Female Urology, Urodynamics, Incontinence, and Pelvic Floor Reconstructive Surgery

# Clinical Epidemiology: Detrusor Voiding Contraction Maximum Power, Related to Ageing

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**OBJECTIVE** To report clinical epidemiology of detrusor (bladder) muscle contraction maximum related to ageing in patients referred with signs and symptoms of lower urinary tract dysfunction.

**STUDY DESIGN AND SETTING** One thousand three hundred and eight urodynamic pressure-flow measurements were analyzed in retrospective. Standard measures of detrusor muscle voiding contraction strength were compared for gender and ranked by age (range 20-90 years).

**RESULTS** A decline in maximum detrusor contraction strength was observed when the results were ranked according to age. Detrusor muscle maximum voiding contraction was on average 30% less powerful in older women and 12% less powerful in the aged men, when compared to the younger. This is transversal data—interpreted in a longitudinal manner—and from persons referred to specialist care with (the full spectrum of) signs and symptoms of lower urinary tract dysfunction. Therefore these results are relevant for clinical epidemiology but not definitely generalizable to (symptom-free) population level.

**CONCLUSIONS** Clinical epidemiologic evaluation of patients referred with lower urinary tract symptoms, found lower detrusor maximum contraction strength in higher-age cohorts, both for women as for men. The maximum detrusor strength difference in association with age was larger in women than in men. UROLOGY 124: 72−77, 2019. © 2018 Elsevier Inc.

Ageing is associated with striated muscle wasting and general decline in muscle contractility function.[1] Ageing may also affect the—not striated−detrusor muscle,[2] and an expert review suggests that one of the causes of the increasing prevalence of lower urinary tract (LUT) dysfunction in the elderly may be detrusor underactivity (DU).[3] The current International Continence Society (ICS) definition of DU limits to a qualitative description [cited:]: "... a contraction of reduced strength and/or duration, resulting in prolonged bladder emptying and or failure to achieve complete bladder emptying in a normal time span."[4] The clinical underactive bladder syndrome (UABs) was recently postulated with a presumed set of symptoms and clinical spectrum.[5] Objective quantification of detrusor voiding contraction and or contractility is done with pressure flow analysis. The sensitivity or specificity of the UAB-syndrome toward objective urodynamically quantified contraction is however, at present, not evident.[6,7] The fact that decay of muscle contractility exists, both in striated, or in smooth muscle as well as in cardiac muscle is undisputed, even when expressed or experienced symptoms that may result from these deterioration(s) are usually not specific, nor pathognomonic or typical.

Detrusor muscle relaxation, contraction and contractility mechanics and molecular pathways share similarity with other smooth muscles in the human body but are also specific to a large extent. An extensive review has summarized the various molecular mechanisms involved in detrusor relaxation and contraction function and identified gaps in knowledge and aims for further laboratory research.[8] Whereas many of the molecular physiology and pathophysiology elements of detrusor muscle contractility have been unraveled, little is known however about clinical epidemiology of detrusor voiding contraction quality, its normal values and the cut off values for DU.[3,5]

Detrusor muscle strength will inevitably vary between persons of every age and strengths will be distributed in a Gaussian manner from persons with a very weak contraction to persons with a very strong detrusor voiding contraction if the sample is large enough. At present, the knowledge regarding clinical relevant cut-off values (between weak and strong) is very scarce, especially in women, but clinical epidemiology of age associated differences may help to increase understanding.

Urodynamic pressure-flow (P-Q) analysis objectively measures detrusor pressure and flowrate throughout the course of micturition and methods to—clinically—assess

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detrusor contraction strength on the basis of these measurements are briefly introduced here below.

