



# Quantifying bladder outflow obstruction in men: A comparison of four approximation methods exploiting large data samples

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## Abstract

**Introduction:** A pressure flow study (PFS), part of the International Continence Society standard urodynamic test, is regarded gold standard for the classification and quantification of the urethral resistance (UR), expressed in the bladder outflow obstruction (BOO). For men with benign prostatic hyperplasia, the minimum urethral opening pressure ( $p_{\text{muo}}$ ), found at the end of the passive urethral resistance relation is considered the relevant parameter describing BOO. However, in clinical practice, direct measurements of  $p_{\text{muo}}$  are easily confounded by terminal dribbling. For that reason, alternative methods were developed to derive  $p_{\text{muo}}$ , and thereby assess BOO using the maximum urine flow rate ( $Q_{\text{max}}$ ) and the corresponding pressure ( $p_{\text{det}Q_{\text{max}}}$ ) instead. These methods were never directly compared against a large data set. With the increasing variety of treatments becoming available more precise grading of UR may become of relevance. The current study compares four well-known methods to approximate  $p_{\text{muo}}$  and examines the relation between  $p_{\text{muo}}$  and  $p_{\text{det}Q_{\text{max}}}$ .

**Methods:** In total, 1717 high-quality PFS of men referred with lower urinary tract symptoms between 2003 and 2020 without earlier lower urinary tract surgery were included. From these recordings,  $p_{\text{muo}}$  was calculated according to three one-parameter methods. In addition, a three-parameter method (3PM) was used, based on a fit through the lowest pressure flank of the pressure-flow plot. The estimated  $p_{\text{muo}}$ 's were compared with a precisely assessed  $p_{\text{muo}}$ . A difference of  $<10 \text{ cmH}_2\text{O}$  between an estimate and the actual  $p_{\text{muo}}$  was considered accurate. A comparison between the four approximation methods and the actual  $p_{\text{muo}}$  was visualized using a Bland–Altman plot. The differences between the actual and the estimated slope were assessed and dependency on  $p_{\text{muo}}$  was analyzed.

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**Results:** A total of 1717 studies were analyzed. In 55 (3.2%) PFS, 3PM analysis was impossible because all pressures after  $Q_{\max}$  were higher than  $p_{\det Q_{\max}}$ . The 3PM model was superior in predicting  $p_{\text{muo}}$ , with 75.9% of the approximations within a range of +10 or -10 cmH<sub>2</sub>O of the actual  $p_{\text{muo}}$ . Moreover,  $p_{\text{muo}}$  according to urethral resistance A (URA) and linearized passive urethral resistance relation (linPURR) appear equally reliable. Bladder outflow obstruction index (BOOI) was significantly less accurate when compared to all others. Bland-Altman analysis showed a tendency of BOOI to overestimate  $p_{\text{muo}}$  in men with higher grades of UR, while URA tended to underestimate  $p_{\text{muo}}$  in those cases. The slope between  $p_{\text{muo}}$  and  $p_{\det Q_{\max}} - Q_{\max}$  increased with larger  $p_{\text{muo}}$ , as opposed to the constant relation proposed within BOOI. Although significant differences were found, the clinical relevance of those differences is not known.

**Conclusion:** Of the four methods to estimate  $p_{\text{muo}}$  and quantify BOO, 3PM was found the most accurate and BOOI the least accurate. As 3PM is not generally available and performance in lower quality PFS is unknown, linPURR is (for now) the most physiologically accurate.

#### KEYWORDS

bladder outflow obstruction, pressure flow study, urethral resistance, urodynamics

## 1 | INTRODUCTION

Bladder outflow obstruction (BOO) in males is a common lower urinary tract (LUT) dysfunction that may lead to LUT symptoms (LUTS). Although BOO in male patients can have several causes, including urethral strictures and bladder neck obstruction, most commonly it is caused by prostate enlargement.<sup>1</sup> Larger prostate size is significantly associated with an increase in the likelihood of BOO in men with LUTS.<sup>2,3</sup> Urethral resistance (UR) during voiding is defined by the ratio of detrusor pressure during voiding ( $p_{\det}$ ) and urine flow rate (UFR) (Q). BOO is diagnosed when the UR is elevated to a limit that is considered clinically relevant.<sup>4</sup> UR can be graded using a pressure flow study (PFS), which is part of the International Continence Society (ICS) standard urodynamic test to evaluate the voiding function.<sup>4</sup>

To interpret the PFS, several physical models for the urethra, that is, the outflow tract, were proposed, which were used for the quantification of BOO. The currently accepted model is based on distensible and collapsible tube hydrodynamics.<sup>5,6</sup> Based on this model, it was proposed that for quantification of BOO, the ideal and most representative relation between  $p_{\det}$  and Q occurs following the point of maximum flow ( $Q_{\max}$ ) during PFS, which was called the passive urethral resistance relation

(PURR).<sup>7</sup> Deviations from this ideal PURR were called the dynamic urethral resistance relation (DURR).<sup>7</sup> In addition, the PFS was presented with a PFS-plot, initially with the uroflow rate on the *x* axis and pressure on the *y* axis, which were later flipped.<sup>8,9</sup>

