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1 Effect of a strong desire to void on walking speed in individuals with multiple
2 sclerosis and urinary disorders

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8

9 **Abstract**

10 **Background.** Lower urinary tract symptoms, especially overactive bladder, are frequent and
11 disabling in individuals with multiple sclerosis (IwMS). An association with gait disorders is
12 common, which could aggravate continence difficulties and affect quality of life. The
13 association between the need to void and walking has never been studied in this population.

14 **Objective.** The primary aim of this study was to assess the effect of a strong desire to void
15 (SDV) on walking speed in IwMS and lower urinary tract symptoms. The secondary aim was
16 to identify clinical or urodynamic factors associated with walking speed impairment at SDV
17 in this population.

18 **Methods.** We included IwMS with urinary disorders and Expanded Disability Status Scale
19 score < 7 in this observational study. Individuals underwent 3 10-m walk tests (10MWT) and
20 one Timed Up and Go (TUG) test at SDV and at post-void (PV).

21 **Results.** Among the 72 IwMS included (mean [SD] age 50.6 [11.6] years; 46 [64%] females),
22 the mean (SD) speed for 10MWT was 1.00 (0.31) m.s⁻¹ at SDV and 1.07 (0.30) m.s⁻¹ at PV

23 (p<0.0001). Time for TUG was also increased when individuals felt SDV: mean 11.53 (4.6)
24 sec at SDV versus 10.77 (3.8) sec at PV (p=0.004). No predictors of greater impairment of
25 walking speed at SDV were identified.

26 **Conclusion.** This study suggests a clinical impact of bladder sensation on walking speed in
27 IwMS and urinary disorders. None of the individual characteristics could predict greater
28 decrease in gait velocity at SDV.

29

30

31 Keywords: Multiple sclerosis, Walking speed, Gait, Urination, Lower urinary tract symptoms

32

33 **Introduction**

34 Multiple sclerosis (MS) causes demyelinating lesions and could be responsible for a number
35 of symptoms, including motor or sensitivity disorders, cognitive impairment, visual
36 disturbances, and urinary and bowel disorders. Gait difficulties are the most visible disability,
37 and about 70% of patients report a psychological impact due to their walking impairment[1].
38 Different neurological presentations can be observed in different individuals: spastic, ataxic,
39 cerebellar, and pyramidal forms, depending on the topography of the cerebral or medullar
40 lesions. Lower urinary tract symptoms (LUTSs) are also very common, with a prevalence of
41 32% to 86%[2]. Overactive bladder with urgency, increased bladder frequency and urgency
42 urinary incontinence is the most common symptoms. Obstructive symptoms are also frequent
43 and may coexist with storage symptoms. Detrusor overactivity is the most frequent
44 urodynamic profile, but the correlation between clinical symptoms and urodynamics data is
45 not perfect. Other urodynamic profiles exist: bladder oversensitivity, detrusor-sphincter

46 dyssynergia, and neurogenic detrusor underactivity, but urodynamics can be normal for 1% to
47 34% of patients with LUTSs[2,3]. Despite a correlation between frequency and severity of
48 LUTSs and severity of incapacity assessed by Expanded Disability Status Scale (EDSS) [4] or
49 with number of falls[5], no strict relationship can be demonstrated between type of LUTS,
50 urodynamics profile and type of neurological presentation (pyramidal, with or without major
51 spasticity, cerebellar etc.)[4,6].

52 The role of bladder filling and need to void on gait has been poorly studied and only in
53 healthy populations. Yet, some hypotheses could support a link between these 2 parameters.
54 The need to void is a sensory stimulus, integrated in different cerebral areas, including insula,
55 periaqueductal gray, cingulate cortex, hypothalamus and prefrontal area[7,8]. A modification
56 in gait velocity with emotions was demonstrated. Jousse et al. showed a decrease in
57 attentional skills with a strong desire to void (SDV)[9]. These 2 studies may suggest a
58 possible impact of the need to void on gait velocity, as a new sensory phenomenon to
59 integrate and modulate, as a function of the locomotion task.

