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Analysis of bladder-outlet function with the linearized passive urethral resistance relation, linPURR, and a disease-specific approach for grading obstruction: from complex to simple

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Summary. The concept of the passive urethral resistance relation (PURR) to quantify bladder outflow conditions in few parameters from the complex pressure/flow relation is generally accepted. The most simple, yet realistic, linearized format is the linear PURR (linPURR). This two-dimensional format allows clear identification of individual outflow conditions with distinction of different obstruction types. Unequivocal grading of obstruction, however, requires a one-dimensional format. Theoretical considerations show that voiding function can be completely defined by a single parameter only when detrusor strength and obstruction type are uniform. This can be achieved with a disease-specific approach such as our pressure/flow diagram, which is specific for prostatic obstruction. It allows grading of obstruction stepwise for clinical decisions making or on a continuous scale for statistical applications using the maximal flow rate with related detrusor pressure as a single data point alone. Adding the actual linPURR to the diagram offers the unique feature of inherent conceptual quality control, relevant for individual assessment. The detrusor-adjusted mean PURR factor (DAMPF) is an alternative format of reducing the PURR to a single number, excluding at least the impact of variable detrusor strength, a conceptual advantage when the obstruction type is less uniform. The voiding pressure at maximal flow is a suitable parameter for most simple obstruction grading. Its validity can be significantly enhanced only when it is used in a disease-specific format, such as our pressure/flow diagram in combination with linPURR and DAMPF. Computerization does not improve the results of manual graphical analysis. Much more important is the clear conceptual definition and transparent application. More sophisticated computer-dependent methods such the original PURR/DURR and the three-parameter model can abstract more detailed information about outflow conditions, which requires expertise in their application and perfect data quality, but this does not result in better obstruction grading.

Basics

The traditional urodynamic parameters recorded during voiding are pressure and flow rate as a function of time, not because they are the ideal pathophysiological variables but because they are easy to measure. The actual pathophysiologically interesting parameters such as outflow conditions or detrusor contraction function are much more clearly reflected by the relation between pressure and flow, which is better represented in a plot of pressure (p) versus flow rate (Q) for each moment of time, a p/Q plot. The information content of such a p/Q plot is clear: every data point reflects the mechanical balance between detrusor power generation, which is the capability to generate pressure and flow in the range between the muscle's maximal contraction velocity and force, and the bladder outflow conditions, which control how much flow can be driven by a given pressure. With adequate biophysical models it becomes possible to separate the contribution of detrusor and bladder outlet to this voiding balance. The contribution of the detrusor follows the general principles of muscle mechanics according to the Hill model, and detrusor contractility can be quantified accordingly [3, 12, 16]. The fluid mechanical model of the bladder outlet follows the general principles of flow through a collapsible tube [3, 4, 11, 13, 14, 28, 30].

The concept of the passive urethral resistance relation

The key to proper data analysis for the bladder outlet is the concept of a flow-controlling zone (FCZ). This means that the p/Q relation is controlled by the mechanical and geometrical properties of the FCZ, i.e., local distensibility and lumen size. Fluid energy loss mainly occurs downstream as a consequence of FCZ properties, but energy loss does not dominate the p/Q relation as assumed in the old resistance or energy loss factors [11, 13, 29]. In a dis-

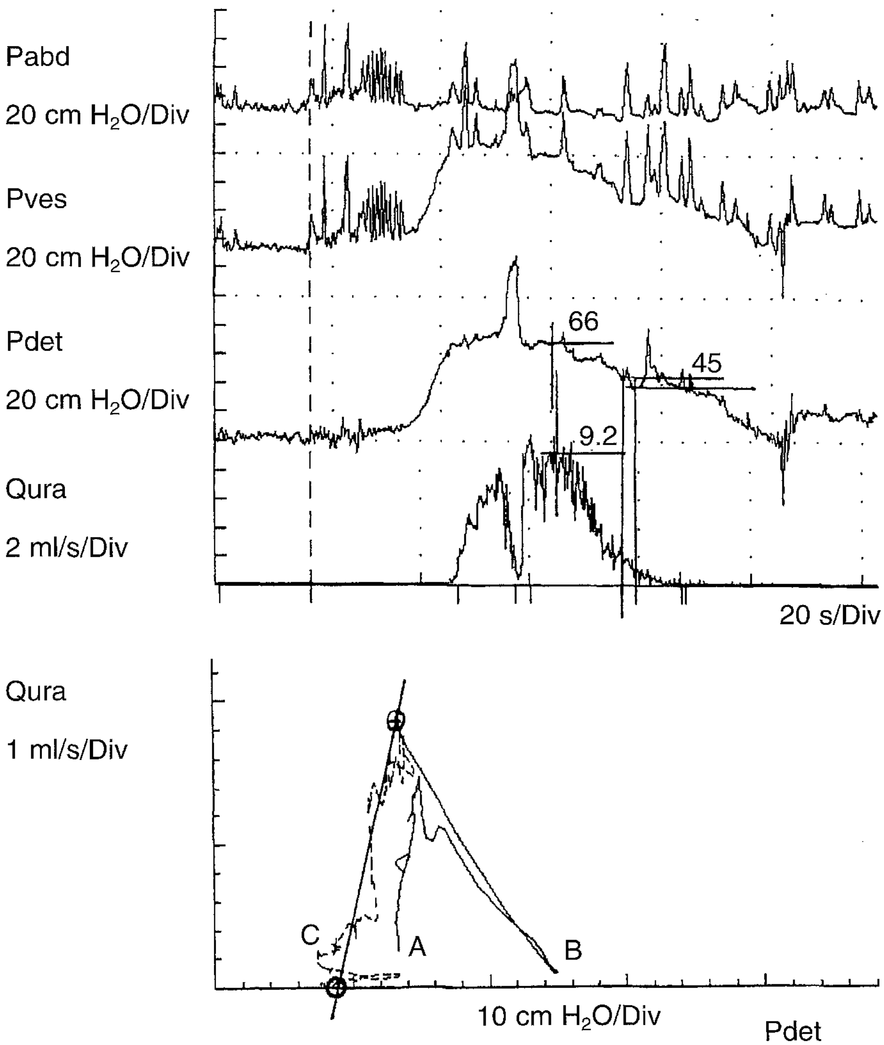


Fig. 1. A typical voiding with a major active change (sphincter contraction) and minor passive changes, as becomes obvious in the p/Q plot *(bottom)*. Voiding begins with pressure at *A*, and flow increases with minor pressure rise. Then the sphincter contraction causes a sharp drop in flow and a rise in pressure *(B)*. When the sphincter relaxes again, the maximal flow is reached but the overall pressure level is lower. The *broken line* in the p/Q plot shows the second part of voiding, ending at *C* at approximately 20 cmH_2O less than at the beginning *(A)*. The *straight line* represents the most simple version of curve fitting according to the PURR concept (for details, see Fig. 7)

tensible tube, a minimal amount of pressure is required to open the FCZ before any flow is possible, and changes in flow rate can occur due to changes in velocity and lumen size. Therefore, the p/Q relation has a complex shape that is difficult to access realistically in detail, particularly as in most cases the bladder outlet properties change actively and passively during voiding (Fig. 1).

