


Lower urinary tract disorders in multiple sclerosis patients: prevalence, clinical features, and response to treatments

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Abstract

Aims: Lower urinary tract symptoms are common in multiple sclerosis (MS) and have a great impact on quality of life. We evaluated prevalence and characteristics of urological symptoms in a cohort of patients with MS.

Methods: This is a cross-sectional study conducted on consecutive patients with MS attending our Center in 2018. We evaluated prevalence, clinical features, and response to symptomatic treatments of lower urinary tract disorders; we investigated the relationship between them and clinical and demographic features. Data of urodynamic studies were also collected.

Results: In our cohort of 806 patients, the overall prevalence of urological symptoms was 52.9% and urgency was the most frequent symptom (59.4%). Symptomatic patients had a higher disability, a longer disease duration, a later age at onset, and a greater mean age at the time of evaluation. Urinary disorders were more frequent in patients with progressive disease and in women. About 41.8% of patients were under treatment for the urological disorder and 81.5% of them reported an improvement of symptoms.

Conclusion: Urinary disorders in patients with MS have a high prevalence. An early and correct characterization of types of symptoms and an early and targeted therapeutic strategy are essential to improve the patient's quality of life and avoid future complications.

KEYWORDS

multiple sclerosis, symptomatic treatments, urinary disorders, urodynamic study

1 | INTRODUCTION

Lower urinary tract symptoms (LUTS) in patients with multiple sclerosis (MS) are common (from 32% up to 96% of patients), appearing on average six years after neurological symptoms, but they may be present at the onset of the disease in about 10% of cases.¹ Overactive bladder (OAB) symptoms, such as frequency and/or urinary urgency associated or not with urge incontinence, are those most frequently reported by patients with MS (37%–99% of patients) and correlate with an alteration of the storage phase due to the presence of detrusor overactivity.² Seconds by frequency, with a prevalence from 34% to 79%, are voiding dysfunction symptoms (hesitancy, interrupted voiding, and feeling of incomplete bladder emptying).² These symptoms are not very informative on the underlying pathophysiological mechanism.² In patients with MS, the most frequent urodynamic profile is detrusor overactivity (average prevalence is 65%, with a range from 34% to 99%), typically associated with frequency, urgency, and urge incontinence; underactive detrusor ranges from 0% to 40%, with an average prevalence of 25%; bladder compliance alterations are present from 2% to 10% of cases.¹ Another common alteration is the detrusor-sphincter dyssynergia, whose prevalence data are greatly influenced by the heterogeneity of the evaluation method among studies.^{1,3} These various clinical features may appear isolated or in association.⁴ Patients with high disability (with an Expanded Disability Status Scale [EDSS]⁵ score > 6.5) and/or with progressive MS phenotype are more likely to present pathological urodynamic study.⁶

Treatment choice should be based on the specific type of disorder presented by the patient. In patients with MS having filling disorders, who complain of urgency and urge incontinence, the treatment is based on the use of antimuscarinic drugs.⁷ Beta-adrenergic agent mirabegron is a valid alternative to antimuscarinics for the management of detrusor overactivity in adults, including those for whom antimuscarinics have proven unsuitable.⁸ In patients with detrusor overactivity refractory to conventional therapy, it is possible to resort to intradetrusor injections of botulinum toxin A (BoNT-A).⁹ In patients who are refractory to symptomatic therapy, electrical stimulation methods can also be considered with the aim of inhibiting micturition.^{10,11} In patients with voiding problems, the first-choice drugs are alpha-blockers.¹² Intermittent self-catheterization is used in patients with poor response to drug therapy.¹³ Only in patients in whom intermittent self-catheterization is not practicable should be considered the placement of an indwelling catheter, possibly suprapubic to avoid urethra injury.¹⁴ Women with symptoms related to detrusor overactivity,

which are often associated with a spasm of the pelvic floor, can benefit from pelvic floor training,¹⁵ however, data on the effectiveness of this practice in patients with MS are scarce.¹⁶

In this study, we evaluated the prevalence, clinical features, and response to symptomatic treatments of lower urinary tract disorders in people affected by MS and investigated the relationship between urological disorders and clinical and demographic features of our cohort.