60 At the medullar stage, a modification of the H-reflex was demonstrated at SDV in healthy
61 individuals[10]. The H-reflex is considered to reflect motoneuronal excitability. The impact of
62 motoneuronal excitability on gait is not clearly established, but some studies revealed a
63 modification of the H-reflex with gait velocity[11,12]. The H-reflex is also used as an indirect
64 measure of spasticity, but its expression is not correlated with spasticity severity[13]. The
65 modulation of the medullar reflex with bladder sensation, and perhaps with bladder filling or
66 detrusor overactivity, with a possible impact on gait may explain a link between gait and the
67 need to void.

68 The consequences of the need to void on other tasks have been little studied and only in
69 healthy populations; however, alterations in attentional condition[9], gait velocity[14] and

70 balance[15] performance were shown. Assessing the effect of the need to void in a neurologic
71 population with frequent gait disorders and LUTSs could be pertinent to better understand the
72 pathophysiological mechanisms and evaluate whether an intervention for one condition may
73 improve the other, with the hypothesis that an appropriate management of LUTSs could lead
74 to an improvement in some locomotor parameters.

75 The primary aim of this study was to assess the effect of an SDV on gait in individuals with
76 multiple sclerosis (IwMS) and LUTSs. The secondary aim was to identify clinical or
77 urodynamic factors (EDSS, symptom severity, detrusor overactivity, cystometric capacity)
78 associated with greater gait impairment.

79

80 **Material and methods**

81 Participants

82 Individuals over age 18 who were consulting for LUTSs linked with MS in the neuro-urology
83 department of a university hospital between February 2017 and March 2017 were invited to
84 participate in this observational study. Individuals who agreed to participate were included
85 where they were admitted for a consultation or urodynamic assessment, and all tests were
86 performed on the same day.

87 Inclusion criteria were MS with EDSS score 1 to 6.5 and LUTSs secondary to MS (storage or
88 voiding symptoms). Participants had to be able to walk 50 m without human help and to hold
89 urine for 5 min, the time required to perform the tests. They could be taking medication for
90 MS or LUTSs. All types of MS were accepted. We excluded individuals with urinary tract
91 infections, relapse of MS in the last 7 days, or severe cognitive impairment (Mini Mental
92 State Examination [MMSE] score < 10).

93

94 Measures and procedure

95 Gait was assessed by 2 clinical tests approved for MS. The same tests were performed under 2
96 conditions: first when the individual felt an SDV, and then immediately after micturition,
97 spontaneously or with self-catheterization (post-void [PV]).

98 The primary outcome was gait velocity assessed by a 10-m walk test (10MWT)[16]. Three
99 trials were recorded, as per Booth et al. [14]. Individuals were instructed to walk the 10 m at a
100 comfortable speed. Maximum speed was not recorded to limit the impact of fatigue on test
101 repetition, because maximal speed improves energetic cost. Only the 6 intermediate meters
102 (meters 2 to 8) were recorded, to limit the effect of acceleration and deceleration. Tests were
103 recorded with a manual chronometer by the same examiner for each individual, with 30 sec of
104 rest at most between each trial.

105 Secondary outcomes were time on the Timed Up and Go Test (TUG)[17,18] and gait
106 variability assessed by the coefficient of variation (CoV) of the 3 trials of 10MWT. The trial
107 began with a non-recorded TUG to understand instructions and to limit the learning effect, but
108 only one trial was recorded to limit the test duration and fatigue induced by the get up
109 exertion.

