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# Bladder and urodynamic changes in multiple sclerosis

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## Abstract

**Background:** Urinary dysfunction is a common symptom during the course of multiple sclerosis (MS). Long-term follow-up of the natural history of bladder dysfunction in MS has been seldom addressed.

**Objective:** To identify the type and the course of voiding dysfunction in MS patients in relation to the urodynamic changes of the lower urinary tract (LUT)

**Subjects and methods:** An observational prospective study including 120 MS patients with urinary dysfunction rated by the American Urological Association (AUA) symptoms questionnaire and assessed by urodynamic studies and followed for 1 year.

**Results:** Irritative symptoms were the most frequently encountered symptoms (90%), whereas overactive bladder was recorded by urodynamic studies in 35% of subjects. Urinary symptoms severity score was higher in patients with initial urodynamic abnormalities by the end of the 1-year follow-up period ( $P < 0.001$ ). A statistically significant relationship was found between urinary symptoms severity score and each of expanded disability status scale (EDSS) and urodynamic pattern of abnormalities ( $P < 0.01$ ).

**Conclusion:** Irritative symptoms and overactive bladder seem to be the most frequent urinary dysfunction in MS patients. Urinary symptoms are related to the degree of disability. The initial urodynamic abnormalities are associated with worse urinary dysfunction outcome after 1 year.

**Keywords:** Voiding dysfunction, Urodynamic studies, Multiple sclerosis, Long-term follow-up

## Introduction

Multiple sclerosis (MS) is the most common demyelinating disorder affecting the central nervous system (CNS). Through the whole course of the disease, up to 90% will suffer from lower urinary tract symptoms including urgency, frequency, urge incontinence, retention, and hesitancy [1, 2].

Lower urinary tract dysfunction (LUTD) in MS patients results from disturbance in the neurological control of the detrusor-sphincter function, leading to detrusor overactivity, detrusor hypocontractility, and detrusor-sphincter dyssynergia (DSD) which can be

assessed by urodynamic evaluation to provide a more evident clue to the nature of the dysfunction [3, 4]. Many studies have explored the relation between urinary symptoms in MS patients and objective urological patterns with different outcome [5–7] also, the relation of LUTD, and clinical parameters of multiple sclerosis as disease severity and disease duration [6].

The aim of this study was to identify the type and fate of bladder symptoms in MS patients during and after 1-year follow-up in relation to initial urodynamic and clinical disability.

## Subjects and methods

An observational prospective study that was conducted in accordance with the principles established by the 18th

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World Medical Assembly Helsinki (1964) [8], International Council for Harmonization guidelines for good clinical practice, and in compliance with all national and international laws and regulations. Written informed consent was obtained from all participants in this study.