2 | METHODS

2.1 | Study design and participants

This is a cross-sectional retrospective study conducted on 806 consecutive patients with MS evaluated from January 2, 2018 to December 31, 2018 at the MS Center of the Policlinico Universitario “A. Gemelli” IRCSS in Rome.

The study inclusion criteria were: definitive diagnosis of MS based on the 2010 revision of McDonald criteria,¹⁷ age more than or equal to 18 years, mental ability to answer questions, stable clinical status (lack of recurrence in the past 3 months and of disability worsening, defined as 1.0-point increase [if baseline EDSS score was < 5.5] or 0.5-point increase [if baseline EDSS score was ≥ 5.5] confirmed 6 months apart and sustained at the end of the follow-up period),¹⁸ lack of LUTS before the onset of MS, lack of history of pelvic surgery/radiotherapy or bladder stones and lack of history of benign prostatic hyperplasia (BPH) or prostate surgery (through patient self-report). The exclusion criteria included recurrence of MS and treatment with corticosteroids in the previous month and a clinical follow-up of less than 6 months.

Demographic and clinical variables were considered for each patient. Demographic variables were age and sex, while the clinical variables were age at MS onset, disease duration, EDSS score, clinical course (relapsing-remitting, primary progressive, and secondary progressive), and the presence or absence of lower urinary tract disorders. The EDSS was performed by certified neurologists (neurostatus.net).

The urological symptoms recorded were frequency, urgency and urge incontinence as OAB symptoms; feeling of incomplete emptying, hesitancy, straining to void, urinary retention, and recurrent urinary tract infections (UTI) (defined as 2 or more UTI in 6 months) as voiding symptoms. Patients were further divided based on the symptom pattern (OAB syndrome, voiding dysfunction, or mixed symptomatology). We finally evaluated the use of symptomatic treatments, adherence, and response to therapy.

2.2 | Urodynamic studies

Data of urodynamic studies performed in 2018 were collected. The following items were recorded for each examination: cystomanometric capacity, bladder compliance, the presence of detrusor overactivity and contraction volume, maximum detrusor pressure, maximum flow and type of flow (intermittent and continuous), and the presence of postvoid residual volume.

2.3 | Aims of the study

The first aim of our study was to evaluate the prevalence of lower urinary tract disorders in patients with MS. As second aims we characterized the lower urinary tract disorders of these patients, evaluated the urodynamic abnormalities in a subgroup of them, and recorded the effect of symptomatic treatments on urinary symptoms. Furthermore, we investigated the relationship between the presence of urological disorders and the clinical and demographic features of our cohort.

2.4 | Statistical analysis

Statistical analysis was realized using the “Statistical Package for Social Science (SPSS)” program. Continuous variables are expressed as mean \pm SD and categorical variables are represented as frequencies. The appropriate statistical tests (Mann–Whitney U test, Kruskal–Wallis test, χ^2 test, and multinomial logistic regression) were used for the analysis of the results. Results with $p < 0.05$ were considered statistically significant.

3 | RESULTS

3.1 | Study population

For the present study, we collected data from 806 consecutive patients with MS who attended the MS Center of the Policlinico “A. Gemelli” IRCSS, in Rome, in 2018.

The mean age of the participants was 45.84 ± 12.86 years with a mean age at MS onset of 31.79 ± 11.24 years and a mean disease duration of 12.54 ± 9.60 years. As expected, most patients were female (68.1%, $n = 549$) and the most common clinical phenotype was relapsing-remitting (76.9%, $n = 620$), followed by secondary progressive (13.4%, $n = 108$) and primary progressive (9.7%, $n = 78$).

