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DEPENDENCE OF MALE VOIDING EFFICIENCY ON AGE, BLADDER CONTRACTILITY AND URETHRAL RESISTANCE: DEVELOPMENT OF A VOIDING EFFICIENCY NOMOGRAM

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ABSTRACT

The influence of age, urethral resistance and bladder contractility on voiding efficiency was evaluated by pressure-flow studies in 138 men of a mean age of 60 years (range 18 to 86). From these studies the urethral resistance parameter was calculated and the maximum bladder contraction strength was determined. Premature fading of the bladder contraction was quantified by a bladder contraction strength decay factor. Voiding efficiency was expressed by the parameter of post-void residual urine volume as a percentage of the initial bladder volume.

Multiple regression analysis showed that voiding efficiency depended significantly in descending order of importance on urethral resistance, maximum bladder contraction strength and bladder contraction strength decay factor. Patient age was not an independent factor. Maximum bladder contraction strength and bladder contraction strength decay factor were not correlated, suggesting that maximum bladder contraction strength and its decay constitute different properties of bladder contractile function. A voiding efficiency nomogram is proposed, making use of the values for maximum bladder contraction strength and urethral resistance in individual patients. Such a nomogram may have predictive value for the occurrence of acute retention but it must be tested prospectively.

KEY WORDS: urethra, bladder, urine, prostatic hypertrophy

The most important determinant of benign prostatic hyperplasia (BPH) is age.[1] The clinical syndrome of BPH has been characterized as a combination of symptoms of prostatism, increased prostate volume and voiding dysfunction, which is best described as bladder outflow obstruction.[2] The relationship among these properties is complex and only partially understood. Voiding function or dysfunction is determined by neurogenic factors, the contractile properties of the bladder and urethral resistance.[3] The interaction of these basic properties can be observed during a urodynamic study. To our knowledge no efforts have been made to relate quantitatively voiding efficiency to urodynamic parameters representing these properties. Such a quantitative relation might, among other things, be predictive of the occurrence of acute retention in patients. As a first step towards this goal, the influence of age, urethral resistance[4] and the bladder contraction strength variable[5] on voiding efficiency was studied in men.

MATERIAL AND METHODS

We studied various obstructive and irritative voiding symptoms urodynamically in 138 consecutive men of a mean age of 60 years (range 18 to 86). Patients with (suspected) neurogenic voiding disorders, malignancies of the urinary tract or diabetes mellitus, or those who had previously undergone operations of the lower urinary tract were excluded. The methods, definitions and units used in the urodynamic studies were based on the standards recommended by the International Continence Society,[6] except for urethral resistance and bladder contraction strength parameters.

The urodynamic examination involved 2 consecutive bladder filling and pressure-flow studies. The bladder was catheterized with 2, 5F catheters, 1 of which was used for medium rate bladder filling with room temperature contrast fluid and 1 was used for pressure recording. The pressures in the bladder and rectum, and flow rate were measured with external pressure transducers and a flowmeter. The residual urine volume at the end of the pressure-flow studies was determined by catheterization unless x-ray screening showed that there was no remaining contrast fluid in the bladder. In the latter situation the residual urine volume was considered to be zero. The rectal pressure was subtracted from the intravesical pressure to derive the detrusor pressure. Throughout the study pelvic floor electromyography was recorded by self-adhesive electrodes and was used to indicate whether the patients were relaxing the pelvic floor muscles during voiding. In some patients there were considerable differences between the 2 pressure-flow studies. To establish uniform data the pressure-flow study with the highest maximum flow rate was used for further analysis in all patients. Since bladder contractility is not likely to change between 2 measurements, the measurement with the highest flow rate represents the measurement with the lowest urethral resistance, that is the most relaxed micturition.

Detrusor pressure and flow rate signals were sampled at a 10 Hz. sampling rate and stored on computer disk. The signals were filtered off-line by a digital low pass filter with a cut-off frequency of 0.5 Hz. Pressure-flow plots were constructed from the filtered detrusor pressure and flow rate signals. A flow delay time correction of 0.8 second was applied.