110 Medical history, treatment, and anthropometric data were collected. An MMSE was
111 administered to identify memory impairment. Urinary symptoms were assessed by the
112 questionnaire Urinary Symptom Profile (USP) with 3 aspects: “stress urinary incontinence”
113 (/9), “overactive bladder” (/21) and “low stream” (/9)[19]. Data for the last cystometry were
114 collected (retrospectively if cystometry was not planned on the day of inclusion): detrusor
115 overactivity, volume at first detrusor contraction, SDV during filling, and cystometric
116 capacity. MS severity was assessed by the EDSS, a score based on measures of impairment in

117 8 functional systems, and on walking ability[20]. Individuals with an EDSS score > 4
118 complained of gait difficulties. Each participant was asked if they had urine leakage during
119 the tests. PV residual volume was measured with a mobile transabdominal ultrasound
120 apparatus (Bladder Scan®); 3 measures were taken, and the highest was recorded. Secondary
121 analyses were planned to identify clinical or urodynamic factors associated with greater gait
122 impairment: age, EDSS score, need for a walking device, severity of overactive bladder on
123 USP score, spontaneous void or self-catheterization, cognitive impairment assessed by the
124 MMSE, detrusor overactivity during the last cystometry, and PV residual volume.

125

126 Ethics approval

127 The study protocol and data collection were conducted in accordance with the ethical
128 standards of the national research committee and the Declaration of Helsinki. This study was
129 approved by the local ethics committee (registration no. 2015-A00125-44). All participants
130 gave their consent to participate. This study was registered on ClinicalTrials.gov:
131 NCT03204747.

132

133 Statistical analysis

134 Statistical tests were performed with R for Windows (Rx64 3.2.3). In a previous study of
135 healthy individuals, the only one assessing the effect of the need to void on gait, Booth et al.
136 [14] showed a mean difference on gait velocity of $0.05 \text{ m}\cdot\text{s}^{-1}$ between SDV and PV. In IwMS,
137 we expected a slightly greater mean difference between the 2 conditions. Thus, based on this
138 previous study, for an expected mean difference of $0.06 \text{ m}\cdot\text{s}^{-1}$, a standard deviation of 0.17
139 (SD 0.18 to 0.19 in the Booth et al. study) and 80% power, we needed 65 participants. Mean
140 gait velocity at SDV and PV were calculated for the 3 trials of 10MWT. Variability of the 3

141 trials was assessed by the CoV (standard deviation/average). The temporal parameters of gait
142 for 10MWT, TUG and CoV data were normally distributed. Thus, these were analyzed by
143 Student's *t* test for paired samples. The effect size was calculated with Cohen's *d* formula.
144 The impact of clinical and urodynamic parameters on the mean difference between TM10 at
145 SDV and PV were analyzed by Student *t* test for qualitative variables and Spearman
146 correlation for quantitative variables. Significance was considered at $p < 0.05$. Missing data
147 were not replaced.

148

149 **Results**

150 We included 72 individuals (mean [SD] age 50.6 [11.6] years; 46 [64%] females).
151 Characteristics are summarized in Table 1. Three individuals performed only 2 trials of the
152 10MWT for each condition because of physical tiredness. The mean speed for 10MWT was
153 $1.00 (0.31) \text{ m}\cdot\text{s}^{-1}$ at SDV and $1.07 (0.30) \text{ m}\cdot\text{s}^{-1}$ at PV ($p < 0.0001$; effect size 0.79). Maximal
154 improvement on mean 10MWT was $0.34 \text{ m}\cdot\text{s}^{-1}$ (5.03 s). Only 10 (14%) participants had a
155 lower performance at PV than SDV. These 10 participants and the others did not differ in
156 EDSS score, use of a walking device, existence of detrusor overactivity, or age. The
157 distribution of gait velocity change between SDV and PV is presented in the Figure. The
158 individual variability of the 3 trials of 10MWT, assessed by the CoV, was significant (mean
159 [SD] 5.2% [3.9] vs 4.2% [3.6], $p = 0.048$). Between the first and second try, 47% of
160 participants showed improved gait velocity at SDV and 40% at PV. Between the second and
161 third try, 68% of participants showed improved gait velocity at SDV and 63% at PV. Mean
162 time for TUG was also increased when individuals felt SDV: 11.53 (4.6) sec at SDV versus
163 10.77 (3.8) sec at PV ($p = 0.004$, effect size 0.35). Only one participant reported a leak during
164 the test.