TABLE 1 Frequency of urinary symptoms

| | Symptomatic patients ($n = 426$) |
|--------------------------------|------------------------------------|
| <i>Urinary pattern</i> | |
| OAB syndrome | 231 (54.2%) |
| Voiding dysfunction | 87 (20.4%) |
| Mixed | 108 (25.4%) |
| <i>OAB symptoms</i> | |
| Frequency | 82 (19.2%) |
| Urgency | 253 (59.4%) |
| Urge incontinence | 177 (41.5%) |
| <i>Voiding disorders</i> | |
| Feeling of incomplete emptying | 123 (28.9%) |
| Hesitancy | 67 (15.7%) |
| Abdominal strain to void | 54 (12.7%) |
| Urinary retention | 40 (9.4%) |
| Recurrent urinary infections | 9 (2.1%) |
| <i>Symptomatic treatment</i> | |
| Treated patients | 178 (41.8%) |
| Untreated patients | 248 (58.2%) |

Abbreviation: OAB, overactive bladder.

3.2 | Urological disorders

The overall prevalence of urological disorders was 52.9% ($n = 426$). The most frequent clinical pattern was the OAB syndrome (54.2%, $n = 231$), followed by mixed symptomatology (25.4%, $n = 108$), and voiding dysfunction (20.4%, $n = 87$). The urgency was the most frequent symptom in our cohort (59.4%, $n = 253$), followed by urge incontinence (41.5%, $n = 177$) and feeling of incomplete emptying (28.9%, $n = 123$). Despite this latter symptom can be characterized as voiding disorder, it was mostly referred by patients with mixed symptomatology rather than purely voiding dysfunction (64.2% vs. 35.8%). Pattern and individual symptoms data are summarized in Table 1.

The pattern of urological disorders (OAB syndrome, mixed symptomatology, and voiding dysfunction) differed in a statistically significant way in relation to the age at onset, earlier in patients with voiding dysfunction and later in those with OAB syndrome, and sex, as the presence of OAB symptoms was greater in women (Table 2).

TABLE 2 Comparison between demographic and clinical characteristics of symptomatic patients—Symptoms patterns

| | OAB syndrome (n = 231) | Voiding dysfunction (n = 87) | Mixed symptomatology (n = 108) | p |
|------------------------------------|------------------------|------------------------------|--------------------------------|--------------------|
| <i>Demographic characteristics</i> | | | | |
| Age | 50.8 ± 12.4 | 48.9 ± 12.2 | 50.1 ± 12.0 | NS |
| Sex | | | | 0.036 ^b |
| Male | 56 (24.2%) | 33 (37.9%) | 26 (24.1%) | |
| Female | 175 (75.8%) | 54 (62.1%) | 82 (75.9%) | |
| <i>Clinical characteristics</i> | | | | |
| Age of onset | 34.8 ± 11.7 | 31.3 ± 11.4 | 32.9 ± 11.2 | 0.048 ^a |
| Disease duration | 14.5 ± 10.0 | 15.9 ± 9.8 | 15.6 ± 10.5 | NS |
| EDSS | 3.8 ± 2.0 | 3.8 ± 2.7 | 4.3 ± 2.0 | NS |
| <i>Clinical course</i> | | | | |
| Relapsing-remitting | 141 (61.0%) | 58 (66.7%) | 63 (58.3%) | NS |
| Primary progressive | 41 (17.7%) | 10 (11.5%) | 13 (12.0%) | |
| Secondary progressive | 49 (21.2%) | 19 (21.8%) | 32 (29.6%) | |

Abbreviations: EDSS, Expanded Disability Status Scale; OAB, overactive bladder.

^aKruskal–Wallis test.

^b χ^2 .

Urinary urge incontinence was more frequent in women, in older patients, in patients with a longer duration of disease, and in a higher level of disability. Urinary retention and recurrent UTI were more frequent in older patients and in patients with a greater disability; urinary retention was more frequent in patients with longer disease duration (Table 3).