Urethral resistance was quantified using a group specific urethral resistance factor (URA), which is based on a statistical approximation of the average urethral resistance relation in a large number of patients. This parameter can be determined for any micturition in which the maximum flow rate and the corresponding detrusor pressure are known. A quadratic urethral resistance relation is then drawn through this point and its intersection with the pressure axis of the pressure-flow plot determines the value of URA.[4]

Bladder contraction strength was quantified using the contractility variable W.[5] This variable expresses the strength of a detrusor contraction in terms of a combination of the detrusor pressure, flow rate and bladder volume. It can be

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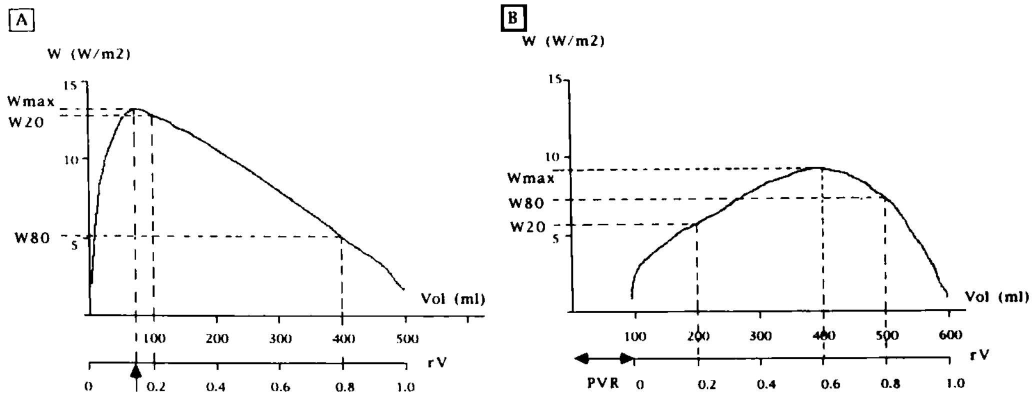

FIG. 1. Schematic examples of variable W (approximation of power per detrusor muscle surface area) as function of bladder volume (*Vol*) and parameters used to quantify shape of function. Graphs trace voiding from right to left starting at initial bladder volume and ending when micturition ceases with or without residual urine. Bladder volume is also expressed on relative scale (*rV*). rV = 1 indicates initial bladder volume at start of micturition and rV = 0 indicates bladder volume when micturition has ceased. *PVR*, post-void residual urine volume. *A*, normal micturition. W increases with decreasing bladder volume and voiding ends without residual urine. W80 (W at rV = 0.8) is lower than W20 resulting in negative value for W80-W20. Arrow indicates rV(Wmax). *B*, prematurely fading bladder contraction. W decreases towards end of micturition leaving 100 ml. residual urine. W80 is higher than W20 resulting in positive value for W80-W20.

considered to approximate the mechanical power developed by the contracting bladder and has the dimension of power per bladder wall surface area. W was plotted as a function of the decreasing volume in the bladder throughout micturition. From the bladder contraction strength variable several parameters were calculated, including maximum value of W during micturition (Wmax), relative volume or percentage of the voided volume at which this maximum of W occurred (rV[Wmax]) and value of W at a relative volume of 80% minus its value at a relative volume of 20% (W80-W20) (fig. 1). The parameters W80-W20 and rV(Wmax) were used as quantitative measures of the decay of bladder contraction strength when a contraction faded away prematurely (fig. 1). W80-W20 has been shown to perform best in the discrimination of patients with normal and fading contractions,[7] and it is referred to as the bladder contraction strength decay factor. A positive value of this parameter indicates that the contraction fades away prematurely.

Voiding efficiency was expressed as residual urine volume as a percentage of the initial pre-micturition bladder volume (%PVR). A value of 50 ml. is often used as the limit above which the residual urine volume is considered significant in prostatism.[8] Others have stated that the residual urine volume is pathologically high if it is more than 10% of the bladder capacity.[9]

In this study we have assumed that a %PVR of more than 10 is significant. The men with more than 10 %PVR included all who had a post-void residual of more than 50 ml. and 7 men with a residual of less than or equal to 50 ml.