165 Secondary analysis did not identify any predictors of impaired walking speed at SDV among
166 the features explored (Tables 2 and 3).

167

168 **Discussion**

169 The results of this study showed an increase in gait velocity after voiding as compared with
170 velocity during an SDV in IwMS and urinary disorders. This finding suggests a negative
171 impact of an urgent need to void on walking speed in IwMS and urinary disorders. We found
172 no clinical or urodynamic factors that predicted reduced gait performance.

173 In their study, Booth et al.[14] proposed that “the experience represents a dual task or divided
174 attention situation” to explain the difference in the SDV and PV situation in healthy
175 individuals. The authors introduced for the first time bladder sensation as a divided attention
176 situation. The role of dual tasks is well established, particularly in older adults and with a risk
177 of falling. The effect of dual tasks, in particular in gait, has been widely studied and
178 demonstrated in IwMS. In a recent review, the presence of cognitive motor interference
179 appeared more frequent in IwMS than in healthy individuals during gait analysis [21].
180 Individuals with mild cognitive impairment seemed more sensitive to the influence of a
181 cognitive task on walking speed[22]. Moreover, emotional perception of the need to void
182 could also influence gait velocity.

183 Functional MRI shows activation of different areas during bladder filling (insula,
184 periaqueductal gray, cingulate cortex, hypothalamus and prefrontal area, amygdala). Most of
185 these cerebral areas are implicated in emotional control, and functional MRI studies found
186 less activation or deactivation of some of these areas in individuals with overactive bladder as
187 compared with healthy individuals, which suggests a lack of control of this unpleasant
188 sensation[23]. A modification of gait velocity has been found correlated with emotion in

189 healthy individuals[24]. In IwMS, only the fear of falling has been studied, but other emotions
190 could also affect gait. We found no relationship between severity of symptoms and greater
191 difference between the 2 conditions. However, the proportion of individuals with regular
192 leaks was higher (no statistical analysis) in individuals with a difference of > 0.1 m/s between
193 SDV and PV, which supports a possible distractible effect of the urge to void and the role of
194 emotional control.

195 A second explanation is the effect of bladder sensation on motoneuronal excitability. Previous
196 studies of individuals with spinal cord injury evoked a gait spinal central pattern
197 generator[25,26]. Furthermore, the H-reflex, which is a spinal motoneuronal response to
198 electrical stimulation, is considered to reflect motoneuronal excitability. Variation in H-reflex
199 amplitude reflects modified spinal cell excitability [27]. During gait, some studies showed an
200 increase in H-reflex amplitude, which suggests an increase in motoneuronal excitability, with
201 variation in function of gait cycle. A proportional increase in the amplitude of the H-reflex as
202 a function of walking speed has been demonstrated[11,12]. Thus, a role of motoneuronal
203 excitability in gait velocity can be supposed, and a decrease in motoneuronal excitability
204 could affect walking speed. A decrease in H-reflex in the soleus muscle occurs at SDV in
205 healthy individuals[10]. However, no study has examined the impact of the need to void on
206 motoneuronal excitability in IwMS, whereas in individuals with spinal cord injury, bladder
207 filling tends to increase H-reflex amplitude[10]. Application of these findings in IwMS is
208 difficult, as far as lesion localizations at cerebral or medullar level could affect H-reflex
209 variability, and a specific study would be necessary.

210 Another possible explanation is that pelvic and trunk muscle activation is modified by bladder
211 filling: the activation of pelvic floor muscles decreases when the bladder is moderately full,
212 and the obliquus internus abdominis and rectus abdominis activation is increased. Bladder
213 fullness also influences balance: an increase in center-of-pressure motions on a force plate

214 was demonstrated when the bladder was full in healthy individuals[15]. These 2 parameters
215 could participate in gait velocity decrease at SDV.

