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Basis of Severity Grade in Detrusor Hyperreflexia

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For both treatment and research it is useful to classify detrusor hyperreflexia/instability according to degree of severity, because it relates to symptomatic impact. However, there has been no systematic evaluation of criteria for severity assignment. This report compares patient classification by urodynamic data according to 3 methods: arbitrary criteria, a severity index, and an empirical cluster analysis. Within the primary urodynamic data there were no natural groupings as a basis for division into discrete patient groups. By all three methods, however, severity level did relate to symptoms. © 1994 Wiley-Liss, Inc.

Key words: detrusor overactivity, severity grade, severity index, cluster analysis

INTRODUCTION

For clinical study there is reason to classify or group cases of detrusor hyperreflexia/instability (DH/DI) according to level of severity. High pressure involuntary contractions at low volume clearly have more impact than mild contractions with onset at near-normal capacity. However, pressure-volume data form an apparent continuum without any obvious interruptions or cut-off points to group the patients.

With arbitrary criteria applied to cystometric data, "severe" cases have been identified by high maximum detrusor pressure (Pdetmax) [Blaivas et al., 1980; Moore and Sutherst, 1990] or by high Pdetmax and low capacity [Coolsaet, 1985; Gajewski and Awad, 1986]. However, these criteria exclude patients with modest Pdetmax at low capacity, a condition associated with troublesome symptoms. Some of these patients may have been captured by pressure-volume indices [Jorgensen et al., 1987; Massey and Abrams, 1986].

An arbitrary cut-off can be useful if it shows a relationship between cystometry and clinical findings, but it may also be subject to disagreement. For example, an arbitrary minimum criterion for instability (Pdetmax 15 cm H_2O) excluded symptomatic patients with "subthreshold" contractions [Coolsaet et al., 1985]. An objective way to find natural clusters or groups might be more acceptable.

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Abbreviations: DH/DI, detrusor hyperreflexia/instability; Pdet, corrected detrusor pressure; Pdetmax, maximal cystometric detrusor pressure; UDS, urodynamic study.

In the present series of 459 consecutive pretreatment cystometries, patients were classified by severity level of DH/DI according to (1) arbitrary pressure-volume criteria, (2) an arbitrary pressure/volume index, and (3) statistical cluster analysis of pressure-volume data. The goals were to determine if patients fall into natural groupings on the basis of urodynamic data, compare the results of patient classification by these three methods, and demonstrate any relationship between severity level and symptoms.

MATERIALS AND METHODS

Patients

This is a retrospective review of 459 consecutive pretreatment urodynamic studies. All patients were referred for evaluation of voiding dysfunction or incontinence. Thirty-two percent were male, 68% were female. The average age was 51.6 years, range 5–92, with 10 patients under age 16 and only 5 patients under 10 years. All were free from urinary infection at study.

Two hundred one patients (44%) had documented neurological disease or conditions that predispose to it. Of these, 113 had intracranial lesions, suprasacral spinal cord pathology, meningomyelocele, or multiple sclerosis, conditions often associated with DH/DI. Another 88 had lumbar spine pathology or diabetes, which may have mixed effects on detrusor reflex function.

Urodynamic Study

The bladder was routinely emptied before infusion, a possibly provocative approach [Abrams, 1985]. Cystometry was done by constant infusion of room-temperature saline via urethral catheter at 60 ml/min with vesical, rectal, and subtracted detrusor pressures. With onset of DH/DI at low volume, the fill was repeated at 30 ml/sec or slower. Large, low-pressure bladders were filled at 100 ml/sec. Of the 459 patients, 378 had both supine and upright cystometry, 56 supine only because of neuromuscular disability, and 25 upright only for varied reasons.

Each fill was interrupted at (1) the onset of phasic or tonic uninhibitable detrusor contraction of 15 cm H_2O or greater, (2) the onset of leakage around the filling catheter, or (3) the subjective sense of complete fullness. This was recorded as Pdetmax and cystometric capacity if the detrusor contraction or leakage continued. Otherwise the fill resumed until one of these 3 conditions appeared again and persisted.