All current analytical approaches follow in principle the concept of the passive urethral resistance relation (PURR) [11]. This concept accepts that the pattern of the complete p/Q relation is too complex for detailed analysis in toto, and the curve of a theoretical p/Q relation is therefore fitted to the low-pressure flank of the p/Q plot. The shape of this curve represents constant properties of the FCZ according to a passive model. The PURR in this way minimizes the impact of variable muscular activity and viscoelastic/plastic relaxation in the outlet as well as abdominal straining. In part, this variability can be assessed by exhibiting the deviation of the original urodynamic data from the PURR as a function of time in the form of the dynamic urethral resistance relation (DURR) [11, 13]. This combination of PURR with DURR emphasizes the difficulty of identifying clearly which parts of the p/Q plot reflect constant mechanical properties and which parts are significantly influenced by active and passive changes in FCZ properties in time.

The careful exclusion of curve elements that do not show realistic pressure/flow gradients as well as the proper consideration of the variable delay between pressure and flow are presently often ignored or not properly considered [11, 13, 23]. Only the PURR in combination with DURR allows a clear description not only of the most relevant aspects of p/Q analysis but also of its limitations.

From PURR to linear PURR

The key parameters of the original PURR are the minimal urethral opening pressure, p_{muo}, and effective lumen size. The three-parameter model of Spangberg et al. [30] attempts to quantify in addition the elastic properties of the FCZ, i.e., the dependency of lumen size on intraurethral pressure. Very often, however, this is rather speculative. It is inherently impossible to distinguish clearly between elastic distension, i.e., an increase in the effective cross-sectional area due to intraurethral pressure increase with constant elastic properties or to viscoelastic/plastic changes in time with variable elasticity. That the p/Q plot frequently shows a typical loop with a decrease in pressure level during the course of voiding indicates that time-dependent changes are important and obscure constant elastic properties (Fig. 2).

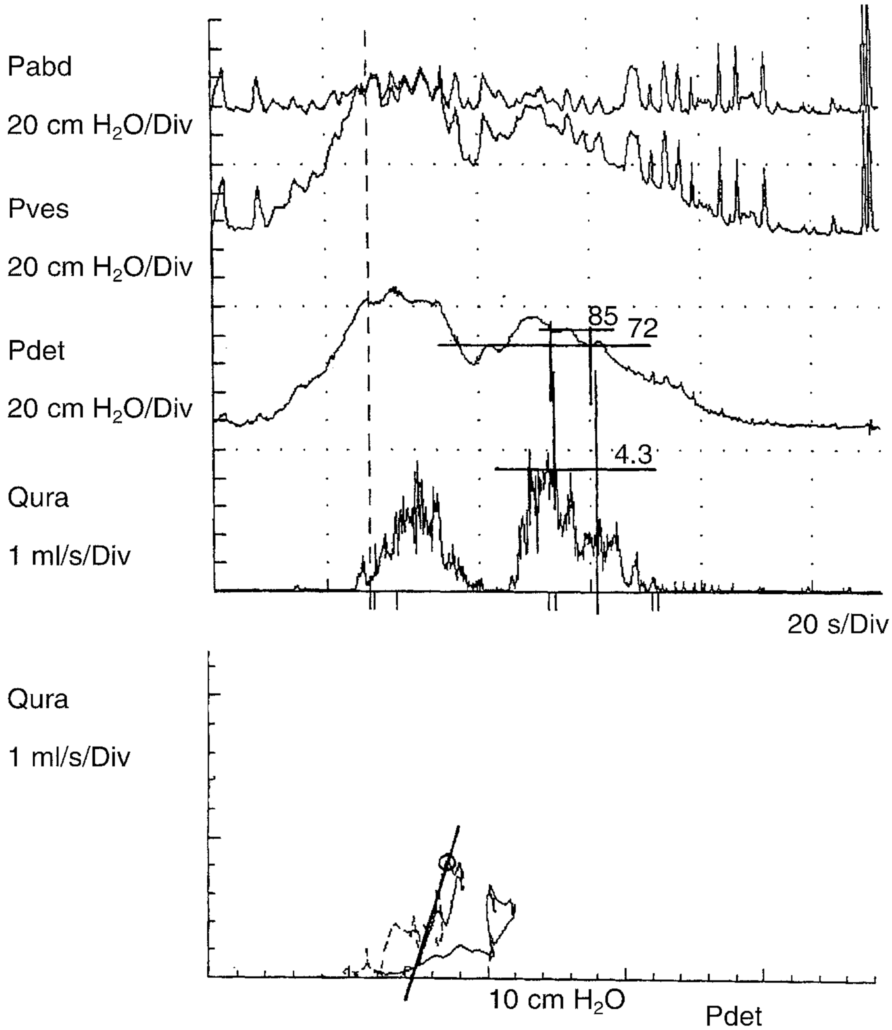


Fig. 2. Interrupted voiding leads to a rather complex p/Q plot *(bottom)*. Typically, the second part shows a lower pressure level, which indicates viscoelastic/plastic changes in the outlet. A *straight line* is fitted to the low-pressure flank, correcting the delay in flow rate (for details, see Fig. 7)

Furthermore, the complex exponential fitting process of the three-parameter model is sensitive to artefacts and is unreliable in many cases. Various combinations of these three parameters result in almost the same curve such that the numbers obtained from the three-parameter model are difficult to judge [14]. The potential additional information has thus far been clinically irrelevant but may be differently weighed for research application.

I have shown by computer simulation that the precise shape of the fitted curve is of only minor importance for the determination of the clinically relevant aspects of bladder outflow conditions [14]. Therefore, I have suggested the use of a simplified approach with a linear curve [15, 17–19, 22]. This linear approach (linear PURR, linPURR) addresses the most relevant aspects, i.e., the position (pressure level) and slope (lumen size) of the curve. In fact, many details of the shape are quite different from voiding to voiding, and even the change from a concave to a convex curvature is quite common in a single patient at repeated voidings. Fitting of orthogonal polynomials shows that any extension beyond a linear fitting is in conflict with the reproducibility and does not perform statistically better [7]. Thus, a linear approximation to the p/Q data is a reasonable compromise for a simple, transparent, yet meaningful assessment of outflow conditions.

The linPURR

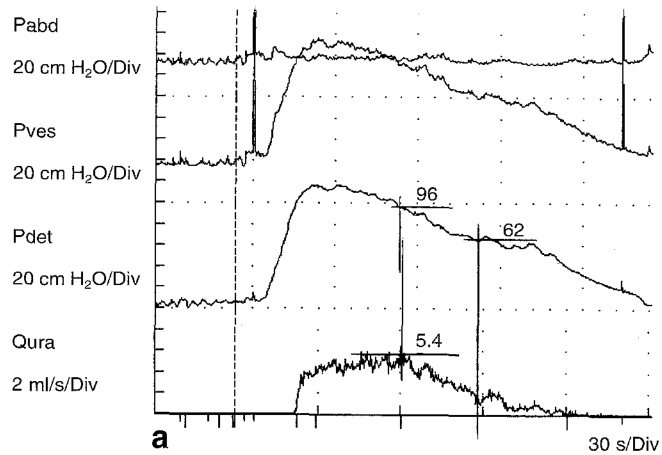
The straight line of the linPURR is completely defined by only two p/Q data points that can be read from the tracings. This opens the way for analysis of outflow conditions by a manual graphical procedure and offers the chance to make the analytical process transparent. It may seem, then, that the determination of this linear PURR is extremely easy, but this is not the case. The result is crucially dependent on the use of an accurate algorithm for the determination of these characteristic data points. Detailed rules for each and every individual tracing cannot be given, but we must refer to intelligent application of the underlying concept. Conceptually it is obvious that the maximal flow rate and related pressure, Qmax/pdet Q_{max}, together with the minimal urethral opening pressure, p_{muo}, are the dominant points for a linPURR. Because p_{muo} is a specifically defined computer-derived value from the original PURR, it is a theoretical value, determined by curve-fitting, and eventually may not actually occur during voiding. Therefore, for a manual graphical concept a realistic substitute for p_{muo} that can be read from the tracings must be clearly defined for the linPURR.