Forty-six patients (11% of symptomatic patients) underwent a urodynamic study. This instrumental investigation was altered in almost all cases (only one examination resulted normal). The most frequent alterations were detrusor overactivity (60.9%, $n = 28$) and increased proprioception (43.5%, $n = 20$). The cystomanometric capacity was normal in 54.3% ($n = 25$) of patients, reduced in 37.1% ($n = 17$), and increased in 4.3% ($n = 2$) of the cases. The pressure/flow study showed detrusor underactivity in 10 patients (21.7%), while in 12 (26.1%) the voiding pattern was suggestive of the presence of detrusor-sphincter dyssynergia. Urodynamic study was completed with pelvic electromyography in 43.5% of the cases (all females): 55% of the tests documented the presence of detrusor-sphincter dyssynergia.

We then compared the clinical-demographic characteristics between asymptomatic and symptomatic patients. Patients complaining of urinary disorders had a higher mean EDSS score, a longer duration of disease, a later age at onset, and a greater mean age at the time of evaluation compared with asymptomatic ($p < 0.001$).

Urinary disorders were more frequent in patients with progressive disease ($p < 0.001$) and in women ($p = 0.02$) (Table 4).

3.3 | Symptomatic treatments

One hundred and seventy-eight (41.8%) symptomatic patients were under treatment for the urological disorder. Adherence to prescribed therapy was high (91.6% of cases). One hundred forty-five (81.5%) patients reported an improvement in the symptomatology attributable to the treatment, 35 of which after a therapeutic adjustment performed during 2018.

Antimuscarinics and alpha-blockers were the most commonly used drugs (42.7% and 34.8% respectively); 12.9% ($n = 23$) of patients performed intermittent self-catheterization and 3.9% ($n = 7$) required indwelling bladder catheter placement. Thirteen patients (7.3%), all women, did pelvic floor rehabilitation. One patient (0.6%) underwent regular intradetrusorial BoNT-A injections; one patient (0.6%) implanted a sacral neurostimulator.

Comparing patients who were responsive and unresponsive to treatment (noncompliant patients were excluded from the analysis), no statistically significant differences emerged regarding clinical and demographic variables. Likewise, there were no differences in response to treatment based on the pattern of urinary disorders,

TABLE 3 Comparison between demographic and clinical characteristics of symptomatic patients