Mann-Whitney's U test was used to compare parameter values between subgroups of patients. Correlations between parameters were calculated using Spearman's rank correlation coefficient (r). The level of statistical significance was set at $p < 0.05$ (1-tailed). Multiple regression analysis was used to examine whether the parameters of age, Wmax, W80-W20 and URA were independent factors determining voiding efficiency expressed in terms of the post-void residual urine volume as a percentage of the initial pre-micturition bladder volume (%PVR).

RESULTS

Table 1 summarizes the urodynamic characteristics of the patients. Of the 138 men 65 (47%) had obstruction based on a discriminating value of URA (more than or equal to 30 cm. water).[10] Half of the men were above or below age 65 years, respectively.

TABLE 1. *Urodynamic characteristics of the study population*

	Mean	Median	Range
Age (yrs.)	60.3	65	18–86
Maximum flow rate (ml./sec.)	8.7	7.5	1.5–27.3
Detrusor pressure at maximum flow rate (cm. water)	55	50	9–143
URA (cm. water)	32.5	28.7	7.8–98.8
Wmax (W/m.^{2})	9.7	9	1.7–20.9
Residual urine (ml.)	151	90	0–800
%PVR	28	23	0–90

TABLE 2. *Urodynamic characteristics of men with (%PVR more than 10) and without (%PVR less than or equal to 10) a significant amount of residual urine.*

	%PVR		
	10% or Less (54 pts.)	Greater Than 10% (84 pts.)	p Value*
Age (yrs.)	55.5 ± 2.3	63.5 ± 1.3	0.008
URA (cm. water)	24.8 ± 1.3	37.4 ± 1.9	0.004
Wmax (W/m.^{2})	10.4 ± 0.5	9.3 ± 0.4	Not significant
Relative vol. (Wmax) (ml.)	0.31 ± 0.04	0.77 ± 0.03	<0.001
W80-W20 (ml.)	−1.0 ± 0.3	1.5 ± 0.3	<0.001

Values are means plus or minus standard error.
* Groups are different for all listed parameters except for Wmax.

Table 2 compares the parameters for urethral resistance and bladder contractility between the men with (%PVR greater than 10) and without (%PVR 10 or less) a significant amount of residual urine. Men with a significant amount of residual urine were older and on average had a fading bladder contraction. They also had a higher urethral resistance but the maximum bladder contraction strength did not differ from that in men without a significant residual urine volume. By inference, men without a significant residual urine volume on average had better flow rates.

The correlation coefficients among patient age, parameters describing bladder contractile function (Wmax and W80-W20), urethral resistance (URA) and residual urine volume as a percentage of the initial bladder volume (%PVR) are summarized in table 3. Maximum bladder contraction strength and bladder contraction strength decay factor were not correlated and seemed to constitute 2 different properties of bladder contractile function. The parameter %PVR seemed to be related more strongly to bladder contraction strength

TABLE 3. *Correlation coefficients among age, Wmax and W80-W20, URA and %PVR*

	Age (yrs.)	Wmax (W/m.^{2})	W80-W20 (W/m.^{2})	URA (cm. water)
Wmax (W/m.^{2})	−0.23 (<0.001)			
W80-W20 (W/m.^{2})	0.20 (0.02)	0.15*		
URA (cm. water)	0.23 (<0.001)	0.31 (<0.001)	0.51 (<0.001)	
%PVR	0.29 (<0.001)	0.22 (0.01)	0.40 (<0.001)	0.46 (<0.001)

Numbers in parentheses represent p values.
* p Value not significant.

decay factor W80-W20 (r = 0.40, p <0.001) than to maximum bladder contraction strength (r = 0.22, p = 0.01) during micturition (table 3). However, W80-W20 strongly depended on URA (r = 0.51, p <0.001). Therefore, a multiple regression analysis is a more appropriate way to determine which parameters are the best predictors of %PVR. Such an analysis with %PVR as the dependent variable showed that URA, Wmax and W80-W20 were the significant independent variables in the regression equation (table 4). Patient age was not an independent factor. If only Wmax and W80-W20 were considered as independent factors in a separate regression analysis, again Wmax (partial F = 33) was a more important factor than W80-W20 (partial F = 14). Thus, in descending order of importance, the urodynamic factors that determined the voiding efficiency (%PVR) were URA, Wmax and W80-W20. Based on these considerations Wmax-URA (fig. 2), (W80-W20)-URA (fig. 3) and Wmax-(W80-W20) scattergrams were constructed.

