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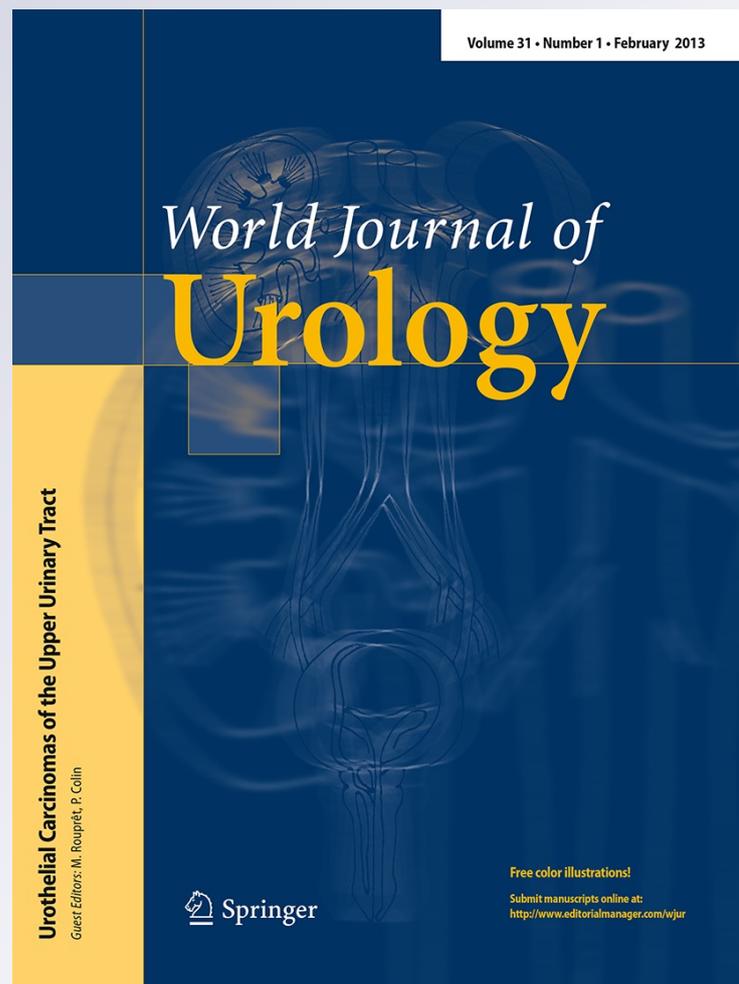
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# Which clinical risk factors determine a pathological urodynamic evaluation in patients with multiple sclerosis? an analysis of 100 prospective cases

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## Abstract

**Background** Urinary tract symptoms are an underestimated problem in multiple sclerosis (MS).

**Objective** Hundred urodynamics of MS patients have been evaluated prospectively.

**Design, setting and participants** In an inpatient rehabilitation, all persons with MS who also suffered from urinary tract symptoms received a voiding diary, post-void sonography and an urodynamic examination according to International Continence-Society-Standard.

**Results and limitations** Between 10/2009 and 3/2011, 100 patients (79 women; 21 men; mean EDSS,  $4.52 \pm 2.26$ ) were examined who had primary progressive MS (9×), relapsing–remitting MS (41×), secondary progressive MS (43×) and CIS (1×). The mean duration of MS was  $10.26 \pm 10.09$  years and mean duration of LUTS,  $6.9 \pm 7.75$  years. Urodynamic testing showed normal findings in 22 patients, detrusor

overactivity in 7, increased bladder sensation without detrusor overactivity in 21, detrusor–sphincter dyssynergia in 26, detrusor hypocontractility in 12, detrusor acontractility in 4 and unclear diagnosis in 8 patients. Statistically significant risk factors for pathological urodynamic findings were as follows: wheelchair dependency, use of more than one incontinence pad per day and a MS type other than relapsing–remitting.