216 Our results agree with the Booth et al.[14] study of healthy individuals (continent,
217 International Prostate Symptom Score 0-7). The authors used a GAITRite® walkway and
218 showed an impairment of 0.05 m.s^{-1} at SDV as compared with PV. Results in our study were
219 obtained with clinical (not instrumental) tests. A potential limitation of the primary outcome
220 is that fast speed usually has better reliability in 10TMW than comfortable speed, but
221 energetic cost is improved at maximal speed. We chose not to record this measure to limit the
222 impact of fatigue on the different tests.

223 Several measures were established to limit bias in recording walking tests. Participants
224 underwent 3 trials for the 10MWT under each condition, to limit intra-individual variability
225 and to observe whether this variability is modified by SDV, as previously described[14]. To
226 prevent inter-judge variation, all tests were recorded by the same examiner using a
227 standardized protocol and the same time-measuring tool. A recent study did not find a
228 significant difference between 3 consecutive short walk tests (Timed 25-Foot Walk) [28],
229 which suggests no spontaneous improved performance with repeated tests. Thus, to reduce the
230 impact of tiredness on recording, we did not randomize by order of condition, and clinical
231 tests at PV were always performed after those at SDV. This minimization of bias is also a
232 potential limitation for highlighting a greater difference between the 2 conditions, because
233 fatigue induced by the first tests can affect subsequent performance with a limited rest time
234 between the 2 conditions. Individuals could also take a rest between the tests to reduce this
235 bias. Our results did not reveal a progressive improvement in performance with the repetition
236 of tests during the same condition. This suggests that the difference shown between SDV and
237 PV is not related to a spontaneous improvement due to the repetition of the same exercise. For
238 the TUG test, the learning effect was limited by a first non-recorded trial to verify

239 comprehension of instructions. Instructions were repeated before each trial to facilitate their
240 memorization.

241 Our study has several limitations. Clinical tests are less precise than instrumental tests, and
242 some gait parameters such as stride length, swing time, and duration of single support could
243 not be studied. The examiner was not blinded to condition (PV or SDV), but participants did
244 not know the expected results and were not informed of the time performed in each test. The
245 sequence of the test after urination can have a negative impact on performance, by the fatigue
246 induced by the first tests and by the fatigue induced by urination, with the different stages of
247 undressing, sitting, etc. This could influence the identification of factors associated with a
248 greater impact of the need to void on walking speed. Moreover, because of the design of the
249 study, the negative impact of the urgent need to void is derived from the interpretation of the
250 increase in speed after urination. An evaluation without the need to void but away from
251 urination could have been interesting to free oneself from possible neurological reflexes
252 induced by micturition, especially in individuals with detrusor overactivity. In secondary
253 analyses, an evaluation of executive functions would have allowed a more specific analysis, in
254 the hypothesis of “dual task” impact, because the MMSE does not properly evaluate these
255 functions.

256 The difference between SDV and PV we found is less than the minimally clinical relevant
257 differences described in the literature, but these have been defined with small numbers of
258 participants with high EDSS score or using a modification of EDSS score as a relevant
259 clinical change, but the EDSS score is not sensitive to minor change[29–31]. Thus, the
260 observed difference in our study can be difficult to interpret; we did not expect a clinical state
261 change as a modification of the EDSS score between SDV and PV, and the comparison of our
262 results with the mentioned thresholds is not wholly adapted (median EDSS or condition to

263 realize the 10MWT differed from those of our study). Therefore, clinical interpretation of this
264 PV improvement is subtle, and our data cannot lead to specific clinical recommendations.

265 There are many different perspectives from this study. First, a new study of the specific
266 population within IwMS could improve the accuracy of results and clinical relevance. The
267 role of detrusor overactivity was not shown, but there was likely a lack of power in secondary
268 analysis, and owing to the study design, 27 of the 62 urodynamic data measurements available
269 were older than 3 months. Also, all individuals did not have urodynamics data, and some
270 measurements were prior to the inclusion date, which limits their interpretation. Further
271 research is necessary to judge the influence on spasticity. Several conditions modify
272 spasticity: urinary tract infections, ingrown nails, lithiasis, temperature[32]. Yet, the
273 possibility of spasticity exacerbation during detrusor uninhibited contraction has never been
274 considered. Moreover, considering the impact of the need to void as a dual task requires a
275 comparison with cognitive tasks during gait evaluation, especially since an impact on
276 attention skills has been demonstrated[9].