In the Wmax-URA scattergram an empty area appeared (fig. 2, *C*), which can be explained theoretically. If there is no urine flow, the value of Wmax in W/m.^{2} equals approximately a tenth of the detrusor pressure in cm. water.[6] Under the same circumstances URA is equivalent to the minimum urethral opening pressure. Inasmuch as voiding cannot occur when the isometric detrusor pressure is lower than the minimum urethral opening pressure, voiding is impossible if the numerical value of Wmax is less than a tenth of the numerical value of URA. Based on these considerations, a line separating *B* and *C* was drawn on figure 2, and below this line voiding was physically impossible. In reality, URA slightly underestimates the minimal urethral opening pressure, which means that the line would move even closer to the data points on figure 2, *B*. Looking at the data in this way shows that voiding was impossible if a certain minimum value of Wmax could not be reached. This necessary minimum value is higher when the urethral resistance is higher. Another pair of lines was drawn to border the data points of those men who voided with a residual urine of less than 10% of the initial bladder volume (fig. 2, *A* and *C*). The area between the drawn lines (fig. 2, *B*) did not contain data points of men with residual urine volumes of less than 10% of the initial bladder volume. In fact, about half (14 of 29) of the cases with residual urine volumes greater than 70% of the initial bladder volume and 14 of 16 cases (88%) with a %PVR greater than 70 are seen in figure 2, *B*. There was an overlap of men with and without a %PVR more than 10 (fig. 2, *A*).

A Wmax-W80-W20 scattergram (not shown) was also studied. Using such a scattergram in the same way as the Wmax-URA scattergram it was not possible to separate patients

TABLE 4. *Multiple regression analysis with %PVR as the dependent and age, URA, Wmax and W80-W20 as the independent variables*

Variable	Coefficient	Standard Error	T Value	Probability	Partial F
Intercept	0.229				
Age	0.001	0.001	0.772	0.442	0.6
URA	0.008	0.001	5.359	0.000	29
Wmax	−0.028	0.006	4.979	0.000	25
W80-W20	0.021	0.008	2.595	0.0105	7

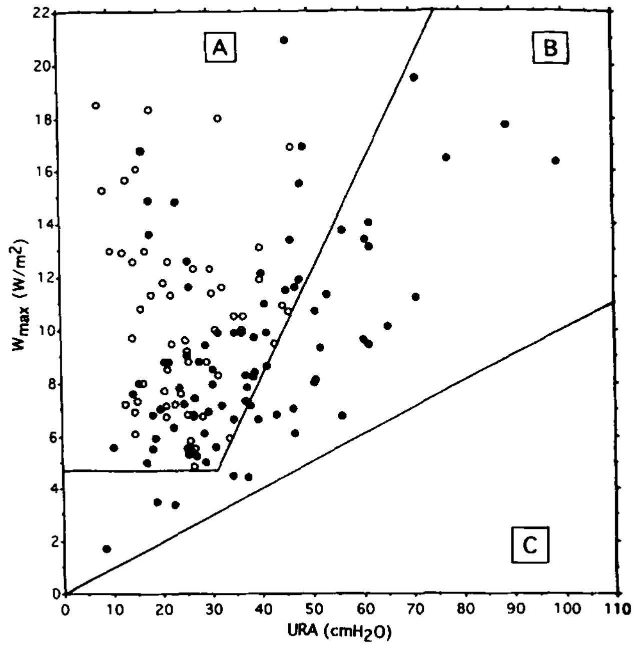

FIG. 2. Scattergram of maximum bladder contraction strength (Wmax) and urethral resistance (*URA*), which can be used as voiding efficiency nomogram. Open circles indicate men with percentage of residual urine less than or equal to 10 of initial bladder volume. Closed circles indicate men with percentage of residual urine more than 10 of initial bladder volume. *A*, contains data points of cases with and without %PVR more than 10. *B*, contains only data points of cases with %PVR less than or equal to 10 of initial bladder volume. *C*, empty area where no voidings have been recorded. Voiding is physically impossible in this area (see text).