In 12% of supine and 13% of upright cystometries the recorded Pdetmax and cystometric capacity were in fact a leak or voiding pressure/volume, not a true reflection of maximal unstable detrusor contraction. It was the most expedient measurement of detrusor reflex in each case, so the resulting pressure and volume were recorded as Pdetmax and capacity. In the remaining 87–88% of cases the Pdetmax and cystometric capacity represented the largest volume or maximal isometric detrusor contraction that the patient would reasonably tolerate.

Severity Grade

By application of arbitrary criteria to both supine and upright cystometry, grade was assigned as follows: Severe, Pdetmax >45 cm H_2O and capacity <200 ml; mild,

TABLE I. Value of r^2 for Cluster Models Considered

	Cystometry	
Model[a]	Supine	Upright
6	0.917	0.920
5	0.888	0.794
4	0.885	0.791
3	0.752	0.426

[a]Number of clusters.

Pdetmax 15–45 cm H_2O at any capacity; stable, involuntary detrusor contractions of less than 15 cm H_2O Pdet or completely stable detrusor.

Severity Index

This was a ratio of Pdetmax to capacity (cm H_2O/ml) with the higher ratio values representative of more significant DH/DI, regardless of capacity. Each supine or upright cystometry was assigned to one of the following arbitrary groups: I20, numeric value 20 or greater; I10, numeric value 10.0–19.9; I1, numeric value 1.0–9.9; IS, numeric value less than 1.

Cluster Analysis

In separate computer runs, supine and upright cystometries were studied by agglomerative hierarchical clustering [SAS/STAT Ordinary User's Guide, 1989; Hartigan, 1975]. This technique identified clusters on the basis of 2-dimensional (Pdetmax vs. capacity) cluster median distances of points between clusters as compared to distances between points within clusters. The clusters were based on standardized data, with equal weight given to Pdetmax and capacity. The 4 cluster model was chosen for comparison because it offered the smallest number of clusters with a high r^2 value in supine and upright (Table I).

Basis for Comparisons

The basis was as follows: (1) for comparison of the grade, index, and cluster methods in regard to component data (Pdetmax and capacity), supine and upright cystometric data are separately presented; (2) for comparison of these methods in regard to patient groups, each patient was assigned the highest level of DH/DI found either supine or upright for each method.

Two approaches were used to detect natural groupings within cystometric data, visual inspection of 3-dimensional graphs (Fig. 1) and analysis of clusters. Of interest is the number of clusters needed to achieve statistically significant differences between clusters. Visual inspection of the resulting scattergram (Figs. 2 and 3) allows further judgement about the presence of divisions between clusters.

The three classification methods were compared by cystometric data (Figs. 4 and 5). If the methods were comparable, one would expect to find similar mean Pdetmax and mean capacities in, for example, the most serious degrees of DH/DI in all methods ("Severe" vs. "I20" vs. "Cluster 1").

