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Urological Neurology and Urodynamics

RELATIONSHIP BETWEEN LOWER URINARY TRACT ABNORMALITIES AND DISEASE-RELATED PARAMETERS IN MULTIPLE SCLEROSIS

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ABSTRACT

Multiple sclerosis affects the lower urinary tract in many patients. The relationship between lower urinary tract abnormalities and disease-related parameters of multiple sclerosis is not well described. We screened urologically and neurologically 212 patients according to a standard protocol. Micturition complaints were noted in 52% of the patients and urodynamic abnormalities were found in 64%. A statistical correlation was found between detrusor hyperactivity and detrusor hypoactivity with disease-related parameters, that is disease duration, disability status, myelin basic protein concentration in the cerebrospinal fluid and neurophysiological investigations. No relationship was found between detrusor hypersensibility or detrusor hyposensibility and the aforementioned disease-related parameters. In 1 patient upper urinary tract abnormalities were noted in combination with urodynamic abnormalities. We conclude that lower urinary tract abnormalities can be found in every patient with multiple sclerosis unrelated to the state of the disease. Severe upper urinary tract abnormalities are rare.

KEY WORDS: multiple sclerosis, urination disorders, urodynamics, urinary incontinence

Multiple sclerosis is a disease in which most of the pathological and clinical features can be related to the destruction and loss of a single type of cell, the myelin-producing oligodendrocyte.¹ This destruction results in decreased nerve conduction in the central nervous system and in varying neurological abnormalities, which tend to remit and exacerbate with time.² Among the many different signs and symptoms of multiple sclerosis, dysfunction of the lower urinary tract is frequent. The incidence is approximately 96% in patients with a disease duration of greater than 10 years³⁻⁵ but even among patients with a short disease duration without micturition complaints 52% had lower urinary tract dysfunction.⁶ Some physicians reported micturition complaints as being the sole initial symptom of multiple sclerosis in 2% of all patients,^{3,7} while others did not note this finding.⁸

The discrepancy between clinical manifestations and anatomical lesions in multiple sclerosis is well documented.⁹ In the case of micturition complaints, a poor correlation was found between symptoms and the underlying pathophysiological condition.^{3,10} In most studies, however, the urological abnormalities were not related to the severity or state of disability of multiple sclerosis. Only a few investigators studied this relationship by comparing urodynamic features with disease duration, physical examination, neurophysiology or disability status.^{3,5,8,11-15} There were few patients in these latter studies (24 to 86), except in the study by Bradley,⁵ and nearly all patients had severe multiple sclerosis.

We evaluated 212 patients with definite multiple sclerosis who underwent a complete urological and neurological diagnostic evaluation. We examined the relationship between urological features and multiple sclerosis features, that is disease activity, disease duration, expanded disability status scale and neurophysiological abnormalities in these patients.

MATERIALS AND METHODS

Between January 1989 and December 1992, 212 patients with a confirmed diagnosis of multiple sclerosis according to the criteria of Poser et al¹⁶ were evaluated. Mean age was 35.9 ± 9.4 years (standard deviation, range 16 to 67) for the 129 female patients and 38.9 ± 10.5 years (range 18 to 64) for the 73 men.

Neurological investigations were performed by 1 neurologist (O. R. H.). After a thorough history was obtained and physical examination performed, the disability was established according to the Kurtzke expanded disability status scale.¹⁷ Based on this scale, patients were divided in 8 groups (table 1). Disease duration intervals in all patients (4 groups) were chosen so that there was an equal distribution of patients in each group. Cerebrospinal fluid was investigated and the amount of myelin basic protein is presented, since values of cerebrospinal fluid-myelin basic protein are considered indicative of the demyelinating activity of the disease.¹⁸ Cerebrospinal fluid-myelin basic protein values of $1.5 \mu\text{g}/\text{l}$. or less were considered normal, while all values greater than $1.5 \mu\text{g}/\text{l}$. were considered abnormal. A distinction was made between twice the normal value and more than twice the normal value. Therefore, 3 groups were formed regarding cerebrospinal fluid-myelin basic protein: group 1—myelin basic protein of $1.5 \mu\text{g}/\text{l}$. or less, group 2—myelin basic protein greater than 1.5 to $3.0 \mu\text{g}/\text{l}$. and group 3—myelin basic protein greater than $3.0 \mu\text{g}/\text{l}$.

Urological investigations consisted of history and physical examinations. Patient complaints were classified as irritative (urgency, frequency, nocturia and pain), obstructive (hesitation, interrupted or weak urine flow and sensation of residual urine) and urinary incontinence (involuntary loss of urine). Urodynamic as well as neuro-urophysiological investigations were performed in all patients. Urodynamic investigation was performed according to the standards of the International Continence Society except when specifically noted.¹⁹ Five days before

TABLE 1. Patient distribution

	No. Pts.
Disease duration (mos.):	
1 to 18	54
19 to 48	51
49 to 108	53
109 or more	54
Expanded disability status scale:	
1	25
2	53
3	46
4	25
5	12
6	19
7	27
8	5
Concentration of myelin basic protein in cerebrospinal fluid:	
Group 1	169
Group 2	21
Group 3	21
Neurophysiological investigation:	
Group 1	48
Group 2	36
Group 3	63
Group 4	53