with %PVR greater than 70 from those with %PVR greater than 10 as well as in the Wmax-URA scattergram. An area equivalent to figure 2, *B* contained only 8 of the 16 men (50%) with a %PVR greater than 70 and only 8 of the 24 cases (33%) in that area had %PVR greater than 70.

Figure 3 shows the (W80-W20)-URA scattergram. The empty area on figure 3, *A* indicates that fading bladder contractions did not occur in men with a low urethral resistance (URA below ± 12 cm. water). This finding is in agreement with the relatively strong correlation between URA and W80-W20 (r = 0.51). The empty area on figure 3, *B* indicates that in this evaluation all patients with a high value for URA (more than 65 cm. water) had a prematurely fading bladder contraction. It is also obvious that the vast majority of patients with %PVR greater than 10 had prematurely fading bladder contractions and that 36 of 55 patients (65%) with a nonfading contraction had %PVR less than or equal to 10. Patients with %PVR greater than 70 were not clustered in a clearly defined area as was the case in the Wmax-URA scattergram. The Wmax-URA plot with its division in the areas A, B and C is proposed as a voiding efficiency nomogram.

DISCUSSION

The relationship between voiding efficiency and patient age, bladder contractility and urethral resistance has been poorly explored in the literature. Equally rare are studies that correlate structural changes in the detrusor muscle with urodynamic findings. In a qualitative electron microscopic study of bladder biopsy specimens from 6 men 72 to 96 years old Elbadawi et al showed that urodynamically proved out flow obstruction was structurally related to myohypertrophy with or without superimposed degeneration of muscle cells and axons.[11] Degeneration was associated with impaired de-

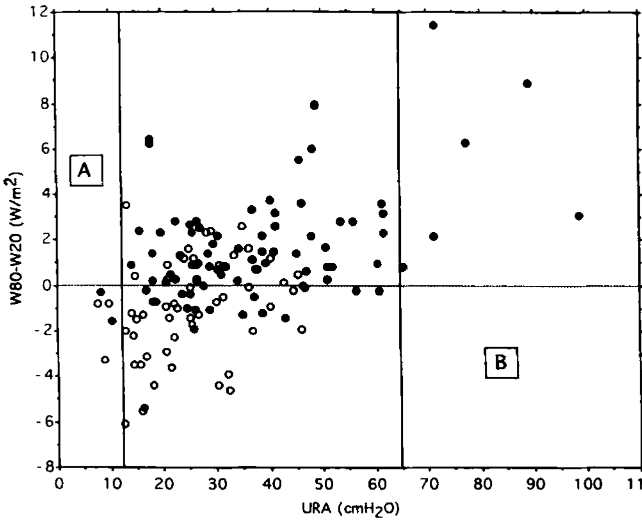

FIG. 3. Scattergram of bladder contraction strength decay factor (*W80-W20*) and urethral resistance factor (*URA*). Open circles indicate men with %PVR less than or equal to 10 of initial bladder volume. Closed circles indicate men with %PVR more than 10 of initial bladder volume. *A*, empty area where no prematurely fading contractions occur. *B*, empty area that indicates that above certain value of URA bladder contractions have faded prematurely.

trusor contractility. In 13 patients (including only 2 men) the same authors established that aging was associated with the occurrence of the so-called dense band pattern in the perimeter of muscle cells,[12] which may affect exchange and storage of ions, with a negative effect on the excitation-contraction coupling mechanism.