Three quantifiers of detrusor voiding contraction strength, or power, have been available at the time of the International Continence Society (ICS)—definition of DU. The (ICS-provisional) bladder contractility index (BCI) is based on detrusor pressure at maximum flow ($p_{det}Q_{max}$) and maximum flowrate ($Q_{max}$). The linearized passive urethral resistance relation (linPURR) nomogram has been developed using the linPURR concept for grading outflow obstruction,[9] based on $p_{det}Q_{max}$ and $Q_{max}$. The linPURR nomogram is generally referred to as the Schaefer Nomogram. It has in addition, independent from linPURR, classes of detrusor contraction strength (also linearized and) based on the bladder working function. These contraction classes can be subdivided on a continuous scale with the projected isovolumetric detrusor pressure (PIP) or detrusor coefficient,[9] similar to the BCI. The bladder Watts factor (W; W/m$^2$) is a third manner to quantify detrusor contraction during voiding. W can be calculated throughout the entire course of micturition although most studies report (W-) contraction maximum. Maximum of W; $W_{max}$, associates with effective emptying in men when quantified in relation to the grade of bladder outflow obstruction.[10] Usually $W_{max}$ occurs just before $Q_{max}$ and $W_{max}$ is therefore not exactly comparable to for example, BCI, based on $Q_{max}$. $W_{max}$ as well as BCI result in continuous scale parameters, suitable for clinical epidemiology. Statistically, LinPURR and BCI correlate with $W_{max}$[11] but the latter is deemed more precise, for research purposes.[12] LinPURR or BCI are not specifically validated for women although hydrodynamic (urodynamic) principles are similar for male and female micturition.[13]

Furthermore, the detrusor muscle activity during voiding is a combination of contraction force and velocity. The methods here used are an indirect reflection of (estimation of) for example, maximum muscle force. A stop-flow test would better reflect maximum contraction however is impractical (inhibits normal contraction function because of mental inhibition as a consequence) in clinical practice.[14] Because the measures used in this study allow ranking of detrusor (estimated maximum) power on a continuum DU can be diagnosed if the value is below a certain cut-off, however this study intends not to conclude about a (clinical) prevalence of DU.

DU can, in general, apart from advancing age, have a variety of causes. These clinical causes are plausible or understandable from clinical history; for example, neurogenic DU or contractility, in patients with caudal or sacral plexus lesion or other relevant neurologic abnormalities. Furthermore, also myogenic DU may exist after acute or chronic overdistention/retention and or in association with polyneuropathy and or microangiopathy with or without for example, diabetes mellitus.[15] DU could however also be a consequence of function decline associated with ageing, without a specific comorbidity as outlined here above. Although sarcopenia; wasting of striated muscle, is more specifically and more frequently studied than smooth muscle ageing[16] the pathophysiology may be similar on the cellular level as has been observable in gastrointestinal and vascular smooth muscle.[17,18] Sarcopenia is objectively quantifiable with however, a variety in clinical expressions.[19] That subjective signs and symptoms differ from stage and grade of disease or dysfunction is not exceptional in healthcare and is also very likely to exist in a similar way, in DU and the UAB-syndrome. The clinical association of all types of LUTD with older age is well described and recently summarized[20] but large scale clinical epidemiology of DU as a specific observation in relation with age is never well reported. One study reports prevalence of DU in men and women for a range of ages, however with—especially for the women—not standard parameters and only reporting dichotomized results.[21] Another study presenting 3 age cohorts to evaluate storage abnormalities (20-39; 40-59; and a third, 30 years covering, cohort of >60) with around 30 women in each cohort, reported that projected isovolumic pressure (-PIP; an extrapolated maximum of detrusor isovolumic contraction) has been lower in the last cohort.[22] The BCI was not reported in this study but is, when calculated from the data presented, not different.[22]

We present clinical epidemiology of age and gender associated—continuous scale—detrusor contraction maximum power ($W_{max}$) on the basis of a large series of precise P-Q contraction analysis results from clinical routine ICS—standard urodynamic P-Q studies.

## STUDY DESIGN, MATERIALS AND METHODS

One thousand three hundred and eight consecutive P-Q studies of micturitions with a volume >100 mL have been entered in the analysis. All, adult, patients included were urodynamically investigated because of bothersome LUT symptoms and signs. Only first urodynamic studies were included. Patients with neurologic disorder, diabetes mellitus, and patients after earlier relevant surgery or with congenital abnormalities affecting the LUT and patients with urinary tract infection (at the time of the study) were excluded.

P-Q studies were performed, after ICS standard, seated, fluid filled external pressure sensor, saline 30-40 mL/min. fill rate cystometry, in privacy and in preferred position; seated for women (N = 374) and for men (N = 795) 75% in standing position, with a 7F double lumen transurethral catheter for all.[23,24] Because the situation during urodynamic testing may provoke unrepresentative micturition when mental stress (≈sympathetic dominance) inhibits detrusor contraction and or outlet relaxation, only micturitions considered representative by the patient were included, but large volume postvoid residual urine has not been an exclusion.