the urodynamic investigation the patient stopped taking drugs that could influence bladder and urinary sphincter behavior. Urodynamic tests consisted of urethral pressure profile measurements and cystometry with water at 37°C and a filling rate of 35 ml. per minute through a 12F silicone catheter with the patient in the supine position. Pressure-flow analysis was performed on a flow chair after cystometry. Intravesical and abdominal pressures were measured with 6F micro-tip transducer catheters. Pelvic floor electromyography was recorded during cystometry with a bipolar wire electrode in the anal sphincter or 2 surface electrodes attached in the vicinity of the anal sphincter. During cystometry special attention was paid to first desire to void and maximal cystometric capacity. A first desire to void of 200 ml. or greater in combination with a maximum cystometric capacity of 500 ml. or more was considered pathological (hyposensitive). In contrast, a first desire to void of 50 ml. or less was considered hypersensitive. Involuntary detrusor contractions with an intravesical pressure increase of more than 15 cm. water during cystometry were considered hyperactive. At the end of cystometry a pressure-flow measurement was performed. Residual urine was measured by catheterization before and after urodynamic investigation. Residual urine volumes of more than 100 ml. and a detrusor contraction with a maximal pressure increase of less than 50 cm. water in combination with a maximum flow of 12 ml. per second or less were considered pathological (hypoactive). Involuntary contraction of the external sphincter (increased electromyographic activity) during a detrusor contraction was considered detrusor external sphincter dyssynergia. A residual urine volume of more than 100 ml. in combination with a maximum flow rate of 12 ml. per second or less, a maximum detrusor contraction of more than 50 cm. water and absence of detrusor external sphincter dyssynergia were considered to indicate obstruction. The upper urinary tract was evaluated by ultrasound of the kidneys or excretory urography.

In every patient cortical somatosensory evoked potentials and sacral reflex latency measurements were obtained according to a previously described technique.²⁰ Somatosensory evoked potentials were obtained with bipolar stimulation (minimum of 200 stimuli) of the posterior tibial nerve at the ankle of the right foot and the dorsal penile or clitoral nerve on the dorsum of the shaft of the penis or on the clitoris. To measure sacral reflex latencies, a concentric needle electrode was inserted in the right upper quadrant of the external anal sphincter muscle with the patient in the lithotomy position. The electromyographic activity of the anal sphincter after insertion of the needle was used to adjust the needle position.

Two stimulation sites were used: the pudendal nerve was stimulated at the penis or clitoris and the proximal urethra was stimulated through a special balloon catheter with 2 ring electrodes, 10 and 20 mm. from the base of the balloon. The catheter was inserted into the bladder and retracted after filling the balloon, thus allowing for direct electrical stimulation of the mucosa of the proximal urethra. The response obtained from the pudendal nerve was recorded as the bulbocavernosus reflex and that obtained from the proximal urethra was the urethro-anal reflex. From each reflex, at least 8 recordings were performed in each patient. If the measurement of a sacral reflex latency (bulbocavernosus or urethro-anal reflex) revealed a delayed or not obtainable response, the electromyographic needle was relocated and the recording was repeated.

Normal and pathological outcomes of the neuro-uropysiological investigations were distinguished by using the measurements gathered in healthy volunteers.⁶ For the purpose of this study, 4 groups were formed from the neurophysiological results: group 1—normal penile/clitoral evoked potentials and sacral reflex latencies, group 2—normal penile/clitoral evoked potentials and abnormal sacral reflex latencies, indicating abnormalities at the level of the conus medullaris, group 3—abnormal penile/clitoral evoked potentials and normal sacral reflex latencies, indicating suprasacral abnormalities and group 4—abnormal penile/clitoral evoked potentials and sacral reflex latencies, indicating suprasacral abnormalities at the level of the conus medullaris (table 1).

For statistical analysis, chi-square tests and the Kruskal-Wallis test were used to compare the data for significant difference among different groups. For pair wise comparisons, the Wilcoxon 2-sample test was used. Test results were considered statistically significant if p values were ≤ 0.05 .

RESULTS

The overall mean duration of disease was 78.3 ± 83.2 months (range 2 to 528, mean 77.8 months for men and 78.6 months for female patients). Table 1 summarizes the group distributions regarding multiple sclerosis classification parameters of disease duration, disability status, cerebrospinal fluid-myelin basic protein concentration and neurophysiological results. Gender differences among the groups regarding the aforementioned classification parameters were not statistically significant.

Of the 212 patients 111 had micturition complaints (table 2). Obstruction complaints were found more frequently in men than in women and incontinence complaints were more frequent in women. Irritative complaints were found equally among the sexes. Of the patients 23 had only irritative, 21 only obstruction and 5 only incontinence complaints. The combination of incontinence and irritative complaints was noted in 3 patients, obstruction and incontinence complaints in 4, obstruction and irritative complaints in 12 and all groups of complaints in 21. Urinary tract infections recurred in 25 patients.

The urodynamic investigation was abnormal in 136 patients. Table 3 summarizes the distribution of the urodynamic abnormalities found. Gender differences were remarkable: hypersensitivity, hyposensitivity and hypoactivity were more frequent in female than in male patients. Hyperactiv-

TABLE 2. Micturition complaints

	Total No. (%)	No. Men (%)	No. Women (%)
Total with complaints	111 (52)	42 (58)	69 (50)
Irritative	81 (38)	27 (37)	54 (39)
Obstructive	58 (27)	28 (38)	30 (22)
Incontinence	55 (26)	15 (21)	40 (29)

TABLE 3. Urodynamic investigation

	Total No. (%)	No. Men (%)	No. Women (%)
Total abnormal	136 (64)	51 (70)	85 (61)
Detrusor hypersensibility	16 (8)	3 (4)	13 (9)
Detrusor hyposensibility	43 (20)	13 (18)	30 (22)
Detrusor hyperactivity	72 (34)	33 (45)	39 (28)
Detrusor hypoactivity	32 (8)	9 (12)	23 (17)
Detrusor external sphincter dyssynergia	27 (13)	12 (16)	15 (11)
Obstructive	10 (5)	6 (8)	4 (3)

ity, detrusor external sphincter dyssynergia and obstruction were more frequent in men. Dilatation of the upper urinary tract was found in 2 patients (0.9%). Of the patients without micturition complaints 51% had an abnormal urodynamic investigation, compared to 81% of patients with irritative, obstruction and incontinence complaints.