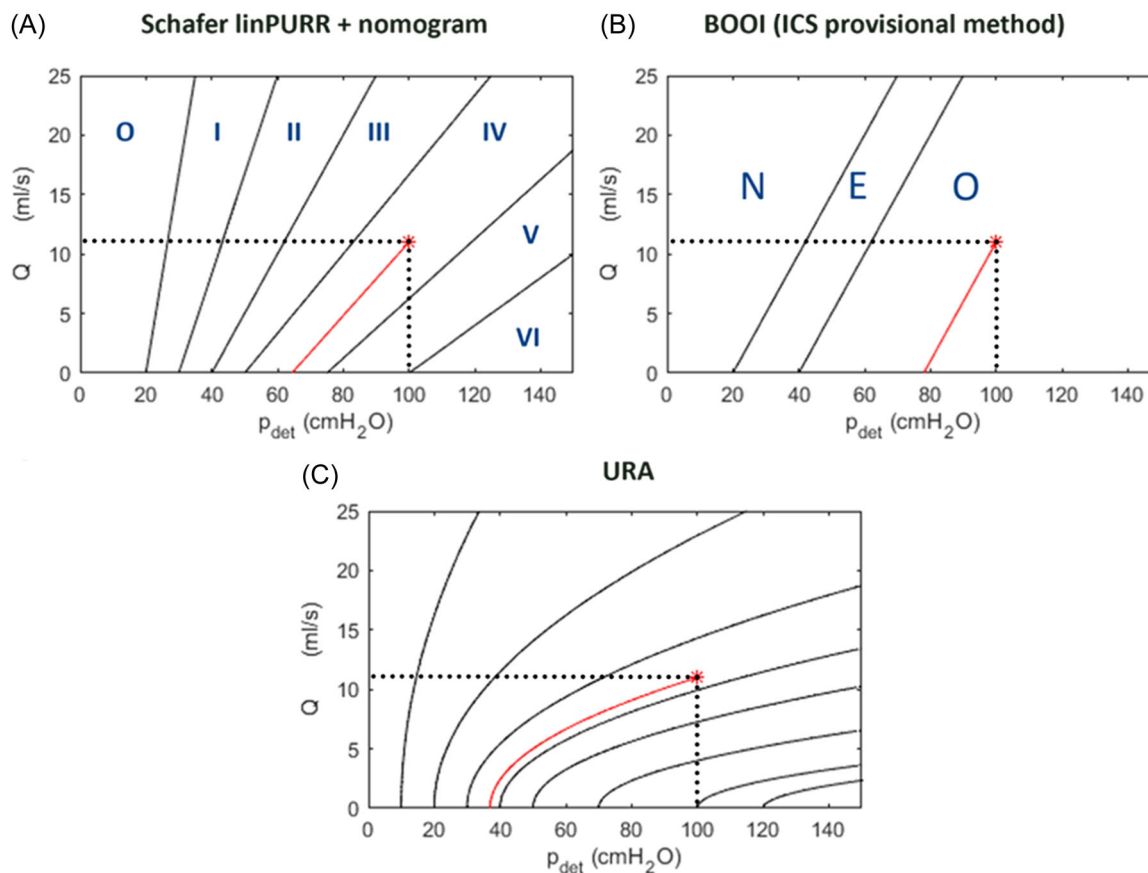
There was agreement that the shape of the PURR as visualized within the pressure-flow plot, showed a polynomial relation between Q and  $p_{\det}$ , with an offset of  $p_{\det}$  on the pressure axis. This offset was called the minimum urethral opening pressure ( $p_{\text{muo}}$ ), representing “the minimum pressure during measurable flow.” Conceptually, within the distensible and collapsible tube hydrodynamics,  $p_{\text{muo}}$  is the least dependent on detrusor voiding contraction strength, and would therefore be the most independent quantifier of BOO in men with LUTS caused by benign prostatic hyperplasia (BPH). However, in clinical practice,  $p_{\text{muo}}$  is often not unambiguously (automatically) detectable because of dribbling and varying pressure-flow delay. For that reason, several methods were developed to mathematically approximate  $p_{\text{muo}}$ , and thereby BOO, mostly based on  $Q_{\max}$  with the corresponding detrusor pressure ( $p_{\det Q_{\max}}$ ). These methods are based on the assumption that the relation between  $p_{\text{muo}}$  and  $p_{\det Q_{\max}}$  which could be expressed in the slope of the linearized PURR, can be defined by a constant or are only dependent on  $Q_{\max}$  and  $p_{\det Q_{\max}}$ . Although these methods all exist, it is not known how

much detailing of BOO-grading is clinically necessary and relevant and/or whether, for example,  $p_{\text{det}Q_{\text{max}}}$  or any other parameter would be theoretically or clinically preferable over  $p_{\text{muo}}$ .

Although formulated decades ago, a direct assessment of UR quantification methods on their accuracy in approximating  $p_{\text{muo}}$ , and thereby BOO, is not performed. One study used manual fitting of the PURR graph against the so-called lower pressure border of the PFS plot and compared this with urethral resistance A (URA),<sup>10</sup> but comparisons with other methods were never published. In addition, since the development of the PFS-UR parameters many new treatments for BOO have been introduced and quantification of UR may become more relevant to select the best type of treatment for a given patient. The current study compares four PURR evaluations (See Figure 1 and below.) on their capability of approximating  $p_{\text{muo}}$ , and examines the relations between  $p_{\text{muo}}$  and the slope of the linearized PURR proposed in these methods.

## 2 | METHODS

All 5657 urodynamic studies including PFS of men, performed between 2003 and 2020 were initially included. All included patients were referred to secondary care after the failure of initial conservative management of their symptoms with a mean IPSS of 17.5 (SD 6.6); a free flow  $Q_{\text{max}}$  12.4 (SD 7.6) and an (ultrasound) prostate size 43.0 (SD 26.7). Men with significant relevant comorbidity (e.g., neurology, diabetes mellitus) were not included. Data selection and analysis steps were performed in Matlab R2022b (The Mathworks Inc.), and statistical analysis was performed in SPSS, version 27 (IBM). The urodynamic studies were performed in accordance with the ICS Good Urodynamic Practices.<sup>4,10</sup> Intravesical and abdominal pressures were recorded with a 7F water-filled catheter using the Ellipse urodynamics machine with AUDACT software (Andromeda Medizinische Systeme GmbH). The UFR was measured using a weight-transducer measurement device. Voiding was typically allowed after strong desire of the