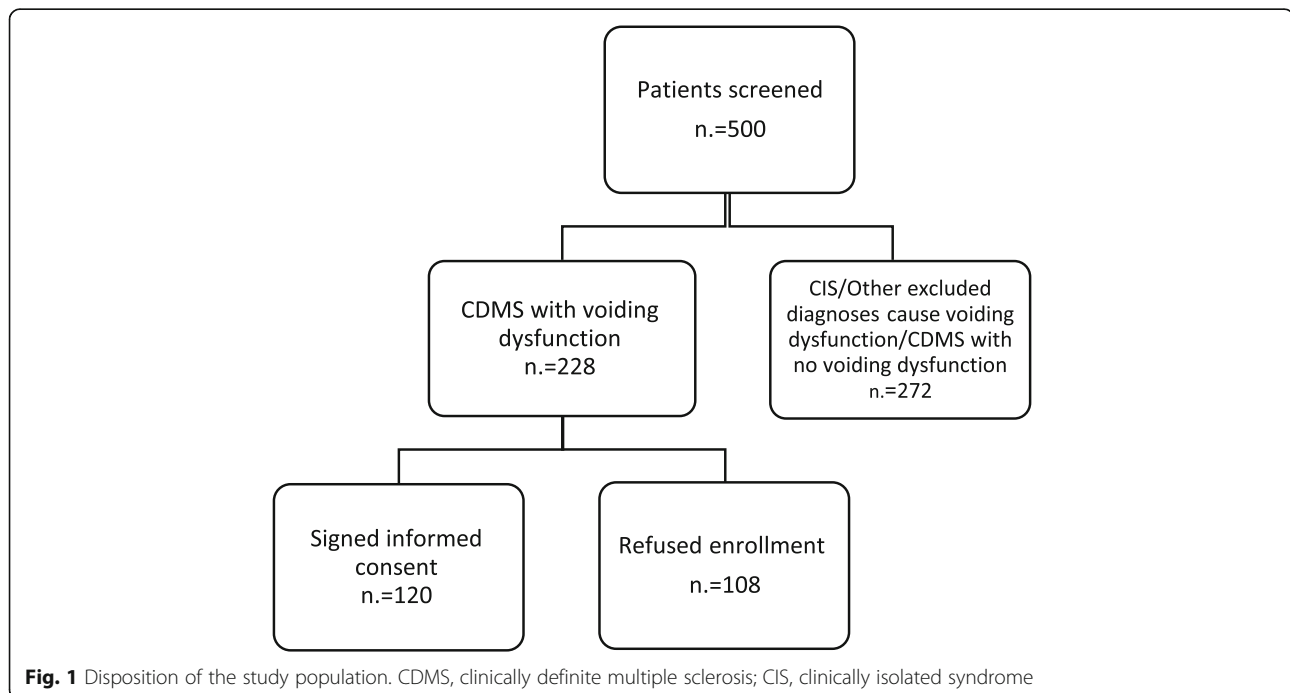
Five hundred patients attending Kasr Al-Ainy MS Clinic, Neurology Department, Cairo University Hospitals, Egypt, from December 2016 to March 2018, were evaluated for MS diagnosis and the presence of bladder dysfunction symptoms. Clinically definite multiple sclerosis (CDMS) according to the revised McDonald criteria (2010) [9] was verified in subjects; 228 of them had voiding dysfunction during their disease course. Eventually, 120 eligible subjects accepted to sign the informed consent (Fig. 1). Patients with other diagnoses such as history of diabetes mellitus, bladder neck surgery, prostate enlargement and fracture spine, and urinary tract infection at time of assessment were excluded.

Full history and neurological examination were carried out via a specialized neurologist, with assessment of disease severity using Expanded Disability Status Scale (EDSS) [10] at baseline and at the end of 1-year follow-up. A careful analysis of urological symptoms was done by a urologist from the “voiding dysfunction unit” Urology Department, Cairo University Hospitals, with the severity of symptoms rated by the American Urological Association Symptom Score (AUASS) [11] at baseline, 3, 6, and 12 months. The AUASS range from 0 to 35, where 0–7 points are considered mild, 8–19 are moderate, and 20–35 are severe.

MRI brain and spinal cord (cervical and dorsal) with and without contrast were done for all patients using 1.5-T MRI machine (Achiva, Philips Medical system, the Netherlands) during the period of patient admission with the following sequences: Axial T1WI, T2WI, Sagittal T1WI, coronal T2WI, and Fluid Attenuated Inversion Recovery (FLAIR).

Post voiding abdominal and pelvic ultrasound, where a residual urine volume  $\geq 100$  ml is considered significant [12], ascending cystography, renal functions, and urine analysis were evaluated for all patients at baseline.

Urodynamic assessment (Laborie, Delphis KT, version 12 with ilist reporting system, Canada 2010) was done for all patients initially at baseline including filling cysto-flowmetry, pressure flow study, and EMG of external sphincter, and the assessment was recorded by a computer-based device that consists of similar input sensors and amplification with the cysto-flowmetry in the standing position or sitting in a urodynamic chair using 6- or 7-Fr dual-lumen urethral catheter along with either a rectal or vaginal catheter to assess extravesimal pressure fluctuations. Urodynamic changes including the bladder volume at the first desire to void (ml), maximum bladder volume (ml), PdetQmax (cmH<sub>2</sub>O), postvoiding residual (PVR) (ml), electromyographic, Qmax (ml/s), and bladder compliance were measured. Detrusor overactivity, detrusor-sphincter dyssynergia, detrusor hypocontractility, and areflexia were defined according to the standardized definitions of lower urinary tract function by the international continence society (ICS) [13].