In a large group of men and women with mixed pathological conditions van Mastrigt found that in women Wmax correlated better (negatively) with age than in men.[13] It was also noted that the maximum or normal contractility values for women decreased almost linearly with age, whereas this trend was less marked in men. It was postulated that this difference between men and women was caused by bladder compensation as a response to out flow obstruction. In our study bladder contraction strength was positively correlated with urethral resistance, which seems to support the view that bladder compensation is a possible explanation for the difference between the sexes. However, our data are cross-sectional. Whether compensation is truly an important factor can only be determined in a longitudinal study. The positive correlation between bladder contraction strength and urethral resistance may alternatively be due to selection bias. Men who are in retention, that is those who would most probably exhibit a relatively high urethral resistance combined with a relatively low bladder contraction strength, cannot be studied by pressure-flow analysis.

In our study voiding efficiency was based on residual urine volume measurements after pressure-flow studies. These residuals may not always be comparable to residuals measured after a free uroflowmetry in the same patient. However, a study of the quantitative relation between voiding efficiency and pressure-flow parameters is most valid when all data originate from the same voiding. Residuals measured after free uroflowmetry cannot be directly related to bladder contraction strength and urethral resistance parameters. Of our patients 39% voided with a clinically insignificant residual urine volume, which indicates that a large proportion of men did not exhibit a voiding efficiency worse than what could have been achieved at a free uroflowmetry. However, it is prudent to say that a patient classified as having borderline voiding efficiency in the Wmax-URA nomogram may have had the voiding efficiency underestimated to some degree.

Maximum bladder contraction strength was negatively and weakly correlated with age ($r = -0.23$, $p < 0.001$). The %PVR was positively correlated with age, although multiple regression analysis showed that age was not a significant independent factor in the determination of voiding efficiency expressed in terms of %PVR. Therefore, %PVR increases with age because URA, Wmax and W80-W20 change with age. The factors on which voiding efficiency depended were, in descending order of significance, urethral resistance (URA), maximum bladder contraction strength (Wmax) and the bladder contraction strength decay factor (W80-W20). Maximum bladder contraction strength and bladder contraction strength decay factor were not correlated, and seem to constitute different properties of bladder contractile function. This is in agreement with findings that a bladder contraction that is fading prematurely preoperatively is usually restored to normal after transurethral resection of the prostate, whereas a low maximum bladder contraction strength is not.[7]

These findings can be explained on the basis of results obtained in animal experiments. Levin et al described the biphasic nature of bladder contraction as an initial phasic contractile response that determines the pressure response and is followed by a plateau phase that determines the ability to empty.[14] The initial phasic response appears to be related to the intracellular adenosine triphosphate concentration, whereas the ability to sustain a contraction may be linked to active mitochondrial respiration. Outlet obstruction has been shown to cause a marked increase in anaerobic metabolism in the rabbit bladder.[15] Malkowicz et al showed in the whole rabbit bladder model of obstruction that the ability of the bladder to empty is impaired to a greater degree than its ability to generate pressure.[16]

The occurrence of acute retention is clinically unpredictable[17] and relatively rare.[18] Spiro et al showed that prostates removed from patients with acute retention differed histologically from prostates of patients without acute retention.[19] Vascular infarctions were noted in 85% of patients with but in only 3% of patients without acute retention. An infarction of the prostate probably occurs rather suddenly but its etiology is unknown.[20] The proposed Wmax-URA voiding efficiency nomogram may be a first step towards a better prediction of acute retention. In its present form the nomogram is divided in 3 areas. C represents the area where voiding is physically impossible and, intuitively, patients who are closer to the borderline between B and C would seem to be more at risk for total retention. A sudden slight increase in urethral resistance could occur in the case of a prostatic infarction with its secondary edema, which could permit crossover between B and C, and result in acute retention provided that Wmax would remain constant. Bladder contraction strength changes (Wmax) have been reported in men but these changes occurred in the course of weeks and months.[21] On the other hand, no significant changes in Wmax were reported following transurethral resection of the prostate.[7] Therefore, it is unlikely that Wmax can increase instantaneously to compensate for a sudden increase in urethral resistance. The voiding efficiency nomogram must be validated in a prospective longitudinal study in which patients presenting with mild to moderate symptoms of prostatism would have to undergo a baseline pressure-flow analysis before being entered into a watchful waiting protocol.

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