) and IPSS-voiding (IPSS-V) sub scores to predicted bladder outlet-related lower urinary tract dysfunction (positive predictive value [PPV] 75% vs PPV 91.4%, respectively) better than IPSS totals [14]. The work suggested that $IPSS-V/IPSS-S > 1$ can differentiate individuals with bladder outlet-related LUTs (obstructive) and bladder-related LUTs (nonobstructive) [14,15]. When predicting voiding and storage LUTs, the area under receiver operating characteristic (ROC) curve was greatest in IPSS-V/S score

compared to other noninvasive tools such as total IPSS, Qmax, PVR, total prostate volume (ROC area 0.81 vs 0.58 vs 0.64 vs 0.63 vs 0.74, respectively). This research is consistent with our findings: IPSS storage symptoms more strongly correlated with UDS findings than total IPSS, suggesting that surveillance in this cohort should include IPSS-V/S ratio in addition to the total IPSS value.

An important limitation of this study was the potential exposure to selection bias in the recruitment of participants from either self- or physician-referral to a tertiary care center. Given LUTs may be under-reported in men, this study likely omits men with MS who did not seek urological consultation. Another limitation is the relatively small size of our cohort, however, to our knowledge, this remains one of largest study in this cohort using UDS as gold standard.

CONCLUSION

IPSS storage symptom questions had a more robust correlation with UDS findings than the total IPSS scores. However, the clinical implications of these findings require further investigation. The lack of correlation between QoL assessments and UDS parameters suggests that QoL may not reflect the complexity of bladder dysfunction in MS and warrants investigation of appropriately metrics. While IPSS shows potential utility in monitoring bladder function in MS patients, our study also highlights the need for large, diverse studies to determine the benefits of integrating disease-specific questionnaires more fully into clinical practice. Further research should explore the standardization and validation questionnaires tailored to the MS population which can reliably guide clinical decision-making.

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