Ideally, the three methods should include the same patients in the respective

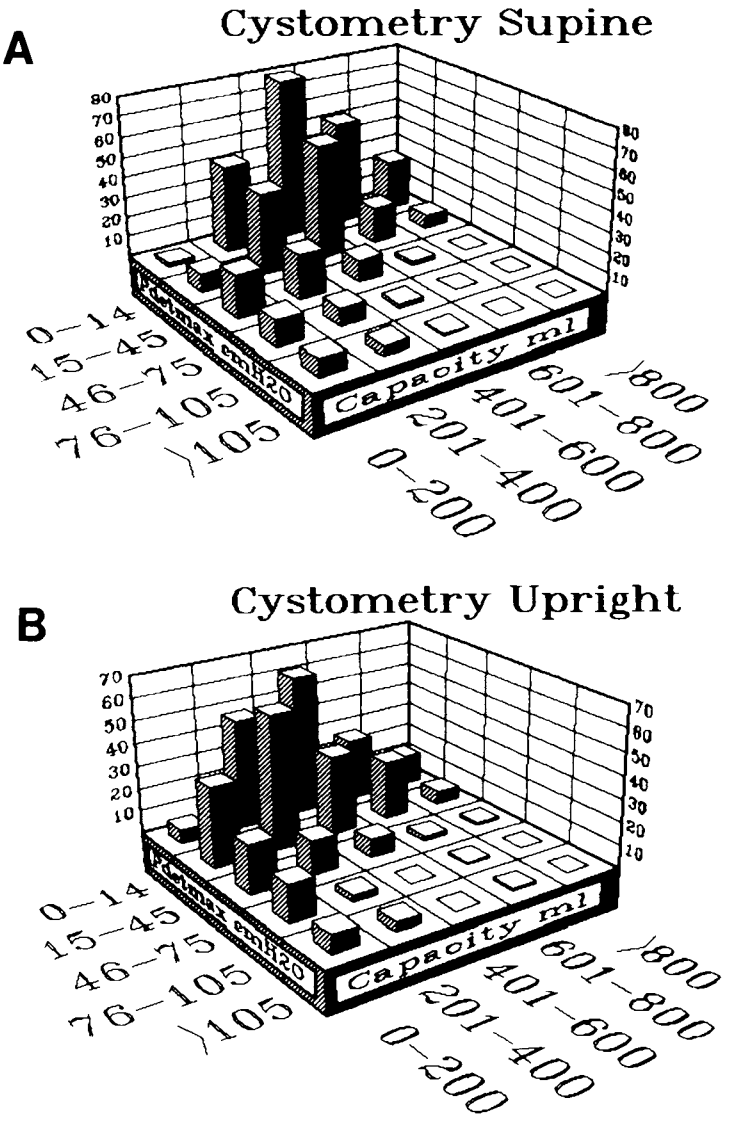

Fig. 1. Number of patients in each group defined by a range of cystometric capacity (ml) and Pdetmax (cm H_2O). **A:** supine; **B:** upright.

highest level or most serious DH/DI groups (Table II). As a measure of agreement among these methods for inclusion in the highest level groups, we used Kappa, a chance-corrected index of agreement [Fleiss, 1981]. On the resulting scale, 1 = perfect agreement, 0 = chance, and <0 = worse than chance.

RESULTS

Cystometric results are displayed in Figure 1 by the numbers of patients in each group defined by an arbitrary range of Pdetmax and cystometric capacity (without

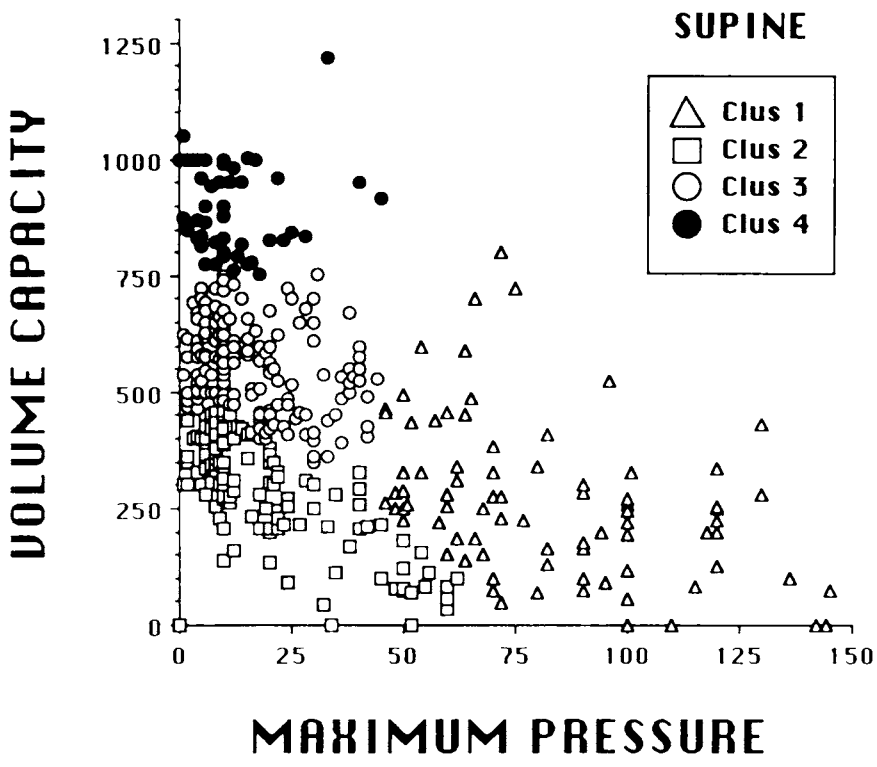

Fig. 2. Cluster analysis of supine cystometries, by cystometric capacity (ml) and Pdetmax (cm H_2O). Cluster 1 (high pressure, low volume) appears in the lower right and cluster 4 (low pressure, high volume) in the upper left.

reference to any of the three classification methods). For any volume range, Pdetmax trends are visually evident, and vice versa. Unique data clusters should stand out in distinct contrast to their neighbors.