**Conclusions** The urodynamic investigation at hand showed urinary tract dysfunction in 78 of 100 MS patients with lower urinary tract symptoms (LUTS). The long latency between the occurrence of MS and/or the beginning of LUTS and the first neuro-urological evaluation indicates a deficit in treatment. Beyond national guidelines, all MS patients should at regular intervals be questioned about LUTS and receive urodynamic assessment especially according to the presented risk profile.

**Keywords** Multiple sclerosis · Lower urinary tract symptoms · Urodynamics

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## Introduction

Multiple sclerosis (MS) is a neurodegenerative disease of the spinal cord and the brain. So far, its causes are not clear, presumably, autoimmune processes play a role. In terms of aetiology, environmental influences [1, 2], genetic factors [3–5], (viral) infections during childhood [6], vitamin D deficiency [7, 8], smoking [9], cerebral venous insufficiency [10] and stress [11] are discussed. Women are afflicted 3–4 times more frequently [12]. First symptoms occur mostly at young adulthood and vary depending on the location of the demyelination focus in the central nervous system. It could be paresis, paresthesia, spasms but

also ataxia, dysphagia, impaired vision and increased fatigue. The course of the disease can be relapsing–remitting or chronic [13, 14]. Lower urinary tract symptoms (LUTS) occur in 75% of affected patients, as do ophthalmologic and neurological symptoms [15, 16]. For MS patients, the probability of urinary incontinence is increased by the factor 21.9 [17]. Not only are there serious impacts on the quality of life [15, 18, 19] but there also exists a potential risk for the upper urinary tract [20].

Urodynamics are rarely conducted. Petersen observed pathological findings in 98 per cent of the 88 patients who underwent urodynamics. An overactive bladder (OAB) with detrusor dysfunction was prevalent. A relation to the latency of symptoms or MS type could not be found [21]. Giannantoni detected urodynamic pathological findings in 89.6% of patients with LUTS; a correlation between the degree of detrusor hypotonia and the neurological status was observed [22].

The guidelines from the German Neurological Society for diagnosis and treatment of MS have no explicit recommendation for regular LUTS screenings for MS patients. It is only mentioned that in case of LUTS, a urinalysis and a frequency–volume chart, and optionally a urodynamic examination should be performed (<http://www.awmf.org/leitlinien/detail/II/030-050.html>). In the diagnostic recommendations for routine diagnosis of MS without disease-modifying therapy, the only indication is, apart from anamnesis in 3 months intervals without any advice to enquire about LUTS, a urinalysis in 6-month intervals.

There might be three reasons for this discrepancy between the frequency of LUTS in MS, the social medical impact and the severity of urodynamically identifiable LUTS:

Apart from the fact that urodynamic examinations do not belong to a neurologist's field of diagnosis and is therefore not in their focus, patients have a significant tendency to keep silent about urinary incontinence, which results in an underestimation of this phenomenon [22, 23]. Furthermore, urodynamic examinations are rarely performed on MS patients altogether. The study on hand aims at eliminating this deficit. In addition, it should resolve whether it is possible to find risk factors that imply an urgent indication of urodynamics on MS patients.

## Patients and methods

In a neurologic rehab clinic, all MS patients who were taken in for rehabilitation during the study period were questioned systematically about LUTS and were asked to keep a frequency–volume chart (FVC) for 3 days. An indication for urodynamics was defined as follows:

frequency  $\geq 7$  micturitions per day or  $\geq 1$  during the night, urgency to void and/or urinary incontinence. It was suggested for 125 out of 400 patients with these inclusion criteria. The examination included urinalysis, sonography of the upper urinary tract, post-void sonography and a urodynamic measurement according to ICS-standard (determination of residual urine by catheterization, cystomanometry in sitting position with filling the bladder at a physiological filling rate with 37°C physiological saline solution, pressure–flow study, urethra pressure profile, optionally urethra stress profile and flow-EMG) and was performed by one physician and one nurse [24]. Exclusion criteria for an urodynamic measurement were defined as follows: urodynamics already done, state that makes urodynamics impossible, that is, immobility (bed-ridden) or lack of ability to communicate, or nitrite-positive UTI. At the end of the prospective study, 100 urodynamic measurements according to the mentioned inclusion criteria could be evaluated.