The patients were prescribed pharmacological treatment based on the nature of their symptoms and the therapeutic plan was modified according to patient's responses, and interventions as clean intermittent catheterization (CIC) and botulinum toxin-A (Botox) were used whenever needed.

### Statistical methods

Data was analyzed using the computer program Statistical package for the Social Science (SPSS version 22, IBM Corp, Armonk, NY, USA) released 2013 for Microsoft Windows. Mean and standard deviation ( $\pm$  SD) was used for numerical data while frequency and percentage for non-numerical data. Student *t* test was used to assess the statistical significance of the difference between means of the two studied groups. Mann-Whitney test (*U* test) was used to assess the statistical significance of the difference of a non-parametric variable between the two studied groups. Correlation analysis (using Pearson's and Spearman's rho method) assessed the strength of association between two quantitative variables. The correlation coefficient (*r*) defines the magnitude and direction (+ or -) of the linear relationship between two 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 urinary symptoms severity score. The probability/significance value (*P* value)  $\geq 0.05$  is not statistically significant and  $< 0.05$  is statistically significant.

### Results

The demographics, neurological and urological characteristics of MS patients are illustrated in (Tables 1 and 2).

Patients were prescribed medications to control voiding dysfunction and the most frequently used anticholinergics (76.6%), selective alpha blockers (35%), and parasymphomimetics (11.6%) in addition to

**Table 1** Demographics and clinical characteristics of multiple sclerosis

<b>Age(years)</b>		35.2 $\pm$ 10
<b>Sex</b>	Males	38 (31.7)
	Females	82(68.3)
<b>Disease duration(years)</b>		6.1 $\pm$ 4.9
<b>EDSS</b>	<b>1st</b>	4.8 $\pm$ 1.8
	<b>last</b>	4.7 $\pm$ 1.8
<b>Total relapse number</b>		4.1 $\pm$ 2.3
<b>Type of MS</b>	CIS	2(1.7)
	RRMS	88(37.3)
	PPMS	18(15)
	SPMS	12(10)

CIS clinical isolated syndrome, RRMS relapsing remitting multiple sclerosis, PPMS primary progressive multiple sclerosis, SPMS secondary progressive multiple sclerosis

Data are expressed as the mean  $\pm$  SD or number (percentage)

intervention, clean intermittent catheterization CIC (20%), and Botox injection for the bladder (15%).

Urinary symptoms severity showed a steady decrease by time, the highest at the 1st month with mean score  $18 \pm 6.6$ , then  $15.8 \pm 5.4$  at the 3rd month,  $12.5 \pm 4.8$  at the 6th month and the least after 1 year with mean score  $10.3 \pm 4.7$  and *P* value  $< 0.001$  (Fig. 2).