| OAB symptoms | Frequency | | | Urgency | | | Urge incontinence | | |
|------------------------------------|---------------------|---------------------|--------------------|--------------------------------|---------------------|--------------------|--------------------------|---------------------|---------------------|
| | Present (n = 82) | Absent (n = 344) | p | Present (n = 253) | Absent (n = 173) | p | Present (n = 177) | Absent (n = 249) | p |
| <i>Demographic characteristics</i> | | | | | | | | | |
| Age | 49.7 ± 12.6 | 50.4 ± 12.2 | NS | 50.2 ± 12.1 | 50.3 ± 12.47 | NS | 54.1 ± 10.9 | 47.5 ± 12.4 | <0.001 ^a |
| Sex | | | NS | | | NS | | | <0.001 ^b |
| Male | 25 (30.5%) | 90 (26.2%) | | 62 (24.5%) | 53 (30.6%) | | 31 (17.5%) | 84 (33.7%) | |
| Female | 57 (69.5%) | 254 (73.8%) | | 191 (75.5%) | 120 (69.4%) | | 146 (82.5%) | 165 (66.3%) | |
| <i>Clinical characteristics</i> | | | | | | | | | |
| Age of onset | 33.2 ± 11.8 | 33.7 ± 11.5 | NS | 33.9 ± 11.6 | 33.1 ± 11.4 | NS | 36.2 ± 11.5 | 31.7 ± 11.2 | <0.001 ^a |
| Disease duration | 14.9 ± 11.4 | 15.1 ± 9.8 | NS | 14.7 ± 10.4 | 15.5 ± 9.7 | NS | 16.2 ± 9.8 | 14.2 ± 10.2 | 0.016 ^a |
| EDSS | 3.8 ± 1.9 | 3.9 ± 2.1 | NS | 3.9 ± 1.9 | 4.0 ± 2.3 | NS | 4.6 ± 1.9 | 3.5 ± 2.0 | <0.001 ^a |
| <i>Clinical course</i> | | | NS | | | NS | | | <0.001 ^b |
| Relapsing-remitting | 49 (59.8%) | 213 (61.9%) | | 157 (62.1%) | 105 (60.7%) | | 85 (48.0%) | 177 (71.1%) | |
| Primary progressive | 13 (15.8%) | 51 (14.8%) | | 41 (16.2%) | 23 (13.3%) | | 35 (19.8%) | 29 (11.6%) | |
| Secondary progressive | 20 (24.4%) | 80 (23.3%) | | 55 (21.7%) | 45 (26.0%) | | 57 (32.2%) | 43 (17.3%) | |
| Voiding disorders 1 | Hesitancy | | | Feeling of incomplete emptying | | | Abdominal strain to void | | |
| | Present (n = 67) | Absent (n = 359) | p | Present (n = 123) | Absent (n = 303) | p | Present (n = 54) | Absent (n = 372) | p |
| <i>Demographic characteristics</i> | | | | | | | | | |
| Age | 47.8 ± 10.8 | 50.7 ± 12.4 | 0.036 ^a | 48.3 ± 12.2 | 51.0 ± 12.2 | 0.037 ^a | 50.53 ± 11.4 | 50.5 ± 12.3 | NS |
| Sex | | | NS | | | NS | | | NS |
| Male | 49 (73.1%) | 262 (73.0%) | | 35 (28.5%) | 80 (26.4%) | | 20 (37.0%) | 95 (25.5%) | |
| Female | 18 (26.9%) | 97 (27.0%) | | 88 (71.5%) | 223 (73.6%) | | 34 (63.0%) | 277 (74.5%) | |
| <i>Clinical characteristics</i> | | | | | | | | | |
| Age of onset | 31.9 ± 10.8 | 33.9 ± 11.7 | NS | 32.3 ± 11.3 | 34.1 ± 11.6 | NS | 31.6 ± 11.2 | 33.9 ± 11.6 | NS |
| Disease duration | 14.3 ± 9.8 | 15.2 ± 10.2 | NS | 14.5 ± 9.6 | 15.3 ± 10.3 | NS | 15.0 ± 8.1 | 15.1 ± 10.4 | NS |
| EDSS | 3.7 ± 2.0 | 4.0 ± 2.1 | NS | 3.7 ± 1.9 | 4.0 ± 2.1 | NS | 4.0 ± 2.1 | 3.9 ± 2.1 | NS |
| <i>Clinical course</i> | | | NS | | | NS | | | NS |
| Relapsing-remitting | 46 (68.6%) | 216 (60.2%) | | 86 (69.9%) | 176 (58.1%) | | 31 (57.4%) | 231 (62.1%) | |
| Primary progressive | 4 (6.0%) | 60 (16.7%) | | 12 (9.8%) | 52 (17.2%) | | 6 (11.1%) | 58 (15.6%) | |
| Secondary progressive | 17 (25.4%) | 83 (23.1%) | | 25 (20.3%) | 75 (24.7%) | | 17 (31.5%) | 83 (22.3%) | |