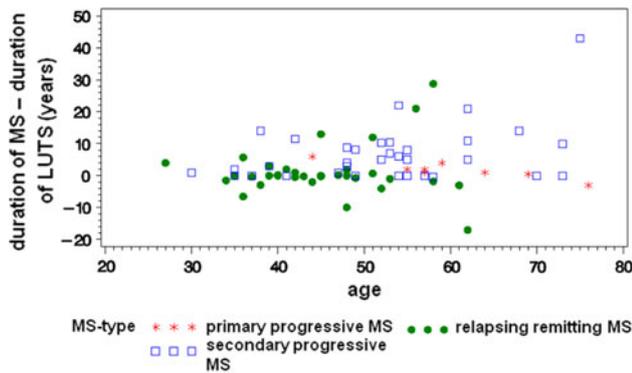
## Statistical methods

Data evaluation was performed with the Software SAS version 9.2. Descriptively, statistical indices like minimum, maximum, median and SD were calculated. Box plots, scatter plots and pie charts have been used for graphic presentation.

Univariately, logistic regression models have been calculated for a selection of potential determinants. The dependent variable is a pathological finding in the final diagnosis of the urologist. For a decision tree, the variable that has univariately the biggest influence on the target variable was successively used as decision criterion. The influence was measured in comparison with the Wald chi-square value in the logistic regression. The process stops as soon as no potential parameter in the Wald test reaches a  $P$  value  $< 0.05$ .

## Results

Between October 2009 and March 2011, 100 patients (mean age:  $49.4 \pm 10.9$  years) were examined. Seventy-nine of them were women (mean age  $50.6 \pm 11.2$  years) and 21 were men (mean age  $45.14 \pm 8.52$  years). According to the records, they were diagnosed primary progressive MS ( $n = 9$ ), relapsing–remitting MS ( $n = 47$ ), secondary progressive MS ( $n = 43$ ) and clinical isolated syndrome CIS ( $n = 1$ ). Patients with an initial manifestation were added to the relapsing–remitting MS since naturally the progression of the disease could not be evaluated at that stage. The mean duration of MS was  $10.26 \pm 10.09$  years, mean duration of urinary tract symptoms was  $6.9 \pm 7.75$  years. The relation

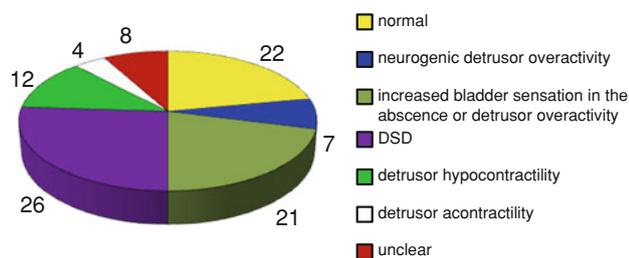


**Fig. 1** Duration of MS—duration of LUTS (years) for the several types of MS

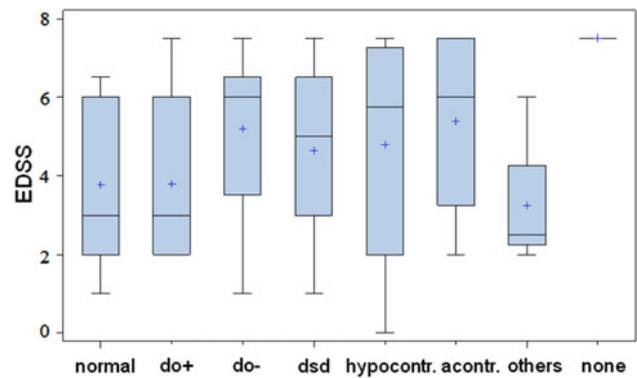
of the two parameters showed a diverse pattern: LUTS partially appeared before MS was diagnosed and partially after a MS duration of several years. For relapsing–remitting MS, a tendency could be seen that LUTS started soon after or before the MS diagnosis (Fig. 1).