Neuro-urophysiological investigations were performed in all patients but in 12 at least 1 of the tests could not be done because of technical or patient related problems. All tests were normal in 43 of the remaining 200 patients (22%). The penile/clitoral evoked potentials were abnormal in 58% of the patients and the tibial evoked potentials were abnormal in 46%. Normal tibial evoked potentials plus abnormal penile/clitoral evoked potentials were found in 36 patients (17%) and abnormal tibial evoked potentials plus normal penile/clitoral evoked potentials were found in 10 (5%). The latter patients had multiple sclerosis plus polyneuropathy. The bulbocavernosus reflex was abnormal in 31% of the patients and the urethro-anal reflex was abnormal in 37%.

Disease duration. Table 4 shows that disease duration is not related to the urological complaints. The same is true for some of the urodynamic abnormalities (fig. 1). Hyposensibility is not related to disease duration. Hypersensibility, hyperactivity, detrusor external sphincter dyssynergia and hypoactivity are related to disease duration.

Disability status. Table 4 also shows that urological com-

TABLE 4. Micturition complaints in relation to parameters analyzed

	Micturition Complaints %		
	Irritative	Obstructive	Incontinence
Disease duration (mos.):			
1-18	30	17	17
19-48	31	31	24
49-108	40	25	34
109+	52	35	30
p Value	0.07	0.11	0.19
Expanded disability status score:			
1	16	16	8
2	15	32	21
3	22	24	11
4	32	48	20
5	42	75	58
6	26	58	32
7	52	52	59
8	80	60	60
p Value	0.001*	0.002*	0.001*
Cerebrospinal fluid-myelin basic protein analysis:			
Group 1	38	24	24
Group 2	33	33	29
Group 3	38	47	38
p Value	0.90	0.06†	0.34
Neurophysiological investigation:			
Group 1	25	13	2
Group 2	36	14	28
Group 3	52	44	41
Group 4	40	30	32
p Value	0.03*	0.001*	0.001*

* $p \leq 0.05$.

† $p \leq 0.06$, nearly statistically significant.