**FIGURE 1** Overview of the three one-parameter methods compared in this study. The value of  $p_{\text{det}Q_{\text{max}}}$  (identical in each of the graphs) is given with the asterisk. The red line represents the relation between  $p_{\text{det}Q_{\text{max}}}$  as proposed in the particular method, while the estimated  $p_{\text{muo}}$  can be found at the red line for  $Q = 0$ . A substantial difference in estimated  $p_{\text{muo}}$  is seen between those three methods, as those estimated  $p_{\text{muo}}$ 's differ substantially (A: 64; B: 79; C: 38). As three-parameter method includes multiple parameters, it is not possible to visualize this method using a simple nomogram.

patient and was performed in their preferred position, usually standing, when possible. The urine flow meter was adjusted to the length of the patient, thereby minimizing the lag induced by the distance between the flow meter and the meatus. The pressures were digitally recorded with a sampling frequency of 20 Hz, while the UFR was sampled at 8 Hz.

## 2.1 | Data selection

PFS of urodynamic studies with missing data (3.1%) and studies of patients with relevant interventions in the past (57.1%) were excluded. PFS with a voided volume <100 mL (4.0%) were excluded from the analysis.<sup>10</sup> In addition, PFS with  $Q_{\max} > 35$  mL/s or <2 mL/s (1.8%) or maximum detrusor pressure during voiding <20 cmH<sub>2</sub>O or >200 cmH<sub>2</sub>O (0.3%) were excluded from further analysis, as those values are considered not physiological, or beyond relevance in men. Studies were automatically analyzed on catheter dislocation during voiding (5.4%) using an algorithm further explained in Supporting Information: Appendix A. The otherwise randomly selected studies were visually checked on remaining large artifacts, resulting in a set of 1717 high-quality PFS, without clinical or technical artifacts, applicable for further analysis. The lag time between the UFR and the pressure signal was corrected with 0.75 s, which is more than the 0.6 proposed,<sup>11</sup> but was convenient for the setup used in the clinic. In addition, all signals were filtered with a 2-s moving average filter as advised for UFR, but with the same reasoning applied for  $p_{\det}$ .<sup>12</sup>

A complementary analysis criterion was established, only including curves following an (almost) pure PURR relation called the PFS-PURR. PFS-PURR includes all studies for which the  $p_{\det}$  or UFR at any point after  $Q_{\max}$  is lower than all pressures or UFRs before. A variation of the UFR of a maximum of 1 mL/s was accepted, while for  $p_{\det}$ , a variation of a maximum of 5 cmH<sub>2</sub>O was accepted.

Therefore, if in the passive collapse, an increase of more than 5 cmH<sub>2</sub>O than the lowest pressure or 1 mL/s than the lowest UFR between  $p_{\det Q_{\max}}$  and the evaluated point is observed, the PFS is excluded. This resulted in a subselection of PFS with a near-perfect PURR, closely following the theoretical PURR, with minimum “accessory bladder outflow tract dynamics” or DURR. The representativity of this subset was analyzed by comparing the age, voided volume,  $Q_{\max}$ ,  $p_{\det Q_{\max}}$ , and UR between all PFS and PFS-PURR.

## 2.2 | Data analysis

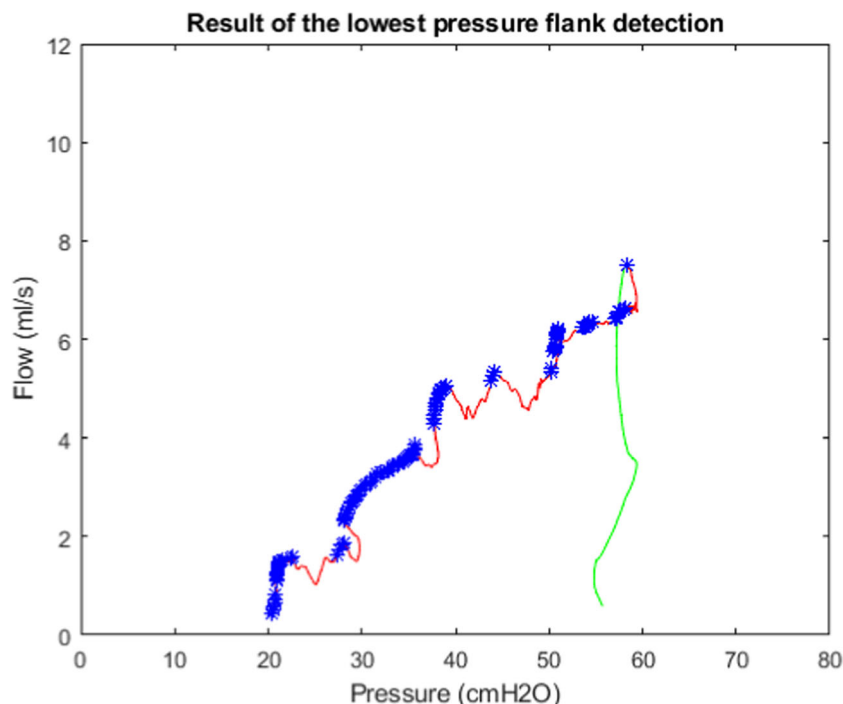
The minimal detrusor opening pressure  $p_{\text{muo}}$  was approximated using four methods, see Table 1 and Figure 1.  $p_{\text{muo}}$  estimated by the linearized passive urethral resistance relation (PmuolinPURR),<sup>13</sup>  $p_{\text{muo}}$  estimated by URA (PmuoURA),<sup>14</sup> and  $p_{\text{muo}}$  estimated with bladder outflow obstruction index (PmuoBOOI)<sup>15</sup> were used. Those three methods are all based on an extrapolation of  $p_{\det Q_{\max}}$ , and are supposed to be an approximation method for  $p_{\text{muo}}$ . In addition, the  $p_{\text{muo}}$  was estimated by the three-parameter method (3PM),<sup>13,14</sup> which has three degrees of freedom (slope, pressure, and curvature) included in the formula.