In the reading of any specific value from a urodynamic tracing, it is indispensable to control the complete curves and to eliminate artefacts. The most important aspect is the proper synchronization of the flow and pressure signals. This is very important for the linPURR and all other p/Q concepts and must therefore be discussed in some detail.

Synchronization of pressure and flow

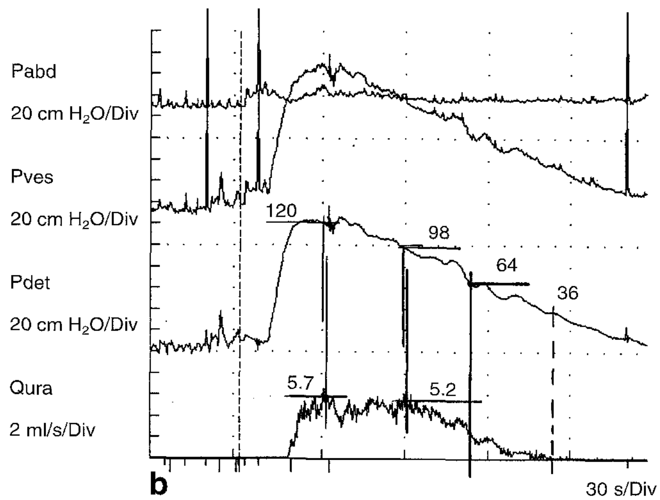
If a value is read from a signal in time, then the gradient of the signal determines how much an error in time affects the value [23]. On a typical urodynamic tracing the correct determination of Qmax and related pressure is usually not very sensitive to correction for a delay of approximately 1 s because the gradient in pressure is much lower than the gradient in flow rate. It mainly relies on correct detection of the maximal flow rate. For p/Q analysis with the PURR, these values have a specific feature. In fact, it is not the absolutely highest flow rate or pressure but the relatively highest flow rate at the relatively lowest pressure that must be determined (Fig. 3). This can be easily decided when all possible p/Q values are compared in a p/Q diagram. According to the PURR, we must focus on the relation and not simply on absolute single values. More difficult is correct determination of the minimal voiding pressure. Theoretically, this is the minimal detrusor pressure at which voiding can occur, which sounds like a rather simple definition. However, usually the pressure gradient toward the initiation and termination of voiding is rather high such that any inaccuracy in time will lead to a rather different pressure value. In benign prostatic hyperplasia (BPH) the lowest voiding pressure is most often found at the end of voiding. Typically, prostatic flow ends with tailing off and postvoid dribbling; thus, it is quite difficult to determine when voiding really ends. According to the concept of the flow in distensible tubes, we must synchronize the signals with respect to the FCZ such that all fluid leaving the meatus after the FCZ has closed must be discarded for determination of the minimum voiding pressure. Our estimate from careful observations is that the last 10 ml of urinary volume must be discarded. This usually leads in BPH to a correct minimal voiding pressure, $pdet_{min}Q$, to be read at approximately 5 or even 10 s before the flow recording ends [17, 23] (see Fig. 3).

I want to emphasize that $pdet_{min}Q$ is a conceptual value and, thus, must be determined according to the concept. This also means that in cases in which the lowest pressure occurs during uninterrupted flow, i.e., is not at all related to the beginning or end of voiding, this pressure is the most appropriate value for $pdet_{min}Q$. In such cases the conceptual aspect of the PURR overrules any other simple rule for correction of delay.



Results (voiding phase)

Max flow rate	6.4 ml/s	Pves at opening	137 cm H_2O
Average flow rate	3.4 ml/s	Pves at max flow	131 cm H_2O
Voided volume	294 ml	Pdet at max flow	95 cm H_2O
Voiding time	98 s	Max Pdet	116 cm H_2O



Results (voiding phase)

Max flow rate	6.5 ml/s	Pves at opening	148 cm H_2O
Average flow rate	3.7 ml/s	Pves at max flow	175 cm H_2O
Voided volume	309 ml	Pdet at max flow	133 cm H_2O
Voiding time	95 s	Max Pdet	136 cm H_2O

Fig. 3 a, b. Two voidings from the same patients are analyzed both with automatically computer-read values and manually according to the recommended procedure for the linPURR. In both cases the relatively highest flow rate is determined for the relatively lowest pressure. In the *upper panel* only a significant reduction in the manually read Q_{max} occurs; in the *lower panel*, quite dramatic changes are obtained from the manual reading. The second, slightly lower, Q_{max} has a much lower pdet, Q_{max}. Here the correction for delay is less important than the correct Q_{max}. However, the pressure at the end of flow, $pdetQ_{end}$, (36 cmH_2O) is much lower than the corrected $pdet_{min}Q$ (62 cmH_2O). Both cases are plotted as linPURRs in Fig. 7 and are discussed in detail there

The urethral opening pressure

Part of the existing confusion regarding the urethral opening and closing pressures, p_{muo} and $pdet_{min}Q$, is related to poor terminology. It is rather misleading to use the terms opening and closing pressure directly for the pressure at which flow begins or ends, because this inherently includes a number of interpretational steps. We should call these pressure values by the properly descriptive terms *the pressure at which flow begins or ends,* i.e., $pdetQ_{beg}$ or $dpetQ_{end}$, and reserve the conceptual conclusion about the interpretation of these values with respect to urethral opening or closure to precisely defined concepts such as $pdet_{min}Q$ and p_{muo}. Relevant for our analysis are also the intrapatient variability of the data and the superimposed interreader variability, both of which are influenced by the conceptual difficulties of precise value definition. Our data show that the intraindividual variability of pdetQ_{max} (10%) is much smaller than that of Q_{max} and pdet$_{min}$Q (20%). It is also noteworthy that the interreader variability is always considerably smaller than the intrapatient variability. This significantly limits the potential advantage of computerized value determination.

Outflow conditions and obstruction

The outflow conditions are clearly defined biomechanically and can be abstracted from the urodynamic data. However, I do not think that "obstruction" is clearly defined urodynamically, nor is the relation between outflow conditions and obstruction. The use of the term obstruction in urodynamics is difficult since we know that *clinical obstruction* is not clearly related to urodynamic data. Obstruction is a traditional clinical term with apparently rather precise qualitative features that are notoriously difficult to quantify. We could clarify the situation by subclassifying the term into *clinical* and *urodynamic* obstruction. However, we first need a clear urodynamic definition of obstruction because the relation between the measured parameters and obstruction is not simple and straightforward. Previously I have suggested the term *voiding efficiency* to describe the energy balance during voiding and have defined obstruction as those outflow conditions that are inefficient. The amount of detrusor contraction energy (work) needed during voiding per unit volume is in first approximation.

$$\frac{\text{Work}}{\text{Volume}} = \frac{\text{Pressure} \times \text{volume}}{\text{Volume}} = \text{Pressure}$$

and, thus, simply the voiding pressure itself. This theoretical result is in agreement with clinical concepts [12, 13, 29].