The neurological rating on the Expanded Disability Status scale [25] (EDSS) showed a mean value of  $4.52 \pm 2.26$ . Forty-nine patients had (limited) walking ability ( $EDSS \leq 5.5$ ), 30 patients depended on walking aids ( $EDSS 6–6.5$ ) and 14 needed a wheelchair ( $EDSS 7–8$ ).

The anamnesis showed urinary incontinence (defined as any loss of urine) for 61 patients, 78.7% of them needed incontinence pads (11 patients, 1 pad; 13 patients, 2; 9 patients, 3, 7 > 4/day). Micturition frequency in 24 h as average from the 3 days recorded in the frequency–volume chart (FVC) was  $9.3 \pm 4$  voidings. FVC showed 7–8 micturitions per day in 33 patients, 9–10 micturitions in 30 patients and 11–12 micturitions in 13 patients; 11 patients even had more than 12 micturitions per day. Accordingly, 38 patients stated 1 voiding per night, 21 two, 17 three, 6 four, 4 patients five voidings and 1 patient more than five voidings per night. The mean value of residual urine that was measured by ultrasound and during urodynamics was 69.1 or 70.3 ml (0–500). The urodynamic assessment showed the following distribution of diagnoses (Fig. 2): In 8 patients, it was not possible to define a clear urodynamic



**Fig. 2** Urodynamic diagnoses



**Fig. 3** Relation between urodynamic diagnoses and the degree of disability (EDSS)

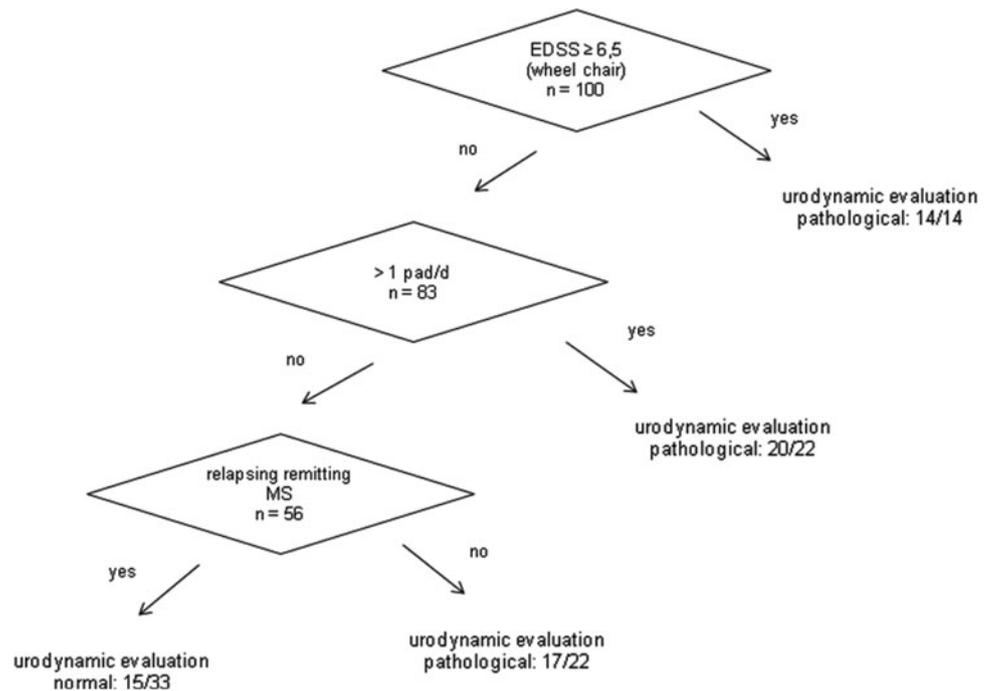
diagnoses, although each urodynamic measurement was intensively discussed due to contrasting findings or artefacts. In all 26 cases of detrusor–sphincter dyssynergia, there were involuntary detrusor contractions. Detrusor pressures due to instable contractions reached an average of 36.3 cm H<sub>2</sub>O (5–53) for neurogenic detrusor overactivity. The relation between the type of urodynamic diagnosis and the grade of disability showed a trend for patients with OAB with involuntary detrusor contractions. For this group, the EDS score was comparable to patients with urodynamically normal findings. For all other types of bladder, inhibitions a higher EDS score and therefore a higher degree of disability could be noticed (Fig. 3).