The  $p_{\text{muo}}$  according to the 3PM (Pmuo3PM) method was calculated using the following steps. First, the low-pressure flank of the  $p_{\det}$ -Q relation (urethral resistance relation [URR]) was determined.<sup>20</sup> This implements the rule that only the flow points with the lowest pressure were included, see Figure 2. Next, the PURR was fitted using the Matlab *fit* function, implementing the formula given in Table 1, with the least squares method and high weight for  $Q_{\max}$  (1000 000 vs. 1 for all other points), so the PURR was forced to pass through this point. Pmuo3PM was found at  $Q = 0$ . If all pressure points after  $p_{\det Q_{\max}}$  were higher than  $P_{\det Q_{\max}}$ , the fit could not be performed and the corresponding PFS were excluded from the analysis.

**TABLE 1** Overview of the four methods to estimate  $p_{\text{muo}}$  based on  $p_{\det Q_{\max}}$ , including the formula used for calculation and the motivation of that formula.

Method	Abbreviation	Formula	Motivation
Three-parameter method <sup>13,14</sup>	3PM	$p = p_{\text{muo}} + A * Q^k, 2/3 \leq k \leq 2$	Theoretical study
Linearized passive urethral resistance relation <sup>15</sup>	linPURR	$p_{\det Q_{\max}} = p_{\text{muo}} + A * Q_{\max}, 0 \leq A \leq 5$	Observational study
Urethral resistance A <sup>16</sup>	URA	$p_{\det Q_{\max}} = p_{\text{muo}} + (p_{\text{muo}}^{2*d}) * Q_{\max}^2, d = 3.8 * 10^{-4}$	Observational study
Bladder outflow obstruction index <sup>17-19</sup>	BOOI	$p_{\det Q_{\max}} = p_{\text{muo}} + 2 * Q_{\max}$	Provisional ICS recommendation

Abbreviation: ICS, International Continence Society.



**FIGURE 2** Low-pressure flank detection algorithm as described by *Kranse*. The green line indicates the pressure-flow relation before  $Q_{\max}$ , while the red line represents the URR. Only the blue dots serve as input for the three-parameter method approximation method. A point is included if no lower pressures can be found for a larger flow. URR, urethral resistance relation.

As the observed  $p_{\text{muo}}$  could be erroneous because of the terminal dribbling, the average  $p_{\text{det}}$  between 1 and 0.5 mL/s at the end of the voiding was used in this study to represent the actual  $p_{\text{muo}}$  ( $P_{\text{muoAct}}$ ), resulting in the mean pressure at a flow of 0.75 mL/s.  $P_{\text{muoInPURR}}$ ,  $P_{\text{muoURA}}$ ,  $P_{\text{muoBOOI}}$ , and  $P_{\text{muo3PM}}$  were corrected to the estimated pressure at a flow of 0.75 mL/s, to enable a comparison with  $P_{\text{muoAct}}$ .

To study the accuracy of an approximation method, the proportion of approximated  $p_{\text{muo}}$ 's which were within a range up to 20 cmH<sub>2</sub>O of  $P_{\text{muoAct}}$  were calculated. Moreover, the percentages of estimated  $p_{\text{muo}}$  within 10 cmH<sub>2</sub>O of  $P_{\text{muoAct}}$  were evaluated using the N-1  $\chi^2$  test for all four methods, as a difference of <10 cmH<sub>2</sub>O was considered to be not clinically significant.<sup>21</sup> In addition, Bland–Altman plots were created, including a linear regression for the differences between the real  $p_{\text{muo}}$  and the estimated  $p_{\text{muo}}$ 's by the four methods, so systemic deviations could be noticed.

Finally, as the one-parameter methods define different relations between  $p_{\text{det}Q_{\max}}$  and  $p_{\text{muo}}$  and expect them to be constant or only dependent on  $p_{\text{det}Q_{\max}} - Q_{\max}$ , the slope of the straight connection line between  $p_{\text{det}Q_{\max}}$  and  $p_{\text{muo}}$  (slope) was further analyzed on the dependency of  $p_{\text{muo}}$ . Therefore, we divided  $P_{\text{muoAct}}$  into six bins of approximately similar widths. The mean slope, according to  $P_{\text{muoAct}}$  and the four approximation methods, was given for each bin, including the 95% confidence interval. Differences between the real slope and the slope based on the estimated  $p_{\text{muo}}$ 's were investigated.

### 3 | RESULTS

A total of 1717 PFSs were included in this study. In 55 studies, all pressure points after  $p_{\text{det}Q_{\max}}$  were higher than  $p_{\text{det}Q_{\max}}$ , preventing the calculation of  $P_{\text{muo3PM}}$ . Consequently, 1662 PFS are included. The mean age of the patients was 59 years (17–93), with 89% of the patients >40 years. The  $Q_{\max}$ ,  $p_{\text{det}Q_{\max}}$ , voided volume, URA, BOOI, and Schäfer grade for all PFS and PURR-PFS are displayed in Table 2. No significant differences in mean UR, according to URA, BOOI, or Schäfer grade were observed between all PFS and PURR-PFS. Age was significantly different, but voided volume was smaller in the PURR-PFS -subgroup.

$P_{\text{muo3PM}}$  was found to be the most accurate, as the proportion of estimated  $p_{\text{muo}}$  according to  $P_{\text{muo3PM}}$  is the highest for all investigated deviations, see Figure 3. URA and linPURR performed similarly, while BOOI showed a lower fraction of estimated  $p_{\text{muo}}$  within an analyzed range.