On visual inspection of these graphs, three observations may be warranted: (1) These data seem to represent a continuum of results, without any conspicuous clusters as a basis for division of patients into discrete groups. (2) There were very few patients above 45 cm H_2O Pdetmax, where severe symptoms often occur. (In fact, most symptomatic patients were in the 15–45 cm H_2O group and some even below that, as pointed out in Table III and also by previous authors [Coolsaet et al., 1985]). (3) On upright cystometry, as compared to supine, there was an unmistakable shift toward lower capacity. Of particular interest were the patients with Pdetmax 15–45 cm H_2O. The upright position was provocative of DH/DI. A given patient may therefore appear in different groups on the two graphs.

The results of cluster analysis appear in Figures 2 and 3. As displayed, the data once again seemed to represent a continuum, rather than obvious groups. For reasons not visually apparent, the clustering algorithm assigned 81 patients to cluster 1 (high Pdetmax and low capacity) on supine cystometry but only 11 patients on upright. Once again, the provocative nature of upright position was evident in a downward shift of capacity and upward shift of Pdetmax (note the expanded Pdetmax scale and the 5 cases of Pdetmax $>$ 150 cm H_2O in Fig. 3).

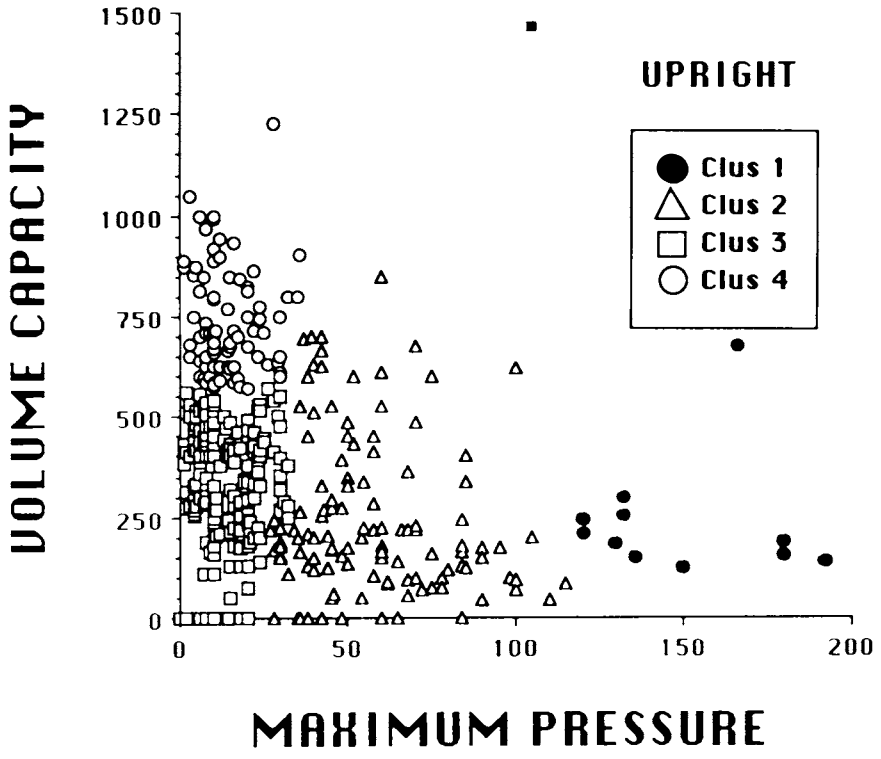

Fig. 3. Cluster analysis of upright cystometries (See Fig. 2 legend for details.).