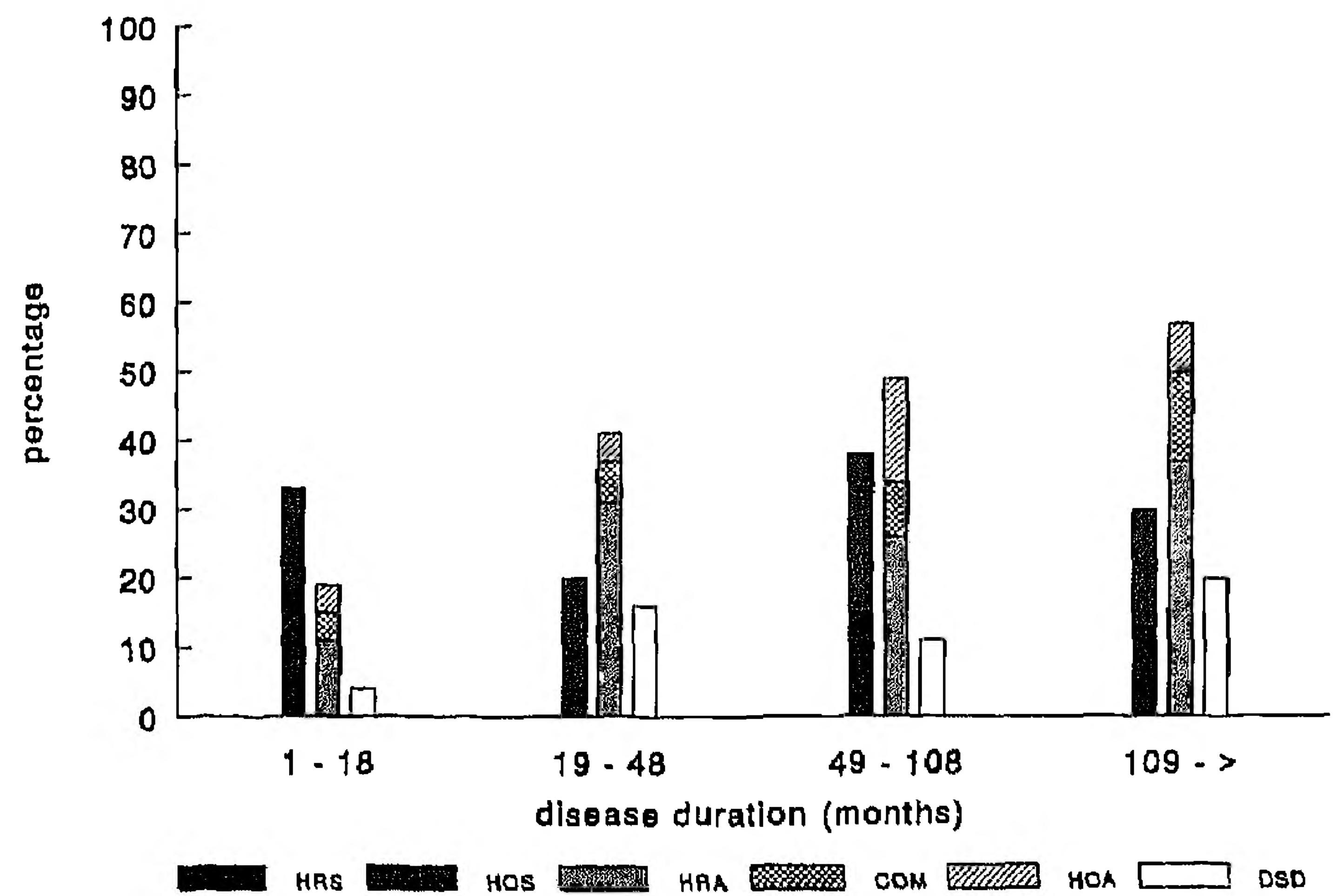


FIG. 1. Relationship between urodynamic abnormalities and disease duration. *HRS*, hypersensibility ($p = 0.02$). *HOS*, hyposensibility ($p = 0.30$). *HRA*, hyperactivity ($p = 0.001$). *COM*, combination of hyperactivity and hypoactivity. *HOA*, hypoactivity ($p = 0.007$). *DSD*, detrusor-sphincter dyssynergia ($p = 0.02$).

plaints are well related to the expanded disability status scale. In case of urodynamic abnormalities only hyperactivity, hypoactivity and detrusor external sphincter dyssynergia were statistically significantly related to the expanded disability status scale (fig. 2).

Cerebrospinal fluid-myelin basic protein. Only urological complaints of obstruction were nearly statistically related to the cerebrospinal fluid-myelin basic protein parameters. For the urodynamic abnormalities, only hyperactivity and detrusor external sphincter dyssynergia were statistically related (fig. 3). Hypersensibility, hyposensibility and hypoactivity were not statistically related to cerebrospinal fluid-myelin basic protein.

Neuro-urophysiological investigations. Urological complaints were statistically related to the outcome of neurophysiological investigations. From the urodynamic abnormalities hyperactivity, hypoactivity and detrusor external sphincter dyssynergia were statistically related to the outcome of the neuro-urophysiological investigations (fig. 4).

Obstruction as a urodynamic abnormality was found in 6 men and 4 women, and was not statistically related to any of the multiple sclerosis parameters. A total of 42 patients had residual urine levels of more than 100 ml. after voiding (9 did