The proportions of estimated  $p_{\text{muo}}$  which differ no more than 10 cmH<sub>2</sub>O from  $P_{\text{muoAct}}$  can be found in Table 3. All proportions for the investigated methods at this range were significantly different from each other (N-1  $\chi^2$  test  $p < 0.025$ ), except for URA and linPURR for all PFS ( $p = 0.291$ ). All the estimation methods performed significantly better for the PURR-PFS ( $p < 0.05$ ), except for the Schäfer method ( $p = 0.204$ ).

The linear regression within the Bland–Altman plots showed a significant correlation for the BOOI and URA

TABLE 2 Basic patient and urodynamic descriptives.

	All (n = 1662) Mean (min–max)	PURR-PFS (n = 376) Mean (min–max)	Mann–Whitney U test for differences p Value
Age (years)	58.8 (17–93)	60.8 (18–88)	0.012
Q <sub>max</sub> (mL/s)	10.1 (2.1–31.7)	9.6 (2.3–30.1)	0.112
P <sub>detQmax</sub> (cmH <sub>2</sub> O)	59 (11–164)	61 (12–151)	0.192
Voided volume (mL)	310 (100–1290)	260 (100–670)	<0.001
URA	31.1 (6.3–108.0)	33.0 (8.9–108.0)	0.158
BOOI	39.0 (–39.7 to 155.9)	42.2 (–23.4 to 143.4)	0.108
Schäfer grade	2.4 (0–6)	2.5 (0–6)	0.141

Note: As there is only minimal difference between all the studies and the PURR-PFS subselection, results are expected to be generally applicable.

Abbreviations: BOOI, bladder outflow obstruction index; PFS, pressure flow study; PURR, passive urethral resistance relation; URA, urethral resistance A.

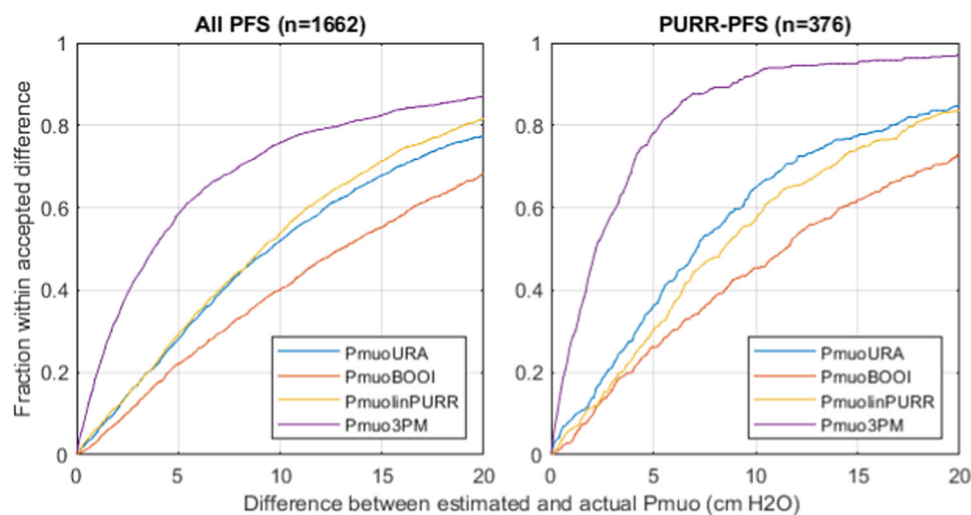


FIGURE 3 Proportion of estimated  $p_{\text{muo}}$  within an accepted difference with the actual  $p_{\text{muo}}$  as a fraction of the total number of pressure flow study (PFS), plotted against the accepted difference between the estimated and actual  $p_{\text{muo}}$ . Abbreviations: see Table 1.

TABLE 3 Values for the proportion of the estimated  $p_{\text{muo}}$  within a range of 10 cmH<sub>2</sub>O of  $p_{\text{muoAct}}$  as a fraction of the total number of studies.

Estimation method	All PFS	PURR-PFS
3PM	0.75	0.93
linPURR	0.53	0.57
URA	0.52	0.65
BOOI	0.40	0.45

