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

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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  <u>Participants</u>

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

## Measures and procedure

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

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

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

Medical history, treatment, and anthropometric data were collected. An MMSE was administered to identify memory impairment. Urinary symptoms were assessed by the questionnaire Urinary Symptom Profile (USP) with 3 aspects: "stress urinary incontinence" (/9), "overactive bladder" (/21) and "low stream" (/9)[19]. Data for the last cystometry were collected (retrospectively if cystometry was not planned on the day of inclusion): detrusor overactivity, volume at first detrusor contraction, SDV during filling, and cystometric 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 $m.s^{-1}$ 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 $m.s^{-1}$, 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) $m.s^{-1}$ at SDV and 1.07 (0.30) $m.s^{-1}$ at PV (p<0.0001; effect size 0.79). Maximal

154 improvement on mean 10MWT was 0.34 $m.s^{-1}$ (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 lwMS 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

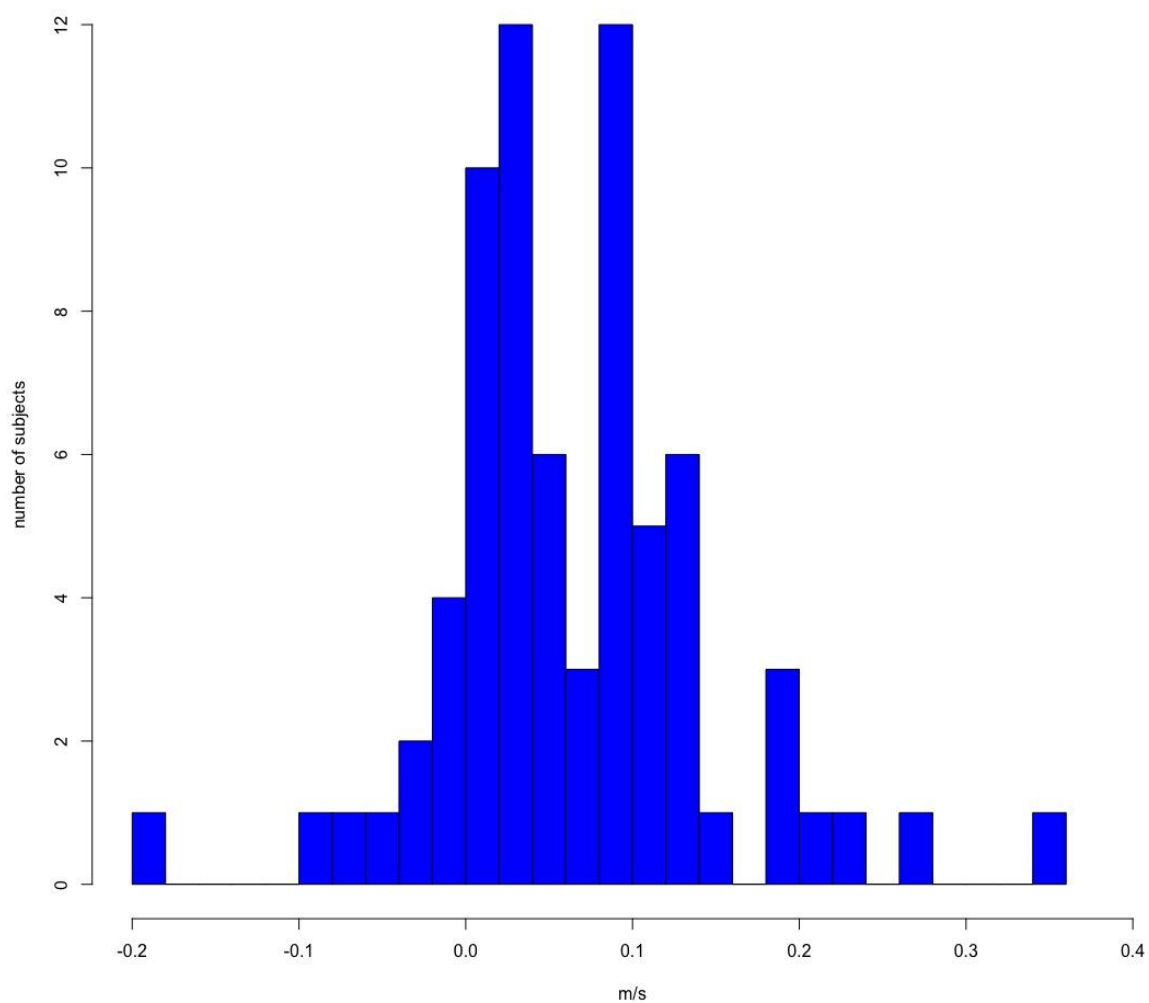285    the influence of a specific factor.

286

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) |
| *Micturition status* |  |  |
| Spontaneous void | 37 (52%) |  |
| CISC | 21 (29%) |  |
| Mixed | 14 (19%) |  |
| *Treatment for LUTS* |  |  |
| 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 | | | 0.91 |
| *Yes* | 1.02 (0.32) | 1.1 (0.32) | |
| *No* | 0.97 (0.25) | 1.03 (0.23) | |
| Way of voiding | | | 0.95 |
| *Spontaneous void* | 1.01 (0.34) | 1.07 (0.33) | |
| *Self-catheterization* | 1.0 (0.27) | 1.07 (0.27) | |
| *Mixed* | 0.98 (0.28) | 1.05 (0.29) | |
| Walking device | | | 0.95 |
| *Yes* | 0.77 (0.24) | 0.80 (0.23) | |
| *No* | 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

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314

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