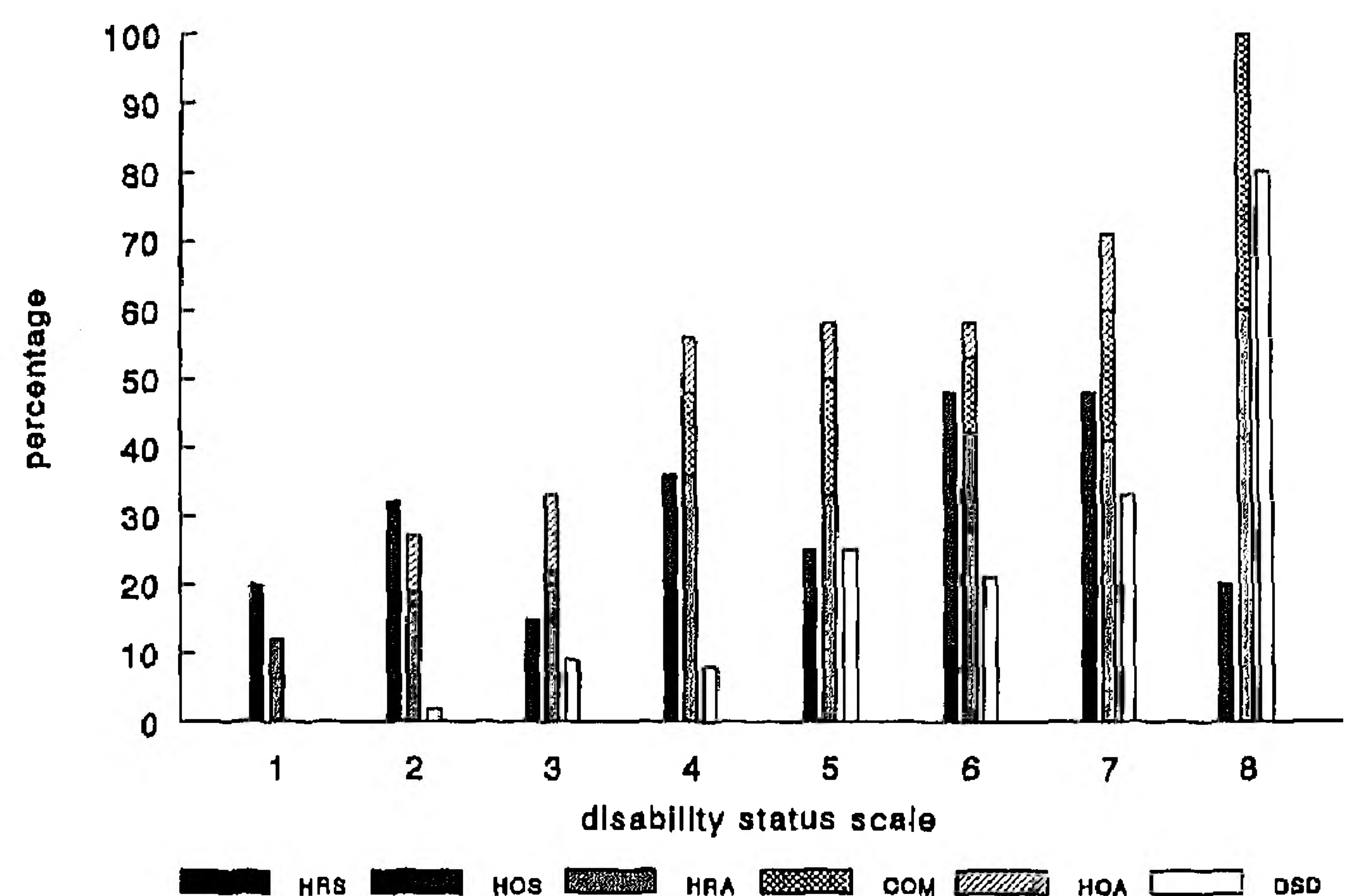


FIG. 2. Relationship between urodynamic abnormalities and expanded disability status scale. *HRS*, hypersensibility ($p = 0.15$). *HOS*, hyposensibility ($p = 0.10$). *HRA*, hyperactivity ($p = 0.0001$). *COM*, combination of hyperactivity and hypoactivity. *HOA*, hypoactivity ($p = 0.0001$). *DSD*, detrusor-sphincter dyssynergia ($p = 0.001$).

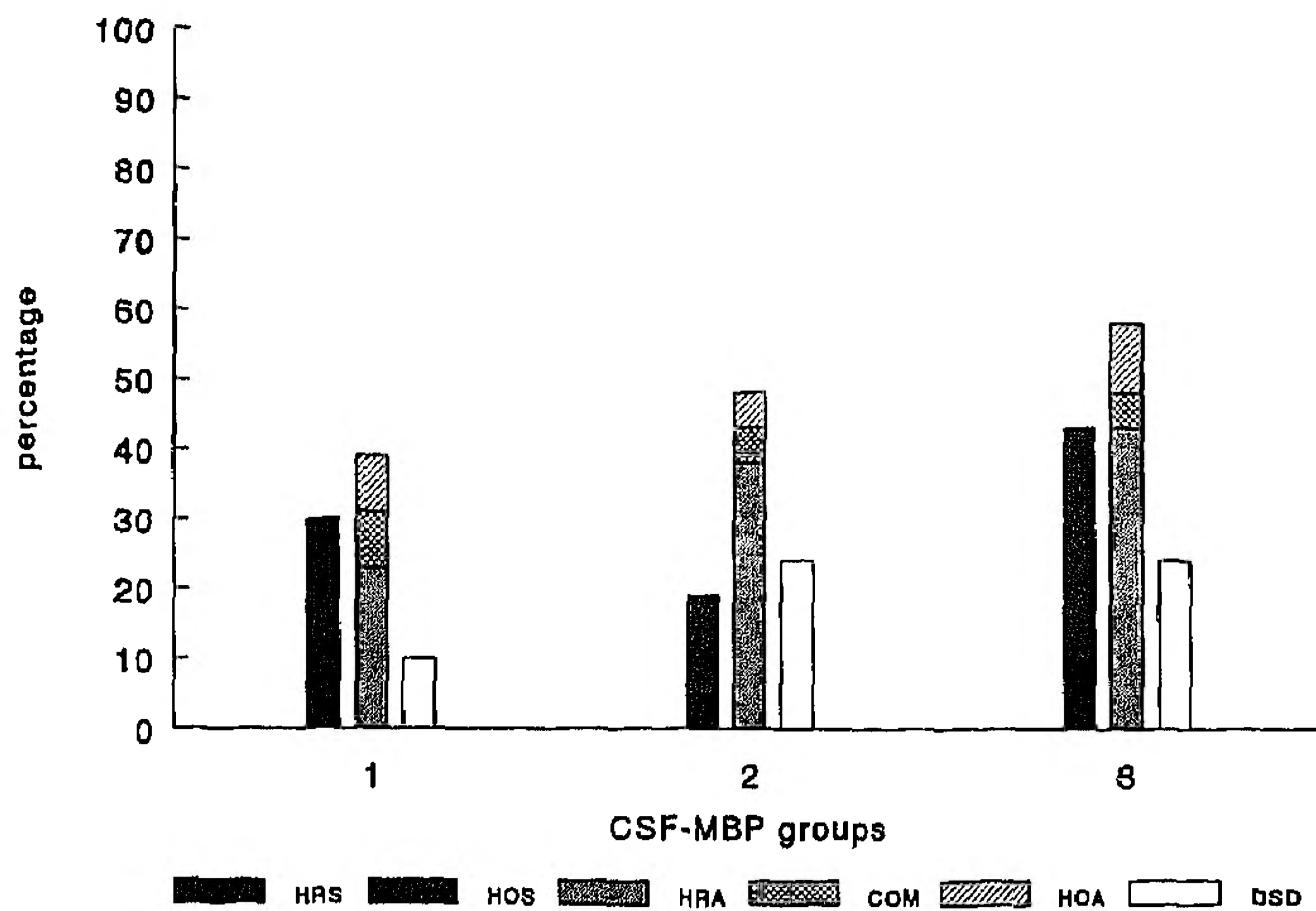


FIG. 3. Relationship between urodynamic abnormalities and cerebrospinal fluid-myelin basic protein (CSF-MBP) analysis. HRS, hypersensitivity ($p = 0.71$). HOS, hyposensitivity ($p = 0.31$). HRA, hyperactivity ($p = 0.01$). COM, combination of hyperactivity and hypoactivity. HOA, hypoactivity ($p = 0.61$). DSD, detrusor-sphincter dyssynergia ($p = 0.05$).