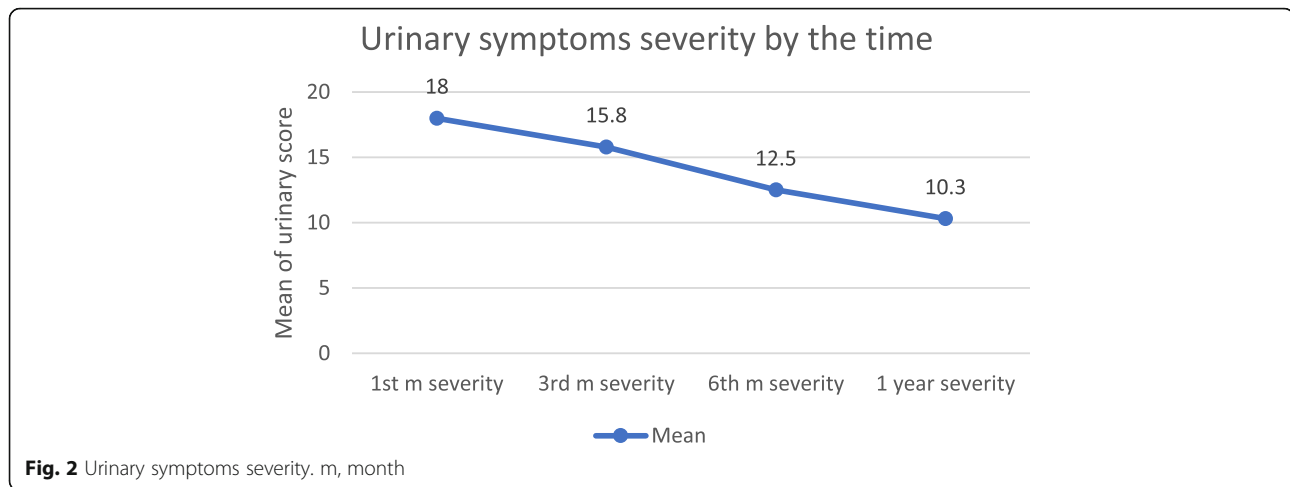
There is statistical significance in the relation of urinary symptoms severity and urodynamic results at all measurements through the year as *P* value was highly significant  $< 0.001$  (Table 3).

A statistically significant relation was found between the type of bladder symptoms and the pattern of urodynamic abnormality (*P* = 0.000) as 72% of patients with irritative symptoms had overactive bladder, and 66.7% of patients with obstructive symptoms had DSD while 64% of patients with mixed urinary symptoms had overactive bladder + DSD (Table 4).

**Table 2** Urological characteristics of multiple sclerosis

<b>Bladder symptoms</b>	Irritative		58(48.3)	
	Obstructive		12(10)	
	Mixed		50(41.7)	
<b>Residual urine via post voiding sonar</b>	$\geq 100$ ml		66 (55)	
<b>Urodynamic studies</b>	Normal		12(10)	
	Abnormal	Atonic bladder		14(11.7)
		Overactive bladder		42(35)
		Overactive bladder + DSD		32(26.7)
		DI		12(10)
		DSD		8(6.7)
		Total		108 (90)

DSD detrusor sphincter dyssynergia, DI detrusor instability  
Data are expressed as number (percentage)



There was a statistically significant positive correlation between 1st total EDSS versus urinary symptoms score at 1st assessment  $r = 0.39$ ,  $P < 0.001$ , and also last EDSS versus urinary symptoms score at 1 year follow-up  $r = 0.27$ ,  $P = 0.003$ , but no correlation was found between neither disease duration nor number of relapses and urinary symptoms score (Table 5).

On regression analysis, baseline total EDSS was a predictor for higher urinary symptoms severity score ( $P = 0.001$ ), however not a predictor for abnormal urodynamic. All other tested variables were not associated with higher urinary symptoms score or abnormal urodynamic (Table 6).

## Discussion

All patients in the current study complained from urinary symptoms with the irritative symptoms which were the most common and this came in agreement with multiple studies which reported that storage symptoms as urgency and frequency are the recurrent urinary symptoms [14–16], while other study stated that obstructive symptoms were more common than storage symptoms in MS patients and interrupted urinary flow was the most frequent symptom [17].

**Table 3** The relationship of urinary symptoms severity through the follow-up between abnormal and normal urodynamic results

Urinary symptoms score	Urodynamic results		P value
	Normal (12)	Abnormal (108)	
	Mean $\pm$ SD	Mean $\pm$ SD	
1st grade	5.8 $\pm$ 1.34	19.4 $\pm$ 5.4	<0.001**
3-month grade	4.8 $\pm$ 1.7	17.0 $\pm$ 4.1	<0.001**
6-month grade	4.3 $\pm$ 1.0	13.4 $\pm$ 4.1	<0.001**
1-year grade	4.0 $\pm$ 1.0	11.0 $\pm$ 4.5	<0.001**

\*\*P value < 0.01 (highly significant)

The severity of urinary symptoms in our study improved with compliance to symptomatic urological medication as anticholinergics decrease bladder pressure, improve muscle spasms, and reduce pain resulting from urine storage. The alpha-1 receptor blockers decrease urethral resistance and relieve emptying symptoms, in addition to intermittent catheterization for MS patients with urinary retention and high residual urine [14].