Our three classification methods (grade, index, and cluster) were compared in regard to the primary urodynamic input data, Pdetmax (Fig. 4) and capacity (Fig. 5). On overview of these graphs, the three methods gave similar results. The only notable exception was the high Pdetmax in cluster 1 upright (Fig. 4), as explained above by the mathematical selection of a small number (11 patients) of the most serious DH/DI cases.

Table II shows the numbers of patients assigned to each level of DH/DI, by classification method. Each method seemed unique in its distribution of patients among the levels. Table IV shows the amount of statistical agreement among methods for the most serious level of DH/DI. The two arbitrary methods (grade and index) were highly in agreement, while the purely mathematical method (cluster) was significantly different.

DH/DI level was not age related in this series. Mean age was essentially the same in all levels, regardless of method, the range of mean ages being 49.3–52.4 years throughout the entire series. However, the more severe levels were male-associated in the cluster method. The percent of males was: cluster 1, 70%; cluster 2, 27%; cluster 3, 20%; cluster 4, 19%. By the other two methods, grade and index, sex distribution was essentially identical in all severity levels.

To show the relevance of classification to clinical presentation, the 4 cluster groups are displayed with symptoms and findings (Table III). The classification

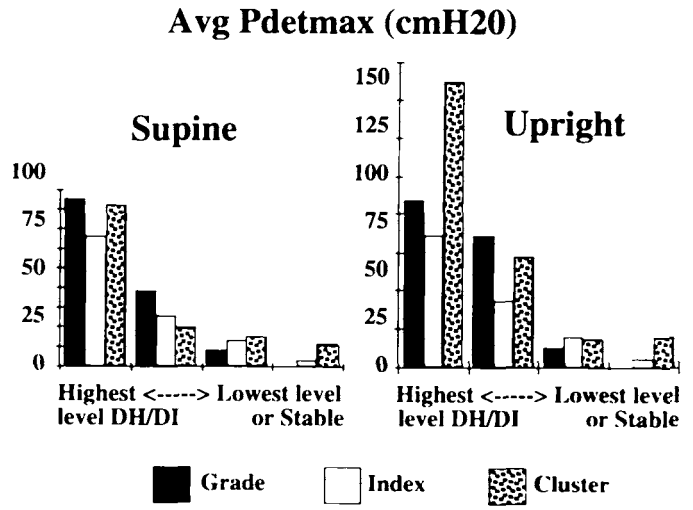

Fig. 4. Average Pdetmax for cystometric results by assigned level of DH/DI and by classification method.

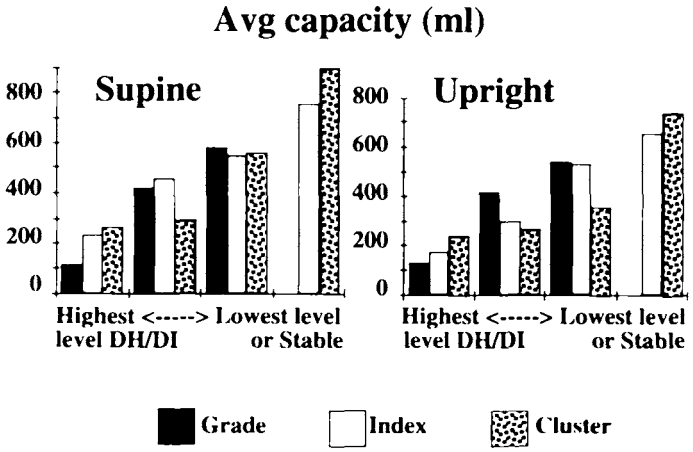

Fig. 5. Average capacity for cystometric results by assigned level of DH/DI and by classification method.

related well to mean voided volumes, urge incontinence by history, and leakage with DH/DI during urodynamic study (UDS), but poorly to other characteristics. On similar displays of severity grade and index methods (not shown), the results were essentially the same.

DISCUSSION

In the Materials and Methods section, the characterization of study subjects includes information about known neurological conditions, potential causes of DH/DI. However, this paper concerns the magnitude of DH/DI, not its cause.