Analysis of the information contained in the p/Q data leads to the conclusion that different voidings can indeed be compared by pressure alone, but only when the same detrusor contraction strength and the same type of bladder outflow conditions are assumed at all pressure levels. Only in such a simplified situation can an easy-to-determine pressure value be used to grade the degree of obstruction by a single number, i.e., one-dimensionally.

In reality, however, the contraction strength of the detrusor can differ considerably from patient to patient, and even in the individual patient the detrusor strength varies physiologically with the bladder-filling volume as reflected by the dependency of the maximal flow on the volume voided. The differences in outflow conditions are less well understood. There are well-defined types of constrictive and compressive obstruction [11], and it is easy to show how they constitute distinctly different pathophysiological conditions that are characteristic of specific diseases. However, the impact of more subtle differences in obstruction type, i.e., in the combination of compressive and constrictive components in complex obstruction forms such as clinical BPH, has not yet been investigated. Nevertheless, it is important to understand why differences in detrusor strength and obstruction type limit the value of any one-dimensional approach to obstruction.

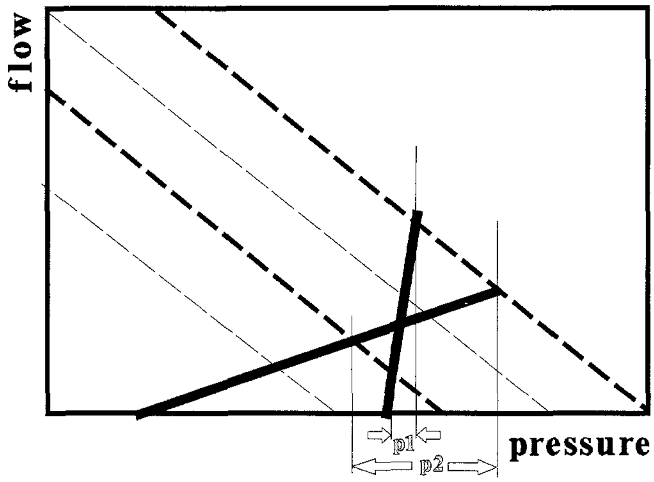


Fig. 4. In a p/Q diagram the detrusor power as well as the outflow conditions can be plotted in a most simplified linearized form. The *steep solid line* represents a compressive obstruction and the *flatter thick line,* a constrictive type. The detrusor power is represented by the *broken lines* for different power levels. The *lower left thin line* shows a weak power, which intersects with the constrictive obstruction and results in low flow at medium pressure but does not intersect with the compressive outlet, which means there is no voiding at all. A power increase between the *thick broken lines* results in a rather small pressure increase *(p1)* for the compressive outlet and a much higher increase *(p2)* for the constrictive type. This schematic example makes clear how the interaction between different detrusor strengths and different outflow conditions complicates any attempt of simple grading in terms of more or less obstructed

Clear definitions of outflow conditions such as the original PURR or the linPURR are independent of detrusor function because they show how the flow rate depends on pressure for any range of detrusor strengths. The relationship between pressure and detrusor strength is dominated by the slope of the PURR; on a compressive PURR the pressure varies little with contractility, whereas in a constrictive PURR even a minor change in contractility has a strong impact on the pressure [11] (Fig. 4).

This multifactorial variability demands a multidimensional approach to describe obstructive outflow conditions realistically and, apparently, may exclude any one-dimensional grading of obstruction. Höfner's CHESS method is an example of a two-dimensional classification technique that does not allow the comparison of patients in terms of more or less obstructed cases [5].

If we consider differences in obstruction type at the same pressure level (i.e., in graphical terms, differing slope and position but intersecting PURRs), it is easy to see that different outflow conditions establish different relationships between detrusor strength and voiding efficiency. A strong detrusor will empty more of the urinary volume at higher pressure with a constrictive PURR than with a compressive PURR. A weak detrusor may achieve complete voiding with a constrictive PURR while being in complete retention with a compressive PURR when the minimal voiding pressure is higher than the maximal isometric pressure, particularly at a larger bladder-filling volume (see Fig. 4). In reality, we do not understand the relevance of such differences in obstruction type, i.e., whether the highest absolute pressure or an elevated minimal voiding pressure is pathophysiologically more important, such that one or the other can be quantified as more or less clinically obstructed. Simple theoretical answers such as *resistance* or *voiding efficiency* quantified as voiding pressure do not help. Thus, our level of urodynamic sophistication has a good theoretical biomechanical basis but no sound connection to the pathophysiological reality, such that simplification is indicated.

The disease-specific approach

If we look at large numbers of PURRs obtained from BPH patients – and this is the only large group with suspected obstruction that we have in the clinic – it is quite obvious that the slope and the position of the PURRs are interrelated: with increasing pressure level the slope decreases. This is confirmed by data from the ongoing International Continence Society (ICS)-BPH study [26, 27]. This pattern suggests that a specific obstruction type exists for BPH, which allows combination of the two PURR factors, slope and position, into a specific BPH-PURR where the pressure level determines the slope (Fig. 5).

Only on the basis of such a BPH-specific obstruction type does it become possible to grade prostatic obstruction unequivocally in simple terms of more or less obstructed cases, to rank patients, and to quantify changes in obstruction grade in BPH. I have had used such an approach for the original PURR and for the linPURR [15, 21, 22]. Similarly, the urethral resistance factor (URA) is derived as a group-specific resistance factor from a group of patients without a specific disease, including men and women [4]. Such a definition of a disease- or group-specific obstruction type leads to a single pressure value for grading of obstruction, most simply the pressure at zero flow, equivalent to p_{muo} or $pdet_{min}Q$. This eliminates the variable influence from detrusor strength. Thus, we have returned to the opening statement that under the condition that we can exclude or control differences in obstruction type and/or detrusor contraction strength, a single characteristic pressure value is a useful measure for outflow conditions and, thus, for one-dimensional obstruction grading.

Stepwise or continuous grading

The disease-specific properties can be presented graphically in a p/Q diagram. There are two simple formats to abstract a single number from a two-dimensional graph. A characteristic data point is read from the original data – in this case, Q_{max}/pdetQ_{max} – and transferred to a disease-(group)-specific diagram. Either we can determine a theoretical minimal voiding pressure on a continuous scale by projecting along the typical PURRs to the intersection with the pressure axis or we divide the graph by typical PURRs into a limited number of classes for stepwise grading (see Fig. 5). Both approaches have specific advantages and disadvantages. A continuous scale is apparently very accurate. A stepwise grading is much easier to use because the grades can be organized according to the needs of clinical decision making, which usually does not follow a continuous scale but is limited to some categories. In our first diagram [21] we have distinguished only three groups (unobstructed, obstructed, and severely obstructed), knowing that transurethral resection of the prostate (TURP) in prostatic outflow obstruction causes dramatic changes; hence, three classes seemed to be sufficient to describe these changes.