Urodynamic abnormalities were found in most of our studied MS patients with detrusor overactivity representing the predominant finding. Similarly, it was reported that the incidence of urodynamic changes in MS patients reaches up to 99% with neurogenic detrusor overactivity is the most frequent abnormality followed by DSD and detrusor hyporeflexia [17–19].

Intracranial plaques present in up to 90% of MS patients [20] but sacral plaques are much less common being found only in about 18% of MS patients. Lesions in the pons, lateral corticospinal and reticulospinal tracts and sacral cord neurons can cause voiding problem and the site of lesion is responsible for the resulting urinary syndrome. Suprasacral lesions especially at cervical level are common interrupting descending inhibitory signals producing irritative symptoms. Plaques in the reticulospinal tract disturbs fibers originating in the pons thus impairing synergistic contraction of the detrusor muscle and relaxation of the external sphincter with (DSD), while lesions in the pons with loss of stimulatory signals result in detrusor hyporeflexia [21, 22].

In our study we initially evaluated the MS patients with urodynamic assessment to provide better diagnosis and improve clinical management and quality of life. On the contrary, other study did not support the use of invasive urodynamic in the initial evaluation of patients with MS and prefer to be restricted to patients with severe urinary symptoms refractory to treatment [23].

**Table 4** Relationship of bladder symptoms type and urodynamic results

Bladder symptoms type			Urodynamic results					P value
			Atonic bladder	Overactive bladder	Overactive + DSD	DI	DSD	
Irritative, n = 58	Number		0	42	0%	12	0	0.000**
	% within bladder symptoms		0%	72.4%	0%	20.7%	0%	
	% within urodynamic		0%	100%	0%	100%	0%	
Obstructive, n = 12	Number		2	0	0	0	8	
	% within bladder symptoms		16.7%	0%	0%	0%	66.7%	
	% within urodynamic		14.3%	0%	0%	0%	100%	
Mixed, n = 50	Number		12	0	32	0	0	
	% within bladder symptoms		24%	0%	64%	0%	0%	
	% within urodynamic		85.7%	0%	100%	0%	0%	

DSD detrusor sphincter dyssynergia, DI detrusor instability

\*\*P value < 0.01 (highly significant)

Through the 1-year follow-up, our study confirmed the result of a previous one with the severity of urinary symptoms in patients who had abnormal urodynamic differ significantly [15]. In contrast to our results, another urodynamic study revealed that there is no association between urinary symptoms severity and urodynamic changes [24].

Our studied MS patients suffered from irritative symptoms resulting from detrusor overactivity and/or incompetent sphincter, while obstructive symptoms denote detrusor-sphincter dyssynergia or detrusor underactivity [6].

Babovic and colleagues agree with our results and mentioned that urgency, frequency, and urge incontinence were well correlated with detrusor hyperreflexia [3]. On the other side, Haggiag and colleagues did not report the value of urinary symptoms assessment in determining the urodynamic changes as they used different questionnaire and limited urological parameters and the effect of other MS disabling symptoms [25].

EDSS initial and 1 year assessment in our study was correlated with urinary symptoms score while no correlation was found with disease duration. This result agrees with a study that showed irritative urinary symptoms were significantly affected by EDSS while obstructed symptoms were not affected by disease duration [6].

**Table 5** Correlation of urinary symptoms severity with EDSS (1st month vs 1st EDSS, 1 year vs last EDSS), disease duration, and number of relapses

		Urinary symptoms severity			
		1st month		1 year	
		r value	P value	r value	P value
EDSS	1st	0.39	< 0.001**	----	
	Last	----		0.27	0.003**
Disease duration in years		0.17	0.19	0.06	0.60
Number of relapses		0.15	0.23	0.1	0.36

EDSS expanded disability status scale

P value ≥ 0.05 (non-significant), \*\*P value < 0.01 (highly significant)

High EDSS score was the only predictor for severe urinary symptoms in our studied MS patients while it was not a predictor for abnormal urodynamic. This was consistent with a prospective study conclusion that high EDSS was associated with frequent urinary incontinence [26]. However, another study demonstrated a significant relationship between EDSS and urodynamic abnormality with risk to upper urinary tract damage. We attributed absence of predictive value of EDSS and other disease parameters in our study to the low number of patients with normal urodynamic that did not reach a statistical significant value [27].