The calculation of a regression model showed in descending order the highest possibility to detect pathological findings in urodynamics when the EDS score was higher than 6.5 (wheelchair dependability), followed by the use of more than one incontinence pad per day, and the diagnosis of a MS type other than relapsing–remitting. All further parameters remained below the significance limit (see Fig. 4). In detail, wheelchair dependability of the patients with an EDS score  $\geq 6.5$  provided the highest prediction probability of a pathological finding in urodynamics; all 14 patients who were wheelchair bound showed pathological urodynamics. For patients who were not wheelchair dependent, this applied for 20 out of 22 patients who used more than one incontinence pad per day; for patients without pad usage, a MS type of non-remitting progression was connected to a pathological results in 17 out of 22 cases ( $P = 0.0361$  resp.  $P = 0.0405$ ). The sensitivity of this regression analysis is 73.9%, the specificity is 68.2% for a positive predictive value of 87.9%.

**Discussion**

With this study, it was possible to show after a systematic questioning of MS patients about LUTS that with an

**Fig. 4** Logistic regression analysis: probability of a pathological finding in urodynamics



appearance of symptoms such as increased daytime frequency, nocturia, urgency or incontinence a functional urological bladder disorder could also frequently be found by urodynamic examinations; only 22 out of 100 patients showed normal findings in urodynamics. Findings were detrusor overactivity, increased bladder sensation without involuntary detrusor contractions, bladder hypocontractility/acontractility or functional obstruction like detrusor–sphincter dyssynergia. Frequently, even experienced examiners had problems to allocate urodynamic findings clearly to a specific disorder. Despite a rather mild symptomatology, there were partly dramatic and potentially dangerous findings: detrusor pressures up to 53 cm H<sub>2</sub>O and a maximal post-void residual urine of 500 ml stood out in our setting for the first time, at the end of the ‘career’ of MS patients in a rehab hospital after termination of the actual diagnosis. This indicates deficits in the care for MS patients in the institutions that carry out primary diagnosis.

Examinations showed for MS patients with involuntary detrusor contractions a degree of disability that was comparable to patients with urodynamically normal findings possibly due to an early form of bladder disturbance. All other urodynamic diagnoses including detrusor acontractility and detrusor hypocontractility were connected to a more serious disability, a finding that has already been described in publications [22].

The logistic regression analysis showed for an EDS score  $\geq 6.5$  a regular use of more than one incontinence pad per day or a MS type that was not relapsing–remitting a

statistically significant risk of pathological findings in urodynamic measurement. These subgroups of patients have to be considered risk groups or risk patients. This should be accounted for in the respective guidelines:

Altogether, the existing recommendation of the German Neurologic Society in the respective guideline to carry out urodynamics ‘optionally’ when urinary tract symptoms appear has to be considered insufficient. With the results of this study, recommendation could be improved by including the recommendation that patients with an increasing degree of disability, use of incontinence pads and a primary or secondary progressive MS should receive urodynamic measurements preventively.

Urodynamics of urinary tract disorders in MS are so different and unpredictable with regard to severity that every MS patient not only has to be questioned actively and regularly about urinary tract symptoms but should also in case of positive answers receive a urodynamic measurement before symptomatic therapies are carried out.

#### Take home message

Patients with MS show a high risk to suffer from serious lower urinary tract disorders, even when the symptoms are rather mild. This regression analysis proved that the risk of a pathological result in urodynamics is especially high for patients with EDSS  $> 6.5$ , use of more than one incontinence pad per day and a MS that is not of the relapsing–remitting type. It has to be demanded that beyond the recommendation in the national guidelines all MS patients

have to be questioned about urinary tract disorders and in case of their existence receive a urodynamic examination according to the described risk profile by an experienced professional.

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