The p/Q diagram

In the p/Q diagram based on the linPURR, I have organized the grades according to the best possible yet realistic resolution of pressure/flow data. I have used the following criteria: a grade width should reflect the reproducibility of the data and the minimal difference that is clinically relevant. The intraindividual variability is approximately 10%–20% for p_{det}, such that a difference between two values has to be larger to be "real." How-

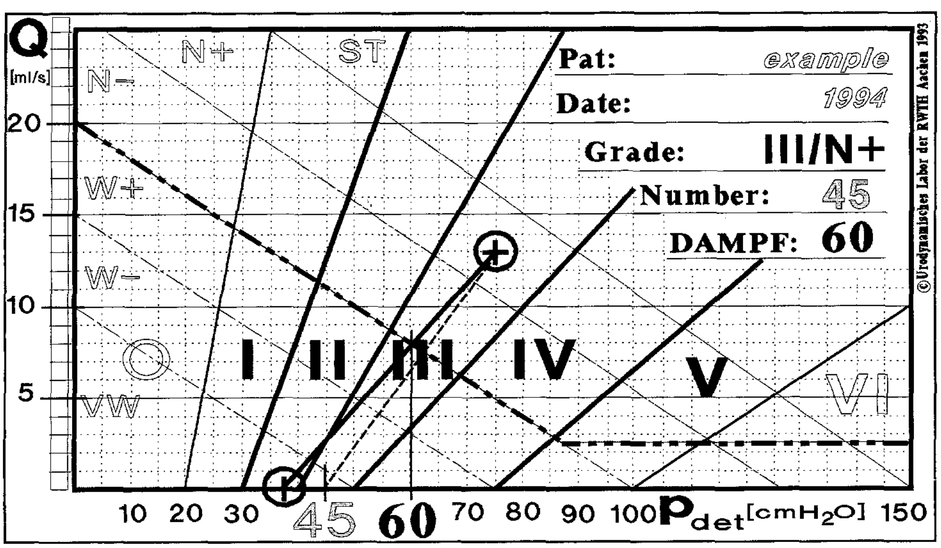


Fig. 5. In the p/Q diagram the slopes of the "statistical" linPURRs are dependent on the pressure level. If a single point of Q_{max} and pdet,Q_{max} is plotted in this disease-specific diagram, one can project to the pressure axis *(thin broken line)* to determine a theoretical minimal pressure *(45 cmH$_2$O)* for simple grading of obstruction. Alternatively, one can use a stepwise grading, with 7 areas being separated in the diagram *(0–VI)*. The full line between the data points is the linPURR, indicating a minor disagreement between this individual case and the diagram. The intersection of the linPURR with the linearized detrusor power line *(thick broken line)* results in the detrusor-adjusted mean PURR factor *(DAMPF)* of 60 cmH$_2$O

ever, it is reasonable to assume that a difference must be even larger than the minimal detectable difference before it becomes clinically relevant.

It is clear that all voidings in the very-low-pressure range (p_{muo} < 20 cmH_2O) and the low-pressure range (20 < p_{muo} < 30 cmH_2O) are unobstructed; thus, further differentiation is clinically meaningless. Urodynamic differences are most interesting in the intermediate pressure range (30 < p_{muo} < 50 cmH_2O), but a finer differentiation than that of 10 cmH_2O is doubtful and not clinically relevant. At higher pressure (50 < p_{muo} < 100 cmH_2O) a differentiation of 25 cmH_2O is sufficient, and above 100 cmH_2O a subdivision can be of only academic interest. This subdivision allows limitation of the number of grades to seven. That the foot points of all grade borders use round numbers underlines our pragmatic approach for definition of these grades (see Fig. 5).

Which urodynamic values are obstructed?

Due to the lack of a relationship between clinical data and urodynamics we cannot use clinical data to "calibrate" a urodynamic diagram with respect to obstruction. Therefore, I have taken a different approach by using a specific surgical definition of *obstruction* as those outflow conditions that improve after surgery. This makes the definition of obstruction in our diagram a uniquely urodynamic grading, based only on comparing urodynamic data before and after surgery, independent of other clinical data. In patients in grade O/I the outflow conditions do not improve after TURP, and in grade 0 they actually become worse. In grade II, some minimal improvement is found (Fig. 6).

From grade III onward we find consistent improvement, with changes being proportional to the obstruction grade and, in general, identical to the numbers of grades above grade I. Therefore, I have defined grade O/I as unobstructed; grade II, as minimally obstructed; and grade III and higher, as increasingly obstructed.

From the patient distribution we now know that typical BPH patients are distributed almost equally, with 20% being classified as grades O–I, II, III, IV, and V–VI, respectively [17, 26]. Therefore, for statistical and clinical application, even a further reduction to the use of only five grades (i.e., including 0 in I and VI in V) may be meaningful, particularly as the subdivision O/I and V/VI has no clinical consequence; patients in these grades are either completely unobstructed or severely obstructed, respectively.

I would like to reiterate that the p/Q diagram is derived by using the linPURR, but the use of this diagram does not depend on constructing a linPURR. By concept, the diagram is valid for using a single point of Qmax/pdet,Q_{max} alone. Then either the correct grade can be directly determined unequivocally in a stepwise format or continuous grading is achieved by projecting from this point to the pressure axis along the separating lines, as for URA or the A/G number [10]. In this way a projected p_{muo} value can be used for grading on a continuous scale. Furthermore, I would like to emphasize again that the proof of a relevant change in *individual* outflow conditions is

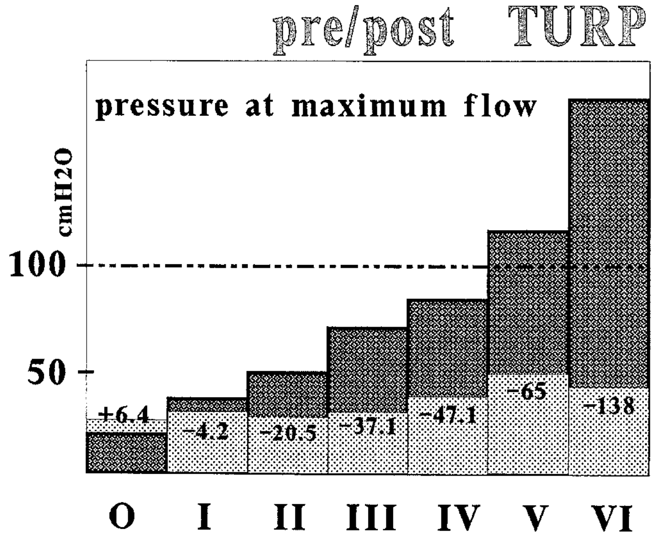


Fig. 6. A comparison of the mean value for pdetQ_{max} before (dark shade) and after TURP in a group of 102 patients reveals a significant decrease in pressure starting in grade II and increasing with the degree of obstruction. This information can be used for a "urodynamic-surgical" definition of obstruction because if surgery removes the obstruction, it is not effective in grade 0/I

obviously not established when the data are on both sides of a borderline separating two grades (see Fig. 7, studies 3, 4). In an individual patient, it follows from the logic of stepwise grading and from the definition of this diagram that only a difference corresponding to a full grade width is relevant [24]. Stepwise grading in a "stupid" simple form can be statistically applied only to a group of patients.