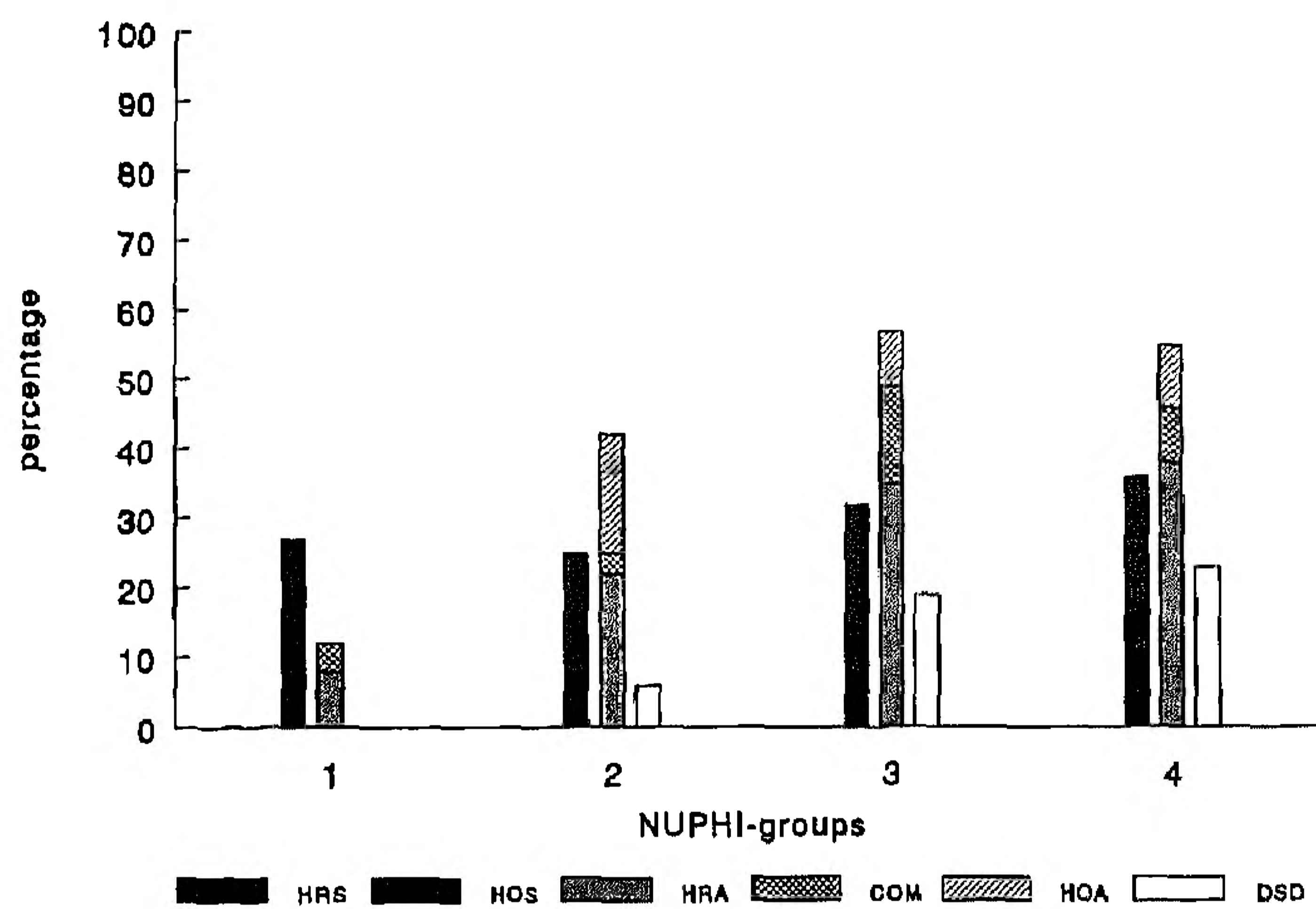


FIG. 4. Relationship between urodynamic abnormalities and neurophysiological investigation (NUPHI). HRS, hypersensitivity ($p = 0.88$). HOS, hyposensitivity ($p = 0.71$). HRA, hyperactivity ($p = 0.0001$). COM, combination of hyperactivity and hypoactivity. HOA, hypoactivity ($p = 0.007$). DSD, detrusor-sphincter dyssynergia ($p = 0.002$).

not have micturition complaints). The amount of residual urine after voiding ranged from 100 to 800 ml. Of the patients with residual urine 11 were not classified as having a hypoactive urodynamic abnormality.

DISCUSSION

In young adults multiple sclerosis is the most recurrent invalidating progressive neurological disease. The risk of multiple sclerosis increases as the region extends further from the equator in the northern and southern hemisphere.²¹ The prevalence in the United States is 41 per 100,000 and in the Netherlands it is 60 to 80 per 100,000.^{21,22} Neurologists are mainly responsible for the treatment of multiple sclerosis patients but in case of urological complaints or abnormalities the help of a urologist will be indispensable. Since 1989, patients with multiple sclerosis admitted to the department of neurology were also screened at the neurourological unit, which provided epidemiological data of urological abnormalities in these patients, and enabled us to study the relationship among different clinical, urological and other related parameters of multiple sclerosis.