277 Finally, our study suggests that clinical walk tests are sensitive to changes in individual
278 variations such as the need to void. The use of the tests in clinical practice and research must
279 be standardized, to reduce bias in their interpretation and clinical significance.

280 **Conclusion**

281 This study suggests decreased walking speed at SDV in IwMS and urinary disorders, showing
282 an increase in gait velocity after voiding with an SDV. Severity of disability and urodynamic
283 parameters were not associated with greater difference in velocity at SDV than PV, but the
284 heterogeneity of the MS population could suggest lack of power in our study to demonstrate
285 the influence of a specific factor.

286

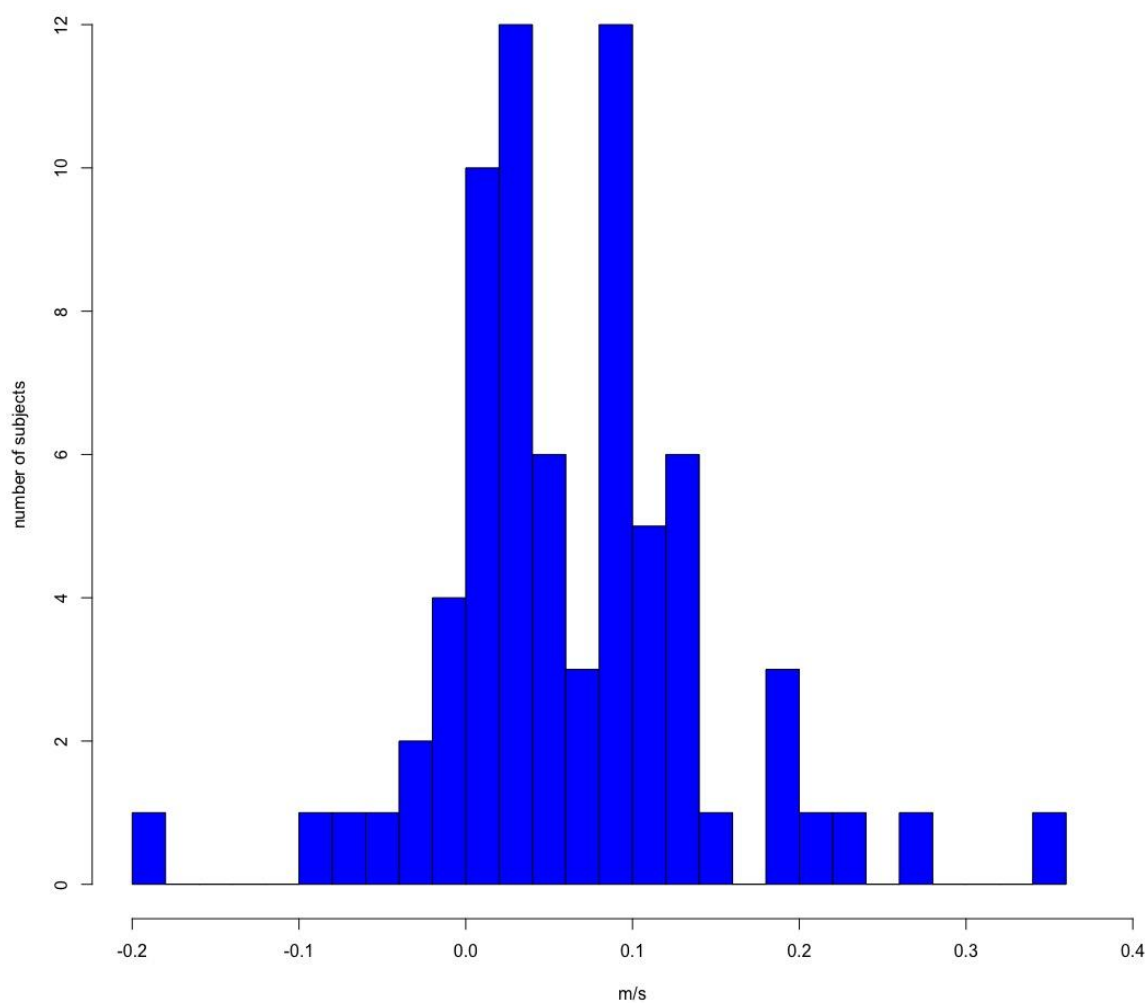
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289 Neurourology), during the conduct of the study.