Also, I would like to make clear what the intended role of the suggested use of the full linPURR in such a diagram is. The only purpose of using the complete two-dimensional linPURR in an attempt to reach a one-dimensional grading is to serve as a quality control. As the borders between the grades of this diagram are defined from the statistical linPURR at a given pressure level, any disalignment or even intersection of an individual linPURR and the borders indicates disagreement between the simplified general concept, the statistics, and the individual case. In this way, the linPURR points out how well the individual case meets the typical BPH obstruction. When we follow strictly the precise algorithm for determination of a linPURR, we rarely find a relevant disagreement with the diagram. LinPURRs that are crossing a whole grade are found in less than 5% of cases. A higher percentage of disagreement, reported by other investigators [7], can be due to a number of reasons: an atypical obstruction type (e.g., bladder-neck sclerosis or stricture), poor data quality (in particular, a slow flowmeter with funnel), or the use of a different algorithm for determination of the linPURR (in particular, insufficient correction of the delay for pdet,$_{min}$Q; see Figs. 2, 3, 7).

In this way our diagram is open to various forms of misuse when either the measurement quality is poor or the definition of linPURR is not followed correctly. However, when this diagram is used together with the linPURR, it is the only concept with an inherent quality-control mechanism. Disagreement between the diagram and the linPURRs in a significant proportion of patients proves nothing but a difference in patient selection or data quality or the misuse of the diagram. I maintain that it is not the diagram that is wrong. When the diagram is used only with the single point of Qmax/pdet,Q_{max}, a disagreement between concept and reality cannot be detected but nonetheless exists, as in any other approach such as URA.

Thus, the specific use of our diagram depends on the information wanted. If statistical analysis of large groups of patients is intended, then a single-point analysis is perfectly adequate. For clinical decision making in an individual patient, an inherent degree of quality control is important and any individual feature of the patient's urodynamic data should be considered; hence, a linPURR should be used in the diagram. This is also true for research in a small group of patients when small changes are expected, e.g., studies on alpha-blockers [24]. Direct inspection of the linPURR graph provides much more information than can be quantified easily. Thus, repeated voiding studies are required and the reproducibility of data as well as the definite decision as to which voiding shows the best outflow conditions can be judged better by visual inspection of the linPURRs than from simple quantification, as the former allows one to overrule the limitation of the disease-specific diagram. This is not possible with any other simple method. Computer programs with our diagram and linPURR are available from a number of urodynamics equipment producers, neither authorized or licensed by me. These programs may make the application easier and reduce interuser variability, but they do not necessarily increase precision and reliability.

The detrusor-adjusted mean PURR factor, DAMPF

Attempts at reducing the complex multifactorial voiding dynamics to a single parameter for grading obstruction with the disease- or group-specific approach have concentrated only on the outflow conditions. Significant disagreement between the statistical obstruction type and the individual case make these obstruction factors dependent on the detrusor contraction strength. URA does not very well represent the typical BPH-induced obstruction at higher pressure levels and deviates frequently from the typical compressive obstruction in BPH. Therefore, URA is inversely related to the detrusor strength, i.e., for the same outflow conditions, the URA value will become smaller with increasing detrusor strength. OBI uses the average pressure level instead of the minimal voiding pressure for derivation of a single number [9]. The average p_{det} on a given linear resistance relation depends on the length of this line and thus, on the maximal flow rate and, hence, on the detrusor strength. Consequently, OBI is by concept dependent on the detrusor contraction strength.

Dependency on detrusor strength has been shown for both parameters from statistical analysis [9]. However, for application of these concepts in an individual patient, it is much more important that a simple conceptual discussion and comparison of URA and OBI come to the result that with identical outflow conditions, two voidings with different maximal flow rates will be classified in opposite directions with URA and OBI, i.e., a higher flow rate is less or more obstructive. Statistically, these differences will be small, but they are relevant individually.

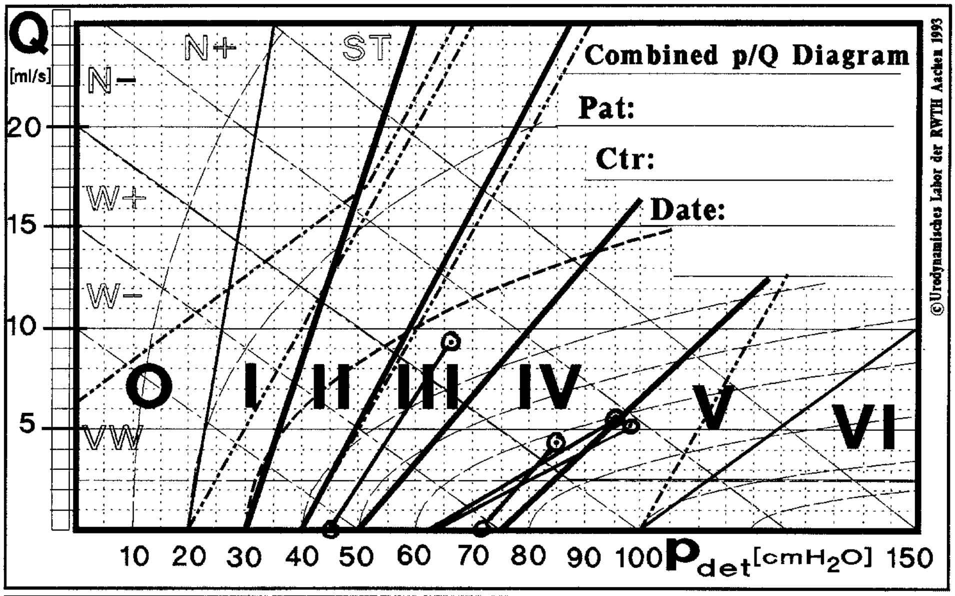
In principle, such an impact of variable detrusor strength is also relevant for our p/Q diagram, whether graded stepwise or continuously, when the obstruction type deviates significantly from the typical form. It is trivial to say that the higher resolution of continuous grading is more sensitive than the stepwise format to such unwanted influences. Therefore, we have suggested a new method of deriving a single number from the two-dimensional linPURR that eliminates by concept the influence of variable detrusor contractility. A "normal" detrusor strength is defined for typical BPH patients in the form of a HILL curve or a Bladder Output Relation (BOR) [3]. Here a very simple linearized form is used (see Figs. 4, 5).

The pressure value at which a linPURR intersects with this detrusor line, I have labelled *detrusor adjusted mean PURR factor* (DAMPF) [20]. Use of "normal" detrusor strength in a linearized form with the p/Q diagram would exclude the very obstructed patients with extremely strong bladders from this new concept. Therefore, it is meaningful to elongate such detrusor line in parallel to the pressure axis to cover all cases (Fig. 5). It also follows from the logic of this concept that in cases in which the linPURR is too "short," i.e., the detrusor is too weak, the linPURR must be elongated to find the intersection at normal detrusor strength.

If this DAMPF concept is used with the linPURR within the BPH-specific diagram, the DAMPF value is a superior format for continuous grading of prostatic obstruction within the definition of the diagram. This concept limits the impact of the two variables, detrusor strength and obstruction type, which make voiding a complex multifactorial event and speak against simple grading by any single value. However, the DAMPF concept can also be applied for simple obstruction grading in general when a disease-specific obstruction form does not exist. Clearly, then, in individual cases a two-dimensional approach is needed, which cannot easily be compared in terms of more or less obstructed cases (see Fig. 4). However, in a statistical approach, DAMPF is a useful general concept because when the variability of outflow conditions cannot be excluded, it is helpful to limit at least the second variable, i.e., detrusor contractility.