| Voiding disorders 2 | Urinary retention | | | Recurrent urinary tract infections | | |
|------------------------------------|-------------------|------------------|---------------------|------------------------------------|------------------|--------------------|
| | Present (n = 40) | Absent (n = 386) | p | Present (n = 9) | Absent (n = 417) | p |
| <i>Demographic characteristics</i> | | | | | | |
| Age | 56.7 ± 10.0 | 49.6 ± 12.3 | 0.001 ^a | 57.9 ± 9.8 | 50.1 ± 12.2 | 0.043 ^a |
| Sex | | | NS | | | NS |
| Male | 16 (40.0%) | 287 (74.4%) | | 2 (22.2%) | 304 (72.9%) | |
| Female | 24 (60.0%) | 99 (25.6%) | | 7 (77.8%) | 113 (27.1%) | |
| <i>Clinical characteristic</i> | | | | | | |
| Age of onset | 32.4 ± 11.7 | 33.7 ± 11.7 | NS | 35.1 ± 5.6 | 33.6 ± 11.7 | NS |
| Disease duration | 22.5 ± 10.4 | 14.3 ± 9.8 | <0.001 ^a | 20.9 ± 9.7 | 14.9 ± 10.1 | NS |
| EDSS | 6.4 ± 1.8 | 3.7 ± 1.9 | <0.001 ^a | 5.8 ± 2.2 | 3.9 ± 2.1 | 0.011 ^a |
| <i>Clinical course</i> | | | <0.001 ^b | | | NS |
| Relapsing-remitting | 8 (20.0%) | 254 (65.8%) | | 3 (33.4%) | 259 (62.1%) | |
| Primary progressive | 9 (22.5%) | 55 (14.2%) | | 2 (22.2%) | 62 (14.9%) | |
| Secondary progressive | 23 (57.5%) | 77 (20.0%) | | 4 (44.4%) | 96 (23.0%) | |

Abbreviations: EDSS, Expanded Disability Status Scale; OAB, overactive bladder.

^aMann-Whitney U test.

^b χ^2 .

nor in relation to the type of evaluation to which the patients were subjected (only clinical or with the integration of the urodynamic study).

Using logistic regression analysis, we looked for potential predictors of response to therapy. We identified as the only independent negative predictor of nonresponse to therapy the need to make frequent therapeutic changes, or the presence of previous failures of symptomatic treatment (Table 5).

4 | DISCUSSION

It is well known that in MS the multifocality of demyelinating lesions is associated with heterogeneous clinical manifestations. The disease can affect several functional systems and frequently involves sphincter functions. Urological disorders have a high prevalence in patients with MS and great impact on their quality of life.^{1,19–21}

Of the 806 patients with MS in our cohort, more than half (52.9%) complained of urological symptoms at the time of evaluation. In line with the data present in the literature,¹ urological disorders were more frequent in older patients, with longer disease duration, later onset of disease, progressive phenotype of disease, and higher disability. Unlike other works, which have documented the same prevalence of urinary disorders between the two sexes,²² in our case series a significantly higher

frequency has emerged in women. This discrepancy could be linked either to a greater degree of disability found in female patients in our sample (EDSS women > EDSS men, $p = 0.019$) or to a lower reporting of mild disturbances by men, as symptoms in the present study were not investigated with specific questionnaires.

According to literature data,¹ the most frequent symptomatic pattern in our sample was OAB syndrome, and the most reported symptoms are urinary urgency and urge incontinence. In our study, OAB symptoms were more frequent in women.

Voiding dysfunction was more frequent in patients with earlier onset of disease. This data may have been influenced by the fact that voiding symptoms, such as hesitancy and a feeling of incomplete emptying, are significantly more frequent in young patients, most of them with relapsing-remitting phenotype and earlier age at disease onset. The frequent complaining of hesitancy, frequency, and feeling of incomplete emptying in younger patients could be linked to a preponderant pelvic muscle component, which with aging tends to reduce.²³ Consequently, the presence of a less performing “scaffolding” justifies the significantly higher frequency of urge incontinence in older patients and with a longer duration of illness and disability. This disorder was also more frequent in women, more likely to have pelvic floor dysfunction with menopause and after childbirth.^{23,24}