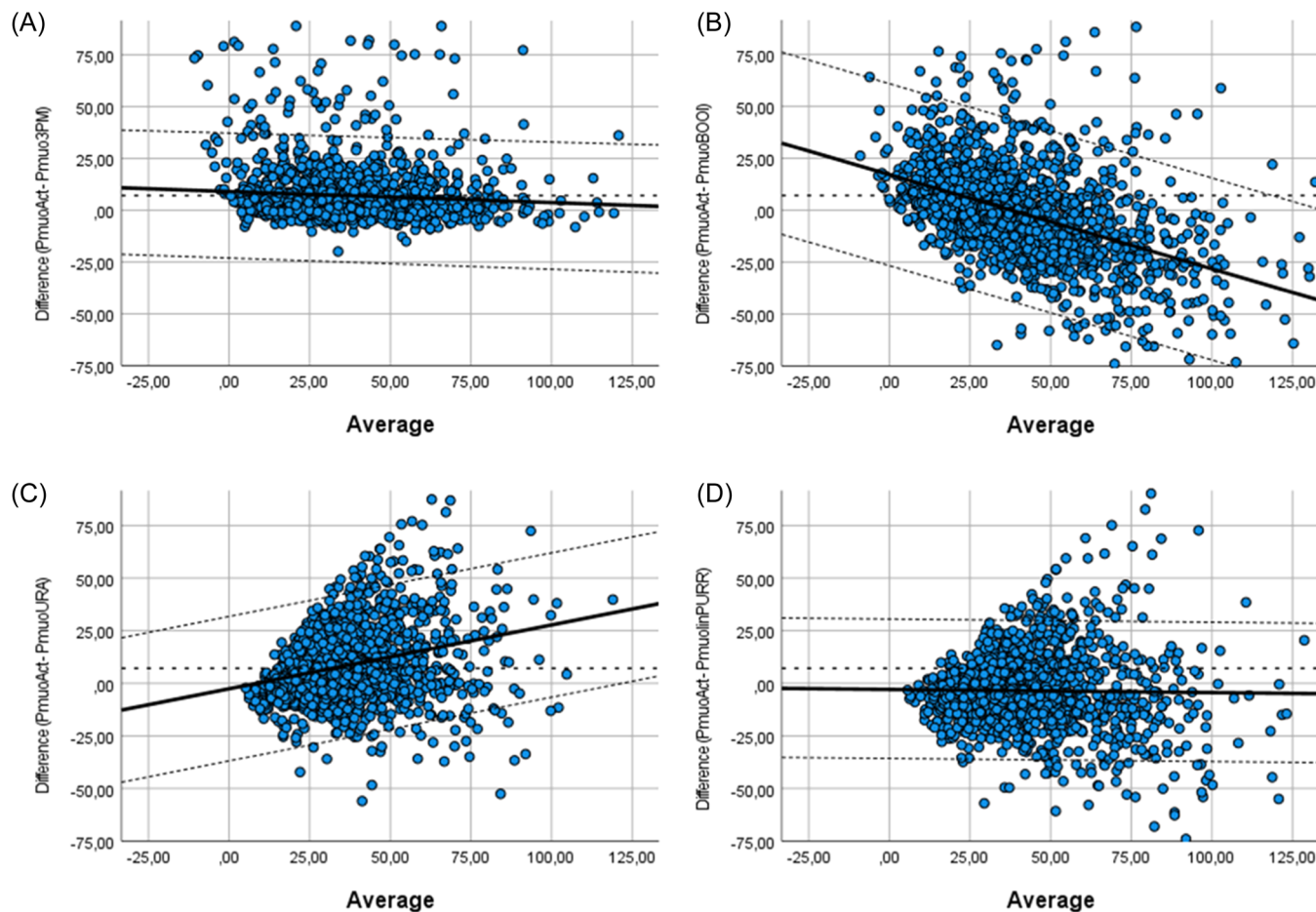
Note: Abbreviations: see Table 1.

Abbreviations: PFS, pressure flow study; PURR, passive urethral resistance relation.

method between the average of the estimated and actual  $p_{\text{muo}}$  and the average of those values, see the regression lines in Figure 4. This correlation was not significant for  $P_{\text{muoURA}}$  within the PURR-PFS, see Figure 5. All other

regressions were found nonsignificant. Overall,  $P_{\text{muo3PM}}$  showed the most narrow confidence interval range, especially within the PURR-PFS. Some outliers are seen for all methods, with some obvious outliers for  $P_{\text{muo3PM}}$ , predominantly caused by a substantial increase of pressure during voiding, visible as a large positive difference in the plot.

$P_{\text{muoAct}}$  was divided into six bins with similar pressure widths and a similar number of observations to allow an analysis of the associations between the slope and  $P_{\text{muoAct}}$ , see Table 4. Figure 6 illustrates that for every method, except BOOI, a positive relationship exists between the slope and  $p_{\text{muo}}$ , which was stronger within the PURR-PFS. The inherently fixed slope within BOOI was found significantly incorrect, as the actual slope was found larger in the higher  $p_{\text{muo}}$  pressure -bins and statistically significantly different with  $P_{\text{muoBOOI}}$  (Wilcoxon  $p < 0.05$ ) for bin 21–29 and higher. The URA



**FIGURE 4** Bland–Altman plots for the difference between PmuoAct and Pmuo3PM (A), PmuoBOOI (B), PmuoURA (C), PmuolinPURR (D) for all measurements. The average of PmuoAct and  $p_{\text{muo}}$  according to the particular method is shown on the x axis. Linear regression is shown (thick line) including the 95% confidence limits (dashed line). Abbreviations: see Table 1.

and 3PM methods did not result in a significantly different slope for bin 29–36 (Wilcoxon  $p > 0.05$ ) and higher, which holds for the PURR-PFS (Wilcoxon  $p > 0.05$ ). There is a significant difference between the mean actual slope for all PFS when compared to the PURR-PFS for bins 45–59 and  $>59$ . In addition, large standard deviations of the actual slope were found, increasing with  $p_{\text{muo}}$ , indicating a wide variation in the slope between  $p_{\text{detQmax}}$  and  $p_{\text{muo}}$ . More characteristics of the distribution of the slope can be found in Supporting Information: Tables B1 and B2.