TABLE II. Number of Patients in Each Level, by Method

	Most serious DH/DI	↔	Moderate DH/DI	↔	Least serious or stable
Grade	72		228		159
	Severe		Mild		Stable
Index	115	66	251		27
	I20	I10	11		IS
Cluster	83	192	152		32
	Clus1	Clus2	Clus3		Clus4

TABLE III. Cluster Classification: Symptoms and Findings Associated With the Patients Assigned to Each Cluster

	Clus 1	Clus 2	Clus 3	Clus 4
Patients (n)	83	192	151	33
No. of patients with urgency (%)	71 (86)	148 (77)	94 (62)	16 (50)
No. of patients with urgency incontinence (%)	58 (70)	105 (55)	77 (51)	11 (34)
Average voids/day (n)	10.7	11.0	9.3	9.0
Average void volume (ml)	162	202	273	338
No. of patients with UDS leak[a]	70 (84)	87 (45)	36 (24)	5 (16)

[a]Urge incontinence demonstrated on UDS supine or upright. The first number is number of patients; the second is percent of patients.

TABLE IV. Summary Measure (Kappas) of Agreement Among Methods for the Most Severe Degrees of DH/DI

		Standard	*P*	
Comparison	Kappa	error	Expected	Observed
Cluster 1 vs. severe	0.537	0.053	0.718	0.869
Cluster 1 vs. I20	0.599	0.045	0.658	0.863
Severe vs. I20	0.717	0.039	0.669	0.906

Previous authors based instability indices on sums of the pressures generated by all unstable detrusor contractions divided by cystometric capacity [Massey and Abrams, 1986] or by volume at first contraction [Jorgenson et al., 1987]. These strategies give prominence to phasic type contractions and may relate to the duration of cystometry after onset of unstable contractions. The present index was based on a single pressure value, Pdetmax, which gives more equal weight to phasic and tonic unstable contractions, regardless of how long the fill volume was maintained after onset of instability.

Of the three methods evaluated here, each has merit. The *index approach* is arbitrary but has theoretical advantages: (1) It gives equal weight to modest Pdetmax/low capacity and high Pdetmax/larger capacity, both being symptomatic conditions sometimes difficult to treat [Cardozo et al., 1978; Coolsaet and Elhilali, 1988]. (2) For correlation with symptoms and clinical factors, it is easy to select index values but difficult to juggle Pdetmax and capacity values simultaneously. The *cluster approach* is purely objective. However, the resulting patient groups were different from the

other two methods. Cluster analysis may involve hours of costly computer application. In the *grade approach*, the arbitrary assignment of cut-off values for Pdetmax and capacity allows one to work directly with familiar urodynamic data but lacks the single value convenience of an index approach.

In the present effort to quantify severity of DH/DI, there was no evidence of natural subgroups (Figs. 1–3, Table IV). Perhaps for that reason, no method was obviously better than the others at face value.

Nonetheless, there is ample reason to quantify the severity of DH/DI and group patients accordingly. Previous authors have done this to identify study patients of interest [Blaivas et al., 1980; Massey and Abrams, 1986] or analyze treatment results [Moore and Sutherst, 1990]. Our data showed a relationship between DH/DI level and symptoms (Table III). Similar analysis revealed that even "subthreshold" DH/DI (<15 cm H_2O) may be symptomatic [Coolsaet et al., 1985]. Quantification can be a way to stratify for treatment assignment and may help to reveal relationships between DH/DI and other clinical factors.

The present data confirm that upright positions provoke or aggravate DH/DI, with a resulting increase of Pdetmax (Figs. 4,5) and lower capacities (Fig. 1) in all three methods. Lesser degrees of DH/DI are therefore more likely to be detected in this position, regardless of diagnostic criteria used.

In the present series the more severe degrees of DH/DI bore no relationship to age, in contrast to previous reports [Abrams, 1985]. Our predominant proportion of women may have obscured the age-relatedness of DH/DI in men.

In conclusion, DH/DI severity classification was accomplished with roughly equal success by the three methods compared here. There were no obvious natural groups on the basis of urodynamic data alone. Apparently the division of patients into discrete groups depends on arbitrary urodynamic criteria, purely mathematical algorithms, or associated clinical conditions of interest. Nonetheless, the level of DH/DI severity did correlate somewhat with symptoms. Classification can therefore be a useful approach to diagnosis, causality, and treatment. Upright cystometry was provocative by way of decreased capacity and increased Pdetmax in patients with DH/DI.

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