| | Symptomatic pt. (n = 426) | Asymptomatic pt. (n = 380) | P |
|------------------------------------|------------------------------|-------------------------------|---------------------|
| <i>Demographic characteristics</i> | | | |
| Age | 50.2 ± 12.2 | 40.9 ± 11.7 | <0.001 ^a |
| Sex | | | 0.02 ^b |
| Male | 115 (27.0%) | 142 (37.4%) | |
| Female | 311 (73.0%) | 238 (62.6%) | |
| <i>Clinical characteristics</i> | | | |
| Age of onset | 33.6 ± 11.6 | 29.7 ± 10.5 | <0.001 ^a |
| Disease duration | 15.1 ± 10.11 | 9.7 ± 8.1 | <0.001 ^a |
| EDSS | 4.0 ± 2.3 | 1.5 ± 2.1 | <0.001 ^a |
| <i>Clinical course</i> | | | |
| Relapsing-remitting | 262 (61.5%) | 358 (94.2%) | <0.001 ^b |
| Primary progressive | 64 (15.0%) | 14 (3.7%) | |
| Secondary progressive | 100 (23.5%) | 8 (2.1%) | |

Abbreviations: EDSS, Expanded Disability Status Scale; OAB, overactive bladder.

^aMann-Whitney U test.

^b χ^2 .

TABLE 4 Comparison between demographic and clinical characteristics—Symptomatic versus asymptomatic patients

TABLE 5 Possible predictors of treatment response

| | Therapy response (n = 145) | | |
|-----------------------|----------------------------|-----------|-------|
| | HR | 95% CIs | P |
| Age | 1.16 | 0.36–3.70 | NS |
| Sex | 2.45 | 0.62–9.74 | NS |
| Age of onset | 0.84 | 0.26–2.70 | NS |
| Disease duration | 0.82 | 0.26–2.63 | NS |
| EDSS | 0.79 | 0.50–1.24 | NS |
| Clinical course | 0.38 | 0.05–2.95 | NS |
| Therapy modifications | 0.24 | 0.07–0.83 | 0.025 |

Abbreviations: EDSS, Expanded Disability Status Scale; CIs, confidence interval; HR, hazard ratio.

Urinary retention was more frequent in patients with advanced age, longer disease duration, greater disability, and progressive phenotype; similarly, patients with older age and greater disability mostly report recurrent UTI. These disorders, in fact, except for the urinary retention due to exacerbations of MS, are referable to the chronicity of urological conditions often underestimated (by the patient himself or by the healthcare professionals) or not adequately treated.²⁵

In the analysis of the small cohort of patients undergoing urodynamic study, the most frequent finding was detrusor overactivity. The pressure/flow study also documented the presence of a dyssynergic pattern in more than a quarter of patients; electromyographic data, although limited, document the presence of detrusor-sphincter dyssynergia in more than half of the cases. In our sample, although less frequent, detrusor underactivity cases are present. Our data are in line with current literature, in which detrusor overactivity and detrusor-sphincter dyssynergia are the most frequent urodynamic alterations in patients with MS.^{1,3,4,25} These alterations correlated with lesions in cortical areas controlling micturition or pyramidal tract with regard to detrusor overactivity and to alterations of pontine regulatory pathways for detrusor-sphincter dyssynergia.¹⁹ The fact that supra- and infratentorial and cervical lesions are much more frequent than those at the sacral or infrasacral level (associated instead with underactive detrusor),¹⁹ explains the difference in frequency of the urodynamic patterns.

Considering symptomatic therapy, our analysis showed that only 41.8% of the patients in the cohort were treated. Antimuscarinics and alpha-blockers are the most frequently used drugs in the management of urological disorders in patients with MS.⁷ Interesting data emerge

from the analysis of patients with indication to pelvic floor training: all treated patients (nine female patients with detrusor-sphincter dyssynergia) report an improvement of symptoms, suggesting that pelvic floor training can be a valid therapeutic option in the female population with pelvic floor disorders,¹⁵ but further studies are needed.