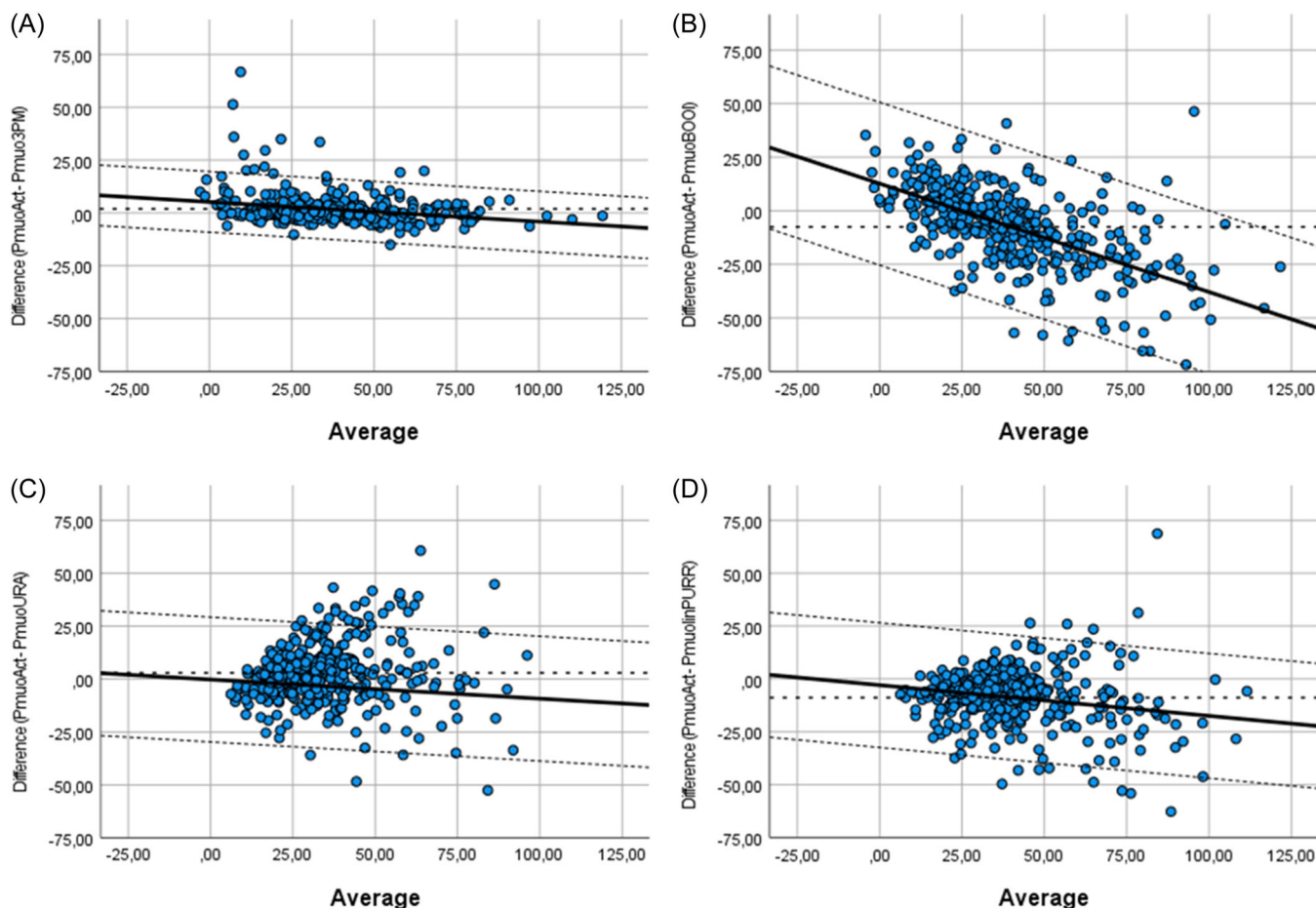
## 4 | DISCUSSION

We found that the use of a multiparameter method resulted in a significantly more accurate estimation of  $p_{\text{muo}}$  when compared to three one-parameter approximation methods in quantifying UR in men.

In addition, a correlation was found between the mean slope of the PURR and PmuoAct, especially within the

PURR-PFS subcohort. However, the large standard deviation suggests that this slope is not constant, indicating that one-parameter approximation methods are less accurate in predicting  $p_{\text{muo}}$ . The one-parameter methods imply a fixed slope for a particular  $p_{\text{detQmax}}-Q_{\text{max}}$  (linPURR and URA) or a constant slope (BOOI). Although the slopes of linPURR as well as URA are adapting to the  $p_{\text{detQmax}}$  pressure, this seems insufficient because of the large variation of slope versus PmuoAct. BOOI was stated to be an easy-to-use tool and resulted in a meaningful possibility to diagnose the presence or absence of BOO.<sup>16</sup> We found that BOOI is significantly imprecise with an overestimation for higher  $p_{\text{muo}}$  in the quantification of BOO. We also found that URA showed a significant underestimation of  $p_{\text{muo}}$  for higher values of  $p_{\text{muo}}$ . While comparing these we found linPURR to be superior within the one-parameter approximation methods.

The use of more degrees of freedom, for example, parameters, within an approximation method will likely result in a more accurate method, albeit at increased algorithmic complexity. In the past, any extension



**FIGURE 5** Bland–Altman plots for the difference between PmuoAct and Pmuo3PM (A), PmuoBOOI (B), PmuoURA (C), PmuolinPURR (D) for the passive urethral resistance relation–pressure flow study. The average of PmuoAct and  $p_{\text{muo}}$  according to the particular method is shown on the x axis. Linear regression is shown (thick line) including the 95% confidence limits (dashed line). Abbreviations: see Table 1.

**TABLE 4** Overview of the distribution of the PFS over the PmuoAct bins, shown as  $\text{cmH}_2\text{O}$  ranges.

$\text{cmH}_2\text{O}$	PmuoAct bins					
	<21	21–29	29–36	36–45	45–59	>59
All PFS ( $n = 1662$ )	247	296	281	303	270	265
PURR-PFS ( $n = 376$ )	71	77	67	66	50	45

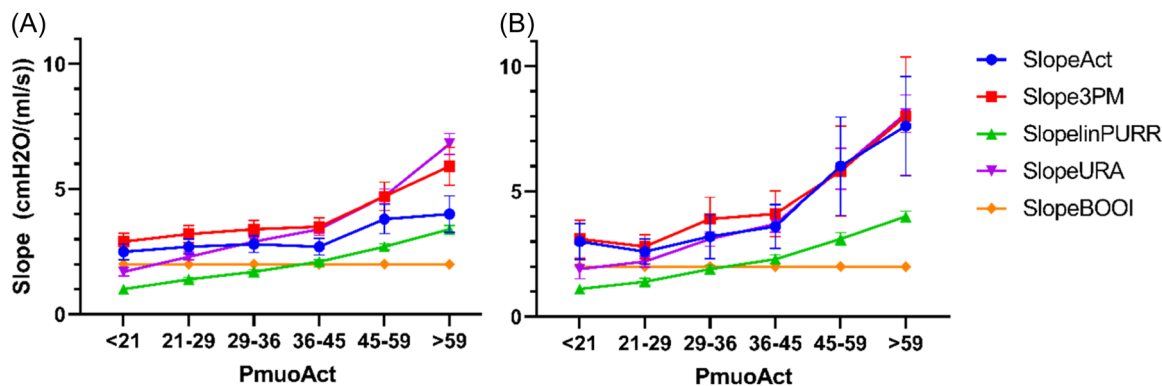
Abbreviations: PFS, pressure flow study; PURR, passive urethral resistance relation.