Our patients represent a cross section through the population of multiple sclerosis patients seen at a multiple sclerosis clinic of a university hospital. Micturition complaints were found in 52% of the patients. Irritative complaints were more frequent than incontinence and obstruction complaints, which is in concordance with other reports.^{3,5,11,15} Micturition complaints were not statistically related to disease duration, which was also reported by Miller et al.⁷ However, Awad et al reported a positive relationship between disease duration and complaints.¹¹ Our finding indicates that multiple sclerosis patients with a short disease duration can suffer from serious micturition problems. On the other hand, micturition complaints were related to the disability status, which has been reported by others as well.^{7,8,11} More than half of the patients with a Kurtzke score of greater than 4 suffered from irritative and incontinence complaints. However, irritative and incontinence complaints did not correlate with the cerebrospinal fluid-myelin basic protein analysis. Obstruction complaints almost correlated with this analysis, indicating that during an exacerbation of multiple sclerosis, when myelin basic protein concentration in the cerebrospinal fluid increases, the risk of obstruction complaints is increased. This finding has been reported by Wheeler et al, who stated that because of the characteristic variability of the illness therapeutic choices must be adjusted accordingly.²² Neurophysiology correlated with micturition complaints, in concordance with other reports.^{3,10} Our data suggest that in multiple sclerosis patients with abnormal somatosensory evoked potentials, indicating spino-cortical tract abnormalities, nearly half suffered from obstruction, irritative or incontinence urinary complaints. It remains unclear why patients with abnormal somatosensory evoked potentials and abnormal sacral reflex latencies, indicating spino-cortical tract abnormalities and abnormalities at the level of the conus medullaris, suffer fewer complaints than those with only somatosensory evoked potential abnormalities. This finding probably results from changes in the neural organization at the level of the sacral micturition center, which is also encountered in spinal cord injury patients.²³

Detrusor hyperactivity was the most frequent urodynamic abnormality in our study and was noted in nearly a quarter of all patients with urodynamic abnormalities. These results are comparable with those reported by others.^{3-5,7} Except for hypoactivity, which was not related to cerebrospinal fluid-myelin basic protein analysis, abnormalities of detrusor activity were statistically related with disease duration, disability status, cerebrospinal fluid-myelin basic protein analysis and neurophysiology. The same finding was true for detrusor-sphincter dyssynergia. Of the multiple sclerosis patients with a disease duration of greater than 9 years nearly 60% suffered from detrusor activity abnormalities, compared to 100% of those with a severe disability status. Patients with an exacerbation of multiple sclerosis, resulting in elevated cerebrospinal fluid-myelin basic protein concentration, are at risk for detrusor hyperactivity.

Somatosensory evoked potentials are a widely used and accepted instrument for the evaluation of the function of certain pathways within the nervous system in multiple sclerosis. Unfortunately, no single neurophysiological test can measure the entire spino-bulbar-spinal micturition reflex because it contains sensory and motor pathways. The pudendal evoked potential measures a part of the spino-bulbar-spinal micturition reflex, that is the conductivity of the sensory portion of the pudendal nerves and the posterior columns. Studies on the usefulness of neurophysiological measurements in the evaluation of the lower urinary tract in multiple sclerosis are contradictory. In our experience the use of these tests is limited.²⁴

Hypersensitivity of the bladder was statistically significantly related with disease duration but no linear relationship was noted. Since no other statistical relationship was

found, it is reasonable to suggest that sensibility abnormalities of the bladder, as defined in our study, were not related with multiple sclerosis, although this has been suggested previously.^{6,25} Changing the definition of hyposensibility, instead of the initial desire to void 300 or 400 ml. and a bladder capacity of more than 600 or 700 ml., was not statistically related to the disease-related parameters. Moreover, the pudendal evoked potential latency and the tibial evoked potential latency were not statistically related to initial desire to void or bladder capacity. Obviously, bladder sensation measured by urodynamic investigation is not a good method to investigate the conductivity of the posterior columns as reported by others as well.²⁶

In our study only 2 patients (0.9%) presented with upper urinary tract abnormalities: in 1 no urodynamic abnormality was found, while 1 had severe detrusor hyperactivity and detrusor-sphincter dyssynergia. In the literature, the incidence of upper urinary tract abnormalities in multiple sclerosis patients is low. In 14 studies (2,076 patients) only 7 patients were reported to have upper urinary tract abnormalities.^{3-5,7,8,10,11,13-15,25,27-29}

CONCLUSIONS

Lower urinary tract abnormalities are frequently observed in patients with multiple sclerosis. For the urologist it is important to realize that every patient with multiple sclerosis can suffer from lower urinary tract abnormalities unrelated to the duration of the disease or the disability status. Since only 1 patient with upper urinary tract abnormalities also had urodynamic abnormalities, multiple sclerosis results in urological morbidity that influences the quality of life, rather than causes life threatening upper urinary tract conditions as observed in spinal cord injury patients.³⁰