Considering only treated patients, we tried to identify the presence of possible correlations between the response to symptomatic therapy and clinical-demographic and/or instrumental parameters, but no significant difference emerged from our analysis. In particular, we expected a greater frequency of response to therapy in patients who underwent urodynamic study. In fact, the first objective of this examination is precisizing the pathophysiology of urinary disorders; secondly, it helps to identify the risk factors in terms of upper tract alterations. In this way, it would make possible to set up an “ad hoc” treatment. However, in our study, there was no significant correlation between the type of evaluation on which the treatment was decided (clinical only or after urodynamic examination) and the improvement of symptoms. In literature, the role of urodynamic tests in the management of urological disorders in patients with MS is still debated and currently, are addressed to this evaluation, patients with complex symptoms and/or in case of failure of empirical therapy.^{1,14} The indication for symptomatic treatment is essentially based on clinical evaluation; however, we know that not all symptoms correlate well with a precise pathological substrate. Especially in the presence of voiding disorders or mixed pictures, it is difficult only with clinical data to identify the specific physiopathological background.² The utility of urodynamic study is not the mere objectivation of detrusor overactivity, but it can be useful in particular in detecting emptying defect through pelvic electromyography, to start targeted therapy (detrusor-sphincter dyssynergia, e.g., may benefit from myorelaxant agents, and/or pelvic floor rehabilitation, whereas detrusor underactivity can provide an indication to intermittent self-catheterization).

Finally, we attempted to identify predictors of response to symptomatic treatment. We identified as the only independent negative predictor of nonresponse to therapy the need to make frequent therapeutic changes, or the presence of previous failures of symptomatic treatment.

We know that, being a cross-sectional retrospective study, there are some limitations including the impossibility in determining parameters such as the time of urological disorders onset, a grading and a better characterization of symptoms, and a possible correlation with neuroimaging

data. However, it involved a large population of patients with MS in which we observed a great prevalence of urological disorders. It is known that these disorders may severely affect quality of life and may cause future complications. Therefore, it is essential to have an early and correct characterization of the type of symptoms and an early and targeted therapeutic strategy. Thus, the use of ad hoc questionnaires, which can help both the clinician and the patient himself in a more accurate characterization of the disorders, should be encouraged. In this study, it also emerges that urodynamic studies do not yet recognize a precise collocation in the management of urological dysfunctions in patients with MS. Currently, they are reserved for complex or nonresponsive cases, in which probably the characterization of the disorder does not seem to increase the possibility of therapeutic success. Instead, it could be helpful to use earlier urodynamic tests to set up targeted therapy. In particular, the presence of voiding dysfunction or mixed symptomatology could justify these tests in patients with mild symptoms, to better characterize the symptom and choose the most appropriate treatment. Further studies are needed to better define clinical and therapeutic aspects of lower urinary tract disorders in patients with MS, which are often overlooked compared to other aspects of the disease.

CONFLICT OF INTEREST

Viviana Nociti has received consulting fees from Novartis, Roche, Mylan, Biogen Idec, Merck, and Bayer; speaker and writing honoraria from Mylan, Teva, Biogen Idec, Bayer, Sanofi Genzyme, and Merck; travel grants from Teva, Biogen Idec, Sanofi Genzyme, Roche, and Novartis. Massimiliano Mirabella: Scientific advisory board membership of Bayer Schering, Biogen, Sanofi-Genzyme, Merck-Serono, Novartis, Teva; consulting and/or speaking fees, research support or travel grants from Almirall, Bayer Schering, Biogen, CSL Behring, Sanofi-Genzyme, Merck Serono, Novartis, Teva, and Ultragenix; principal investigator in clinical trials for Biogen, Merck Serono, Novartis, Roche, Sanofi Genzyme, Teva, and Ultragenix. Matteo Lucchini has received travel grants from Biogen and Sanofi-Genzyme and speaker honoraria from Biogen. The other authors have nothing to disclose. For the present work the authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTIONS

Dr. Seddone, Dr. Nociti, and Dr. Lucchini designed the study and drafted the paper. Material preparation, data collection, and analysis were performed by Dr. Seddone. Dr. Marturano and Dr. Bientinesi provided the urological data. Dr. Nociti, Prof. Mirabella, and Prof. Bassi reviewed and edited the paper. All authors read and approved the final manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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