The observed limitation of our study was that all included MS patients had urinary complaints so no chance for value of urodynamic in patients without urinary symptoms.

**Conclusion**

Irritative bladder symptoms and overactive bladder are the most frequent lower urinary tract problem in MS patients. EDSS is a predictor for urinary symptoms severity. The type of bladder symptoms can reflect urodynamic abnormalities.

**Table 6** Predictors of abnormal urodynamic and severity of urinary symptoms

Predictors	Abnormal urodynamic			Severity of urinary symptoms		
	OR	95% confidence interval	P value	Regression coefficient	95% confidence interval	P value
EDSS	1.38	0.92–2.08	0.11	1.49	0.89–2.10	< 0.01**
Disease duration (years)	1.10	0.82–1.48	0.49	0.21	– 0.08 to 0.52	0.15
Number of relapses	1.42	0.73–2.72	0.29	0.30	– 0.32 to 0.94	0.34
MS type	0.36	0.00	1.00	– 1.02	– 2.64 to 0.59	0.21

EDSS expanded disability status scale, MS multiple sclerosis, OR odds ratio P value ≥ 0.05 (non-significant), \*\*P value < 0.01 (highly significant)



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Not applicable.

### Authors' contribution

HT participated in study design, urodynamic study, collection, and analysis of data. NS participated in study design and helped to select the type of patients. SH helped to draft the manuscript and in the diagnosis of selected participants. HA participated in study design. SZ participated in the follow-up of urodynamic study. MS participated in study design sequence alignment. AY performed the laboratory work. SM performed abdominal and pelvic ultrasound for all participants. All authors read and approved the final manuscript.

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### Availability of data and materials

The datasets used during the current study are available from the corresponding author on reasonable request with permission of Faculty of Medicine, Cairo University, Egypt.

### Ethics approval and consent to participate

The study was approved by the ethical committee of the Urology Department, Faculty of Medicine, Cairo University (I-131016, on the 26th of December 2016). The procedures and follow-up were explained to every participant and an informed written consent was obtained from all participants.

### Consent for publication

Not applicable.

### Competing interests

The authors declare that they have no competing interests.