290

291 **Conflict of interest.** None declared.

292 **Legend**

293 **Figure.** Walking speed change between post-void and a strong desire to void.



294
295

296 **Table 1.** Initial characteristics of individuals with multiple sclerosis (n=72).

		Median (Q1-Q3)
Age, years	50.6 (11.6)	51 (40.7-60.2)
Female	46 (64%)	
EDSS	4.8 (1.2)	5 (4-6)
MMSE (/30)	27 (2.8)	
BMI	23.4 (2.8)	23.1 (19.9-25.8)
USP stress score (/9)	1.2 (2.3)	0 (0-1)
USP OAB score (/21)	6.3 (3.7)	6.5 (4-9)
USP low stream score (/9)	4.9 (3.6)	4 (2-9)
<i>Micturition status</i>		
Spontaneous void	37 (52%)	
CISC	21 (29%)	
Mixed	14 (19%)	
<i>Treatment for LUTS</i>		
Anticholinergic	31 (43%)	
Alpha blocker	20 (28%)	
PTNS	6 (8%)	
Botulinum toxin in detrusor	21 (29%)	
Botulinum toxin in sphincter	4 (6%)	
None	22 (30%)	
Treatment for multiple sclerosis	52 (72%)	
Urodynamics data available	62 (86%)	
Detrusor overactivity	31 (50%)	

297 Data are mean (SD) or number (%).

298 EDSS, Expanded Disability Status Scale; MMSE, Mini Mental State Evaluation; BMI, body
 299 mass index; USP, Urinary Symptom Profile; OAB, overactive bladder; CISC: Clean
 300 Intermittent Self Catheterization; PTNS: Posterior Tibial Nerve Stimulation; LUTS, lower
 301 urinary tract symptoms

302

303

304 **Table 2.** Secondary analysis: predictive factors of higher impairment of walking speed at a
 305 strong desire to void (SDV) and post-void (qualitative variables).

	SDV	PV	t-test P-value
Detrusor overactivity			
<i>Yes</i>	1.02 (0.32)	1.1 (0.32)	0.91
<i>No</i>	0.97 (0.25)	1.03 (0.23)	
Way of voiding			0.95
<i>Spontaneous void</i>	1.01 (0.34)	1.07 (0.33)	
<i>Self-catheterization</i>	1.0 (0.27)	1.07 (0.27)	
<i>Mixed</i>	0.98 (0.28)	1.05 (0.29)	
Walking device			0.95
<i>Yes</i>	0.77 (0.24)	0.80 (0.23)	
<i>No</i>	1.07 (0.29)	1.15 (0.28)	

306 Data are mean (SD).

307

308

309 **Table 3.** Secondary analysis: predictive factors of higher impairment of walking speed at a
 310 strong desire to void (quantitative variables).

	rho (p)
EDSS	0.12 (0.32)
Age	0.09 (0.48)
USP OAB	0.06 (0.63)
MMSE	-0.11 (0.39)
PV residual volume	-0.07 (0.58)

311 EDSS, Expanded Disability Status Scale; MMSE, Mini Mental State Evaluation; USP,
 312 Urinary Symptom Profile; OAB, overactive bladder; PV, post-void

313

314

315

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