Confusion in methodologies

Although all recently proposed methods have a common basis, not their similarities but their differences have been emphasized for a variety of reasons. Gross misinterpretation of methods is quite easy because terminology is often vague, methodology is often poorly defined, and computer application does not enhance transparency. Furthermore, the discussion mostly uses statistical comparison instead of conceptual arguments.



Study	Qmax	$pdet_{Qmax}$	$pdet_{minQ}$	Grade	Number	DAMPF	A/G	A/G No	URA	OBI
1	9.2	66	45	III/N-	45	62	obs	48	34	61
2	4.3	85	72	IV/N-	71	82	obs	76	63	86
3	5.4	96	62	IV/N-	74	83	obs	83	60	92
4	5.2	98	64	V/N-	79	85	obs	88	64	98

Fig. 7. The combination p/Q diagram allows classification and grading of obstruction according to Schäfer grade and number, DAMPF, the A/G nomogram and number, URA, and OBI from a reading of the values recorded for Qmax, pdet,Q_{max}, and $pdet_{,min}Q$ from the original tracings. Here the 4 cases from Figs. 1–3 are plotted and analyzed according to all these methods. Overall, all methods lead to comparable results. However, typical and, I think, relevant individual differences can be abstracted from the graphics. *Study 1* (Fig. 1): a typical case of mild BPH-induced obstruction. From the different slope between the linPURR and URA results, that if detrusor contraction becomes stronger (e.g. by larger volume) and the flow rate increase for just 3 ml/s, i.e., a longer linPURR, then URA would classify this patient as unobstructed. It is easy to see that with increasing pressure level, URA, linPURR, and A/G number diverge increasingly. Using the concept of the linPURR, one can create examples to study the effects of various slopes, pressure levels, and curve lengths representing detrusor strength. This is the only way to understand the information content of this diagram and, thus, the differences between the concepts. For example, the A/G 100 line (thick broken line in grade V) relates to possible URA values between 40 and 100 with different detrusor strength. Study 1 is derived from Fig. 1; study 2, from Fig. 2; and studies 3 and 4, from Fig. 3. For study 4 it is interesting to consider the impact of reading wrong values from Fig. 3b with p_{det},Q_{max} = 120 cmH_2O and p_{det}, $_{min}Q$ = 36 cmH_2O

Some methods are proposed for a specific use such that a comparison beyond this intended application is misleading. This would be disclosed by a conceptual discussion but is disguised in statistics. It is particularly confusing that different methods are proposed by the same authors but are not compatible with each other [1, 3, 4, 10, 32]. The Abrams/Griffiths (A/G) nomogram [3] is a quite simple method to diagnose obstruction and was never intended to be used for grading obstruction. The delineation of an *equivocal* and an *unobstructed* range in the A/G nomogram is now historical and has been de facto revoked by the recently suggested A/G number for grading obstruction [10]. Simple consideration of the conceptual differences between the A/G number, our p/Q diagram, and the URA nomogram leads to the result that the methods are rather close in the unobstructed range and diverge with increasing obstruction. This may not be important statistically but is relevant individually. A very simple statistical comparison cannot show this in its numerical results, but if a scattergram of A/G versus URA is inspected carefully, the expected deviation with obstruction level becomes obvious [10].

Van Mastrigt and Rollema converted Griffiths' intriguingly simple URA nomogram, suggested for manual graphical use, for commercial purposes into a computer program, CLIM, although neither a clinically relevant increase in reliability nor a scientifically meaningful increase in precision can be expected from a computer-derived URA. Furthermore, they offer the *group-specific resistance factor URA* as a method of obstruction grading for general application in clinical routine, in particular for BPH, and ignore all limitations of URA as explicitly specified in the original publication: "... changes in URA in individual patients are not necessarily reliable..." and "... URA may not necessarily be a useful parameter for the diagnosis of obstruction" [4]. Although by concept meaningless, they compare continuous with stepwise grading of obstruction and continue to suggest new and differently superior concepts of obstruction grading using various forms of automated computerized fitting of the p/Q data with "orthogonal polynomials" [10], in fact "a first order orthogonal polynomial," an impressive term for nothing but a straight line, i.e., a linearized PURR. Recently they suggested that slope and position be quantified separately and confirmed that statistically the significance of differences between two single factors can be enhanced by combination [32].

In conclusion, when individual authors suggest a variety of inconsistent and incompatible methods for analyzing voiding function and grading obstruction, it would be very helpful if they would clarify either the specifically different application of these methods or which one should be used and how the differences are to be interpreted. Nevertheless, when commercial/personal/political interests are ignored, it is possible to identify significant common features from a variety of methods that can be combined into a single comprehensive methodology for interpretation of p/Q data.

Comparing different methods

I have used all methods of manual graphical data analysis, including A/G nomogram and number, Schäfer p/Q diagram, stepwise and continuous, with and without linPURR, URA, OBI, and DAMPF, in a large number of patients. The bases for this analysis are Qmax/pdet,Q_{max} and pdet,$_{min}$Q properly corrected for delay on quality-controlled urodynamic tracings [26]. These data points are transferred to a combination diagram including all methods (see Fig. 7).

When these methods are combined graphically, it may be confusing for the nonspecialist that today different positions of axes are in use for presentation of p/Q data. Traditionally in urodynamics, data presentation has been uniform according to general scientific convention, with the flow rate being the dependent variable on the vertical axis, as the flow rate has been considered to be dependent on pressure. In 1979, however, a standardization committee of the ICS accidentally inverted the position of the axes for the specific purpose of presenting the data point for the maximal flow rate and pressure at maximal flow rate in a simple diagram for rough classification. Consequently, differing selection of axes came into use in urodynamics practice, with those analyzing the causal relation between flow and pressure continuing with the scientific convention [5–7, 11, 13, 15] and others using the inverted format [1, 4, 30, 32].

Recently, attempts have been made to return to a uniform selection of axes, as such optical uniformity, although irrelevant for the derived results, may make it easier to compare the different methods [2]. However, this reflects a considerable misunderstanding of the underlying concepts. In spite of the observation that graphical presentation of data is possible for all methods currently in use, a meaningful comparison simply by graphical superposition is inadequate. Furthermore, the current discussion makes it clear that the different selection of axes reflects very well conceptual differences. Whereas some methods, such as the PURR and its derivatives linPURR and DAMPF, are based on the assumption that the flow rate depends on the pressure, other methods are independent of any causal relation (A/G nomogram) and have no preference in terms of axis position (Abrams, personal communication). Recently, some authors have denied any causal relation between pressure and flow (van Mastrigt, personal communication) or have even postulated that the detrusor pressure is causally dependent on the flow rate [8] and that the pressure must therefore be plotted along the vertical axis in their analysis.

Therefore, the different position of axes is related to profound scientific differences in the conceptualization of bladder outflow conditions and should thus be maintained to visualize these differences until an agreement on the scientific foundation of the p/Q relationship is reached, which should lead to a uniform format of data presentation.

Apart from these trivial formal differences, all methods perform very similarly for large groups of patients, as would be expected from their common basis. Statistically, the correlation coefficient between the different gradings is very high, ranging between 0.85 and 0.95. However, the correlation coefficient between all obstruction factors and the straight value for pdet,Q_{max} is in the same order. Also, a separation between obstructed and unobstructed cases will be provided statistically by all methods with a high degree of agreement if a reasonable, common cutoff value is used. Therefore, it would seem interesting to discuss the different delineations between obstructed and unobstructed cases in more detail.

Obstructed, unobstructed, equivocal?