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### References

1. Compston A, Coles A. Multiple sclerosis. *Lancet*. 2008;372:1502–17.
2. Wein AJ. Lower urinary tract dysfunction in neurologic injury and disease. In: Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA, editors. *Campbell-Walsh Urology*. 9th ed. USA; 2007. p. 2011–2045.
3. Babović R, Miličević S, Radovanović S, Jančić J. Testing of urodynamic dysfunctions in patients with multiple sclerosis. *Vojnosanit pregled*. 2014; 71(5):446–50.
4. Shah P. Symptomatic management in multiple sclerosis. *Ann Indian Acad Neurol*. 2015;18(Suppl 1):S35.
5. Kirchhof K, Fowler CJ. The value of the Kurtzke Functional Systems Scales in predicting incomplete bladder emptying. *Spinal Cord*. 2000;38(7):409.
6. Araki I, Matsui M, Ozawa K, Nishimura M, Kuno S, Saida T. Relationship between urinary symptoms and disease-related parameters in multiple sclerosis. *J Urol*. 2002;249(8):1010–5.
7. DasGupta R, Fowler CJ. Bladder, bowel and sexual dysfunction in multiple sclerosis: management strategies. *Drugs Rev*. 2003;63(2):153–66.
8. World Medical Association. Declaration of Helsinki. Ethical principles for medical research involving human subjects. Adopted by the 18th World Medical Association General Assembly. Helsinki, Finland. 1964.
9. Polman CH, Reingold SC, Banwell B, Clanet M, Cohen JA, Filippi M, et al. Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. *Ann Neurol*. 2011;69(2):292–302.
10. Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). *Neurology*. 1983;33(11):1444.
11. Roehrborn CG. The American Urological Association Symptom Index—concerns and confirmation. *J Urol*. 1996;6(155):1975–6.
12. Kelly CE. Evaluation of voiding dysfunction and measurement of bladder volume. *Rev Urol*. 2004;6(Suppl 1):S32.
13. Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U, et al. The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. *Neurourol Urodyn*. 2002;21(2):167–78.
14. Wang T, Huang W, Zhang Y. Clinical characteristics and urodynamic analysis of urinary dysfunction in multiple sclerosis. *Chin Med J*. 2016;129(6):645.
15. Tadayyon F, Etemadifar M, Bzeih H, Zargham M, Nouri-Mahdavi K, Akbari M, et al. Association of urodynamic findings in new onset multiple sclerosis with subsequent occurrence of urinary symptoms and acute episode of disease in females. *J Res Med Sci*. 2012;17(4):382.
16. Engeler DS, Meyer D, Abt D, Müller S, Schmid HP. Sacral neuromodulation for the treatment of neurogenic lower urinary tract dysfunction caused by multiple sclerosis: a single-centre prospective series. *BMC Urol*. 2015;15(1):105.
17. Nakipoglu GF, Kaya AZ, Orhan G, Tezen O, Tunc H, Ozgirgin N, et al. Urinary dysfunction in multiple sclerosis. *J Clin Neurosci*. 2009;16(10):1321–4.
18. De Sèze M, Ruffion A, Denys P, Joseph PA, Perrouin-Verbe B. International Francophone Neuro-Urological expert study group (GENULF). The neurogenic bladder in multiple sclerosis: review of the literature and proposal of management guidelines. *Mult Scler*. 2007;13(7):915–28.
19. Kobashi KC. Review of the 2008 annual meeting of the Society of Urodynamics and Female Urology (SUFU) at the American Urological Association. *Curr Bladder Dysfunct Rep*. 2009;4(1):5–10.
20. Aharony SM, Lam O, Corcos J. Evaluation of lower urinary tract symptoms in multiple sclerosis patients: review of the literature and current guidelines. *Can Urol Assoc J*. 2017;11(1–2):61.
21. Araki I, Matsui M, Ozawa K, Takeda M, Kuno S. Relationship of bladder dysfunction to lesion site in multiple sclerosis. *J Urol*. 2003;169(4):1384–7.
22. Litwiller SE, Frohman EM, Zimmern PE. Multiple sclerosis and the urologist. *J Urol*. 1999;161(3):743–57.
23. Çetinel B, Tarcan T, Demirkesen O, Özyurt C, Şen İ, Erdoğan S, et al. Management of lower urinary tract dysfunction in multiple sclerosis: a systematic review and Turkish consensus report. *Neurourol Urodyn*. 2013; 32(8):1047–57.
24. Onal B, Siva A, Buldu I, Demirkesen O, Cetinel B. Voiding dysfunction due to multiple sclerosis: a large scale retrospective analysis. *Int Braz J Urol*. 2009; 35(3):326–33.
25. Haggiag S, Bolla G, Picconi O, Galgani S, Gasperini C. Discrepancies between urinary symptoms assessment and objective bladder dysfunctions in multiple sclerosis. *Mult Scler Demyelinating Disord*. 2017;2(1):11.
26. Wiedemann A, Kaeder M, Greulich W, Lax H, Priebe J, Kirschner-Hermanns R, et al. Which clinical risk factors determine a pathological urodynamic evaluation in patients with multiple sclerosis? An analysis of 100 prospective cases. *World J Urol*. 2013;31(1):229–33.
27. Ineichen BV, Schneider MP, Hlavica M, Hagenbuch N, Linnebank M, Kessler TM. High EDSS can predict risk for upper urinary tract damage in patients with multiple sclerosis. *Mult Scler*. 2018;24(4):529–34.

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