After manual (peak) artefact correction of $Q_{max}$; $p_{det}Q_{max}$; bladder outflow obstruction index (BOOI) and BCI, and also bladder outflow resistance (URA) have been calculated. Outlier $W_{max}$ values, occurred most frequent just before the end of complete micturition. They were however not removed for this analysis. Age association was statistically analyzed with ANOVA as

**Table 1.** Pressure flow study parameters *t* tests (corrected for variance): male vs female and correlation with age; male and female. Significant 2-tailed correlations: ** at 0.001 level; * at 0.005 level

| Pressure Flow Parameters: | | $Q_{max}$ | $P_{detQmax}$ | URA | BOOI | BCI | $W_{max}$ |
|---|---|---|---|---|---|---|---|
| Female | N | 375 | 375 | 360 | 375 | 375 | 375 |
| | Mean | 19.2 | 27.6 | 12.7 | −10.9 | 123.7 | 11.9 |
| | S.d. | 10.3 | 27.4 | 8.3 | 36.2 | 55.4 | 8.6 |
| Male | N | 800 | 798 | 795 | 797 | 797 | 793 |
| | Mean | 11.2 | 59.5 | 29.8 | 37.2 | 114.9 | 13.6 |
| | s.d. | 6.0 | 27.6 | 16.2 | 33.3 | 33.6 | 8.6 |
| *t* test | **Female/Male** | <0.001 | <0.001 | <0.001 | <0.001 | 0.001 | 0.003 |
| ALL | Mean | 13.7 | 49.3 | 24.5 | 21.8 | 117.7 | 13.0 |
| | S.d. | 8.5 | 31.3 | 16.3 | 40.9 | 41.9 | 8.6 |

| Pressure flow vs age correlation | | $Q_{max}$ | $p_{detQmax}$ | URA | BOOI | BCI | $W_{max}$ |
|---|---|---|---|---|---|---|---|
| Age female | Pearson | −0.231** | −0.230** | −0.023 | −0.005 | −0.343** | −0.305** |
| | Sig. P | <0.001 | <0.001 | 0.661 | 0.926 | <0.001 | <0.001 |
| Age male | Pearson | −0.286** | 0.081* | 0.205** | 0.162** | −0.132** | −0.191** |
| | Sig. P | <0.001 | 0.023 | <0.001 | <0.001 | <0.001 | <0.001 |
| Age all | Pearson | −0.327** | 0.069* | 0.234** | 0.216** | −0.183** | −0.243** |
| | Sig. P | <0.001 | 0.012 | <0.001 | <0.001 | <0.001 | <0.001 |

well as in a correlation matrix and visualized, with addition of a regression coefficient in scatter-graphs per gender.

## RESULTS

Table 1 shows the gender specific mean values of P-Q study parameters, and the result of *t* testing, corrected for variance, as well as the (Pearson) correlation of these parameters with age. Gender differences are statistically significant although the largest absolute mean differences are seen in outflow-related parameters $Q_{max}$, URA and BOOI. Men have higher $P_{det}Q_{max}$ and lower $Q_{max}$ when compared to women. URA and BOOI are not correlated with age in female patients however they are in men. On the other hand, $P_{det}Q_{max}$ is lower in females than in males and correlates with age in female patients.

The 2 scatter graphs in Figure 1 show that older men as well as older women had lower $W_{max}$ (Y-axis). In men however the decline, associated with older age (X-axis), was less than in women, as is demonstrated with the linear (regression) $R^2$. For men $R^2$ for the depicted age range (18-96 years) is 0.018 and $R^2$ for women is 0.118. We will translate this into a clinical perspective here below. Table 2 provides the mean values of $W_{max}$ per age decade with ANOVA for age-group, and the *t* tested differences per age group. Figure 2 is a visualization of the data of Table 2.

## DISCUSSION

These data show that $W_{max}$ is 10.1 W/m$^2$ lower for women in the oldest age group, compared with the youngest. For men the difference between the youngest and the oldest is 7.5 W/m$^2$. On average the difference is 0.08 W/m$^2$ per year in men and 0.17 W/m$^2$ per year in women. The differences in $W_{max}$ between men and women are however most obvious in the age cohort from 50 onwards (Fig. 2). A $W_{max}$ of 10.6 W/m$^2$ is reported normal[12,13] and a negative difference of 1 W/m$^2$ may crudely translate to a ≈5% loss of (maximum) contraction power; Longitudinal interpretation of