The A/G nomogram was based on the assumption that urodynamics correlates with the clinical features of BPH [1]. The separating lines were found intuitively by trying to separate urodynamic values of patients with clinical classifications of obstructed, doubtfully obstructed, and unobstructed. The separation line between *equivocal* and *obstructed* has a slope of 0.5 (ml/s)/cmH_2O at a minimal voiding pressure of 40 cmH_2O. Further subclassification of the data in the *equivocal* range is possible with additional criteria, such that almost 20% of *obstructed* patients have a lower pressure than those classified as *obstructed* [1].

Using the concept of the linPURR, Schäfer found at the same pressure level a rather similar value for the slope (0.53 (ml/s)/cmH_2O) for BPH. However, for a urodynamic separation of obstructed from unobstructed cases without using clinical data, he found much lower pressures. The lower border for grade II *(minimally obstructed)* has a minimal voiding pressure of 30 cmH_2O and a slope of 0.83 (ml/s)/cmH_2O. The vast majority of the patients in A/G *equivocal* who were originally classified as *obstructed* [1] belong to Schäfer's grade II. In addition, the borderline between grade I *(normal)* and grade II *(minimally obstructed)* has been confirmed by Spangberg et al. [31], who found an upper limit for normal older men to be 33 cmH_2O and a slope of 0.82 (ml/s)/cmH_2O, which is almost identical to Schäfer's lower border for *obstructed* (Fig. 8).

Although it is in principle difficult to compare a parabolic cutoff curve for URA and Höfner's A1 CHESS classification with a straight line, it is noteworthy that for low flow values both are in Schäfer's grade II. Thus, there is good agreement on those patients which are "definitely obstructed" between the old A/G nomogram and Schäfer's grade III and higher. However, there is significant disagreement about the definition of "unobstructed", by concept and numbers, between the A/G nomogram and all other methods. It is currently generally accepted that the delineation for *unobstructed* in the old A/G system is unrealistic in terms of position and slope. Abrams has recently suggested a new grading with the A/G number and Griffiths has proposed a new limit for *unobstructed* following the A/G number 20 (Griffiths, personal communication). This could be interpreted as a redefinition of the A/G nomogram. There is, however, no scientific evidence in terms of either position or slope for such a new line.

Furthermore, I think it is in principle not meaningful to qualify urodynamic data as *equivocal*. All recent data confirm that a definite relation between *clinical obstruction in BPH* and the urodynamic quantification of obstruction does not exist [15, 17, 21, 24, 26]. When a correlation does not exist, we must use one or the other source of information, clinic or urodynamics, as a standard for *obstruction*. This decision should not be ob-

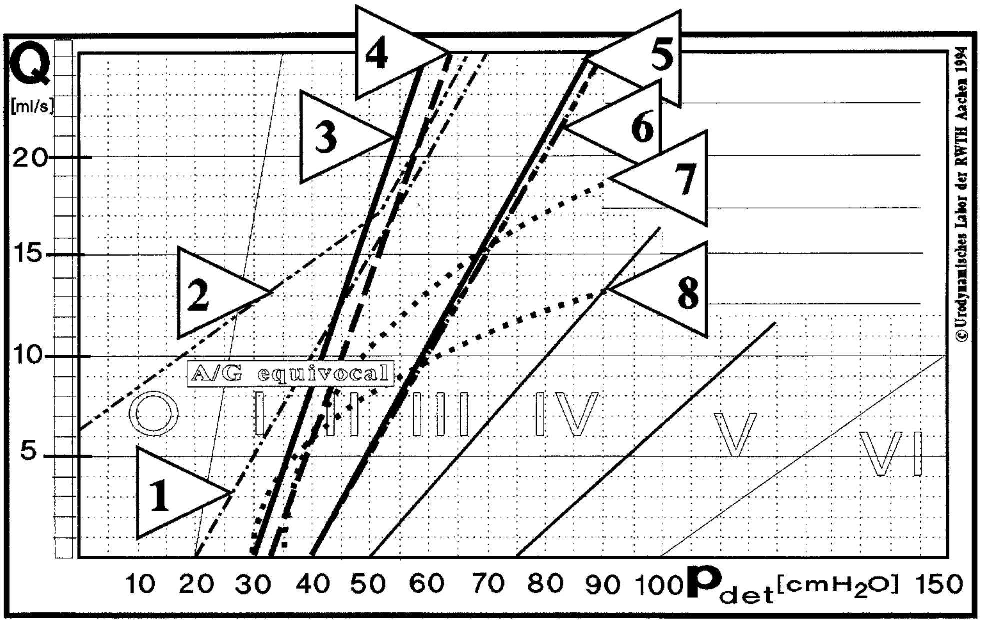


Fig. 8. Different separating lines used for grading are superimposed on the p/Q diagram. *1,* A/G number 20; *2,* A/G nomogram separating unobstructed and equivocal; *3,* Schäfer's upper limit of unobstructed, i.e., grades I/II; *4,* Spanberg et al.'s upper limit for normal older men; *5,* Schäfer's lower limit of real obstruction, i.e., grades II/III; *6* A/G separation line between equivocal and obstructed; *7,* Höfner's A1 line; *8,* URA 29 for separating unobstructed and obstructed

scured by an *equivocal* range. There can be no doubt, that I favour urodynamics as the reference standard for definition of obstruction, simply because it is measurable in a strict sense [2, 13, 15, 21].

Conclusions

The urodynamics of micturition is well developed today. The biomechanical concepts of data analysis allow the theoretical elaboration of details that have not been investigated in vivo. We can investigate the outflow conditions in detail, but we do not know the pathophysiological relevance of the measured changes for the clinical situation. At least it is currently generally accepted that the discrepancy between urodynamic measurement and clinical findings does not prove that urodynamics is wrong but indicates that the clinical diagnosis is unreliable. Accepted general features are used in all concepts, such as fitting to the low-pressure border of the p/Q plot (PURR). The discussion starts when details of application are considered. Unfortunately, the scientific discussion is currently confronted with commercial and political interests. However, rather soon we will know which methodologies have stood the test of time.

If we theoretically had the need for a most simple grading method, then we should use the most simple value straight away, which is the voiding pressure, specifically the pdet,Q_{max} in proximal obstruction, or the mean detrusor pressure during voiding, or an equivalent intravesical pressure in distal obstructions and in women. If we deal with a specific disease or any otherwise defined group of patients, we can improve analysis significantly by using a disease- or group-specific format, because then we abstract more information from the p/Q relation and so improve the accuracy. Our linearized p/Q diagram is defined for BPH, and a different diagram could be defined for other diseases. Similarly, a specific URA nomogram could be defined for BPH. The A/G nomogram, new or old, cannot be used for grading. The A/G number is unspecific and will therefore result in more individual misclassification. Statistically, the A/G number cannot perform better than pdet,Q_{max} alone but has the unusual feature of classifying normal patients with negative values.

However, for individual analysis of outflow conditions, any one-dimensional grading amounts to a dangerous reduction in the available information [7, 11, 13, 15, 24]. Therefore, the combination of our p/Q diagram with linPURR and DAMPF is an optimum compromise on the way from complex to simple. These concepts can be used also for grading obstruction from non-invasive p/Q measurements [25]. On the sophisticated level of urodynamics the combination of PURR and DURR is still the most comprehensive form of data analysis of voiding function in an individual patient.

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