beyond a linear fit was found to be not reproducible and not of added value for describing the PURR.<sup>14</sup> However, we showed that a linear fit is rather inaccurate when only based on  $p_{\text{detQmax}}$ , as all (linear) one-parameter methods were found significantly less accurate in predicting  $p_{\text{muo}}$  when compared to the three-parameter method. Within the linPURR, a two-point linear fit of the PURR was originally proposed, which was based on both the real

$p_{\text{muo}}$  and  $p_{\text{detQmax}}$ . Later,  $p_{\text{muo}}$  was found not consistently determinable, and deviations of the real  $p_{\text{muo}}$  from the estimated  $p_{\text{muo}}$  by the nomogram were thought of to be not representative for men with BPH/LUTS.<sup>14</sup> In this study, however, the proportion of deviations of PmuolinPURR of more than  $10 \text{ cmH}_2\text{O}$  from PmuoAct was found almost 50% in men with LUTS. Therefore, the neglecting of this deviation by one-parameter methods could result in different quantification of UR in a significant part of men, as the real  $p_{\text{muo}}$  could significantly be higher or lower than estimated.

We found a positive correlation between  $p_{\text{muo}}$  and the slope of the PFS curve between  $p_{\text{muo}}$  and  $p_{\text{detQmax}}$  for all PFS, even stronger in the PURR-PFS. This agrees with the linPURR nomogram and URA but is not included in the currently used ICS standard.<sup>16</sup> Using ICS standard BOOI only will result in an overestimation of the UR in men with higher grades of BOO. Additional classification of men with BOO, for example, severely obstructed,





**FIGURE 6** Slope with estimated error bars for the actual mean slope and the mean slope as estimated by the four methods, grouped by PmuoAct bins, for all pressure flow study (PFS) (A) and the passive urethral resistance relation (PURR)-PFS (B). Abbreviations: see Table 1.

should take this into account. Additionally, the large standard deviations for the higher  $p_{\text{muo}}$  bins suggest a variable association between  $p_{\text{detQmax}}$  and  $p_{\text{muo}}$ , indicating that a one-parameter method is probably not sufficient for the precise approximation of the UR. This was earlier observed, as a distinction between constrictive and compressive PURR was made<sup>7</sup> and the value of the slope was included in the CHES classification.<sup>22</sup> This study suggests that two-parameter linPURR analysis (including both  $p_{\text{det}}$  and the slope) as included in the CHES classification could extend the currently used classification of UR. However, this is not included in the currently used ICS standard.

The found inaccuracies of the one-parameter estimation methods could be expected as those methods are, as originally stated, approximations of  $p_{\text{muo}}$ ,<sup>15,16</sup> or only to be used at the basis for classification of BOO.<sup>19</sup> However, as those are continuous variables, they suggest that a larger value implies more BOO, with comparable outcome values, so a comparison between those methods can be made on their mathematical accuracy. As there is currently no clinical implication in the guidelines on the “amount” of BOO, and the estimation methods yield similar results in the classification of BOO,<sup>23</sup> the clinical relevance of the found differences in estimation accuracy is not known.

This study has a few limitations. First, the actual  $p_{\text{muo}}$  is taken as a gold standard for evaluating the other methods. It is known that this actual  $p_{\text{muo}}$  value is often not unambiguously automatically detectable. Therefore, we only included PFS of high quality by using strict quality selection criteria, including the complementary analysis of the PURR-PFS, and used a derivative for  $p_{\text{muo}}$  within the analysis, which removed the influence of terminal dribbling. In addition, although the three-parameter PURR was found superior, it is not known whether this method (but also the other methods), also

performs well on lower-quality measurements. Theoretical performance in those lower-quality studies is not easily studied, as the actual  $p_{\text{muo}}$  is expected to be inaccurate.

In clinical practice, only the classification of BOO as obstructed, unobstructed, or equivocal is currently used in the treatment decision. It is known that there is a correlation between the effect of (surgical) treatment and the quantification of BOO.<sup>14</sup> Hence, the quantification of BOO could be used for the quantification of the treatment effect. However, as a wider variety of treatment options became available, new studies on this correlation or of disease stage: subtyping of the UR-shape; more or fewer dynamics; more or less slope; constrictive or compressive may bring additional value. As the 3PM method is expected to represent the most precise prediction of  $p_{\text{muo}}$ , and thereby the UR for men with LUTS, subtyping and more precise grading of UR in men with BPH is more accurate with 3PM than with BOOI only. Therefore, the 3PM method can be used to evaluate proof of principle of the treatment options and to individualize management.

## 5 | CONCLUSION

In conclusion, to approximate  $p_{\text{muo}}$  for the quantification of bladder outflow obstruction in men, we found that the three-parameter PURR model performed significantly better in approximating the actual  $p_{\text{muo}}$  than the one-parameter methods in all PFS in our database with high technical quality. Subanalysis of the PFS most accurately following the expected theoretical URR, showed similar results. The linPURR method performs better than BOOI and URA, and has little systemic deviations over the whole range of BOO. Two or more parameter linPURR analysis will be relevant to improve diagnostic accuracy.

## AUTHOR CONTRIBUTIONS

Wouter van Dort and Peter F. W. M. Rosier contributed to the design and implementation of the research, to the analysis of the results. Peter F. W. M. Rosier, Bernard J. Geurts, and Thomas R. F. van Steenberg supervised the work. All authors were involved in the writing of the manuscript and provided input for the analysis.

## CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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