REFERENCES

1. Prineas, J. W.: The neuropathology of multiple sclerosis. In: *Handbook of Clinical Neurology: Demyelinating Diseases*. Edited by J. C. Koetsier. Amsterdam: Elsevier Science Publishers, vol. 3, chapt. 8, pp. 213-257, 1985.
2. Waxman, S. G.: Membranes, myelin, and the pathophysiology of multiple sclerosis. *New Engl. J. Med.*, **306**: 1529, 1982.
3. Goldstein, I., Siroky, M. B., Sax, D. S. and Krane, R. J.: Neurourologic abnormalities in multiple sclerosis. *J. Urol.*, **128**: 541, 1982.
4. Andersen, J. T. and Bradley, W. E.: Abnormalities of detrusor and sphincter function in multiple sclerosis. *Brit. J. Urol.*, **48**: 193, 1976.
5. Bradley, W. E.: Urinary bladder dysfunction in multiple sclerosis. *Neurology*, suppl. 1, **28**: 52, 1978.
6. Bemelmans, B. L. H., Hommes, O. R., Van Kerrebroeck, P. E. V., Lemmens, W. A. J. G., Doesburg, W. H. and Debruyne, F. M. J.: Evidence for early lower urinary tract dysfunction in clinically silent multiple sclerosis. *J. Urol.*, **145**: 1219, 1991.
7. Miller, H., Simpson, C. A. and Yeates, W. K.: Bladder dysfunction in multiple sclerosis. *Brit. Med. J.*, **1**: 1265, 1965.
8. Betts, C. D., D'Mellow, M. T. and Fowler, C. J.: Urinary symptoms and the neurological features of bladder dysfunction in multiple sclerosis. *J. Neurol. Neurosurg. Psych.*, **56**: 245, 1993.
9. Poser, C. M.: Exacerbations, activity, and progression in multiple sclerosis. *Arch. Neurol.*, **37**: 471, 1980.
10. Blaivas, J. G., Bhimani, G. and Labib, K. B.: Vesicourethral dysfunction in multiple sclerosis. *J. Urol.*, **122**: 342, 1979.
11. Awad, S. A., Gajewski, J. B., Sogbein, S. K., Murray, T. J. and Field, C. A.: Relationship between neurological and urological status in patients with multiple sclerosis. *J. Urol.*, **132**: 499, 1984.
12. Eardley, I., Nagendran, K., Lecky, B., Chapple, C. R., Kirby, R. S. and Fowler, C. J.: Neurophysiology of the striated urethral sphincter in multiple sclerosis. *Brit. J. Urol.*, **68**: 81, 1991.
13. Hassouna, M., Lebel, M. and Elhilali, M.: Neurourologic correlation in multiple sclerosis. *Neurourol. Urodynam.*, **3**: 73, 1984.
14. Blaivas, J. G. and Barbalias, G. A.: Detrusor-external sphincter dyssynergia in men with multiple sclerosis: an ominous urologic condition. *J. Urol.*, **131**: 91, 1984.
15. Philp, T., Read, D. J. and Higson, R. H.: The urodynamic characteristics of multiple sclerosis. *Brit. J. Urol.*, **53**: 672, 1981.
16. Poser, C. M., Paty, D. W., Scheinberg, L., McDonald, W. I., Davis, F. A., Ebers, G. C., Johnson, K. P., Sibley, W. A., Silverberg, D. H. and Tourtellotte, W. W.: New diagnostic criteria for multiple sclerosis: guidelines for research protocols. *Ann. Neurol.*, **13**: 227, 1983.
17. Kurtzke, J. F.: Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). *Neurology*, **33**: 1444, 1983.
18. Barkhof, F., Frequin, S. T., Hommes, O. R., Lamers, K., Scheltens, P., van Geel, W. J. and Valk, J.: A correlative triad of gadolinium-DTPA MRI, EDSS and CSF-MBP in relapsing multiple sclerosis patients treated with high-dose intravenous methylprednisolone. *Neurology*, **42**: 63, 1992.
19. Abrams, P., Blaivas, J. G., Stanton, S. L. and Andersen, J. T.: Standardisation of terminology of lower urinary tract function. *Neurourol. Urodynam.*, **7**: 403, 1988.
20. Bemelmans, B. L. H., Meuleman, E. J. H., Anten, B. W. M., Doesburg, W. H., Van Kerrebroeck, P. E. V. and Debruyne, F. M. J.: Penile sensory disorders in erectile dysfunction: results of a comprehensive neuro-urophysiological diagnostic evaluation in 123 patients. *J. Urol.*, **146**: 777, 1991.
21. McDonald, W. I.: The mystery of the origin of multiple sclerosis. *J. Neurol. Neurosurg. Psych.*, **49**: 113, 1986.
22. Van der Ploeg, H. M., Molenaar, M. J. and Tiggelen, C. W. M.: Use of alternative treatments in patients with multiple sclerosis. *Dutch J. Med.*, **138**: 296, 1994.
23. Koldewijn, E. L., Van Kerrebroeck, P. E. V., Bemelmans, B. L. H., Notermans, S. L. H., Lemmens, W. A. J. G. and Debruyne, F. M. J.: Use of sacral reflex latency measurements in the evaluation of neural function of spinal cord injury patients: a comparison of neuro-urophysiological testing and urodynamic investigations. *J. Urol.*, **152**: 463, 1994.
24. Kornips, F. H. M., Rosier, P. F. W. M., Hommes, O. R., Vingerhoets, H. M., Debruyne, F. M. J. and Van Kerrebroeck, P. E. V.: Critical analysis of the correlation between urodynamic and neurophysiological findings in patients with multiple sclerosis. *Neurourol. Urodynam.*, **13**: 345, 1994.
25. Schoenberg, H. W., Gutrich, J. and Banno, J.: Urodynamic patterns in multiple sclerosis. *J. Urol.*, **122**: 648, 1979.
26. Gänzer, H., Madersbacher, H. and Rumpl, E.: Cortical evoked potentials by stimulation of the vesicourethral junction: clinical value and neurophysiological considerations. *J. Urol.*, **146**: 118, 1991.
27. Wheeler, J. S., Jr., Siroky, M. B., Pavlakis, A. J., Goldstein, I. and Krane, R. J.: The changing neurourologic pattern of multiple sclerosis. *J. Urol.*, **130**: 1123, 1983.
28. Bradley, W. E., Logothetis, J. L. and Timm, G. W.: Cystometric and sphincter abnormalities in multiple sclerosis. *Neurology*, **23**: 1131, 1973.
29. Van Poppel, H., Vereecken, R. L. and Leruitte, A.: Neuro-muscular dysfunction of the lower urinary tract in multiple sclerosis. *Paraplegia*, **21**: 374, 1983.
30. Van Kerrebroeck, P. E., Koldewijn, E. L., Scherpenhuizen, S. and Debruyne, F. M.: The morbidity due to lower urinary tract dysfunction in spinal cord injury patients. *Paraplegia*, **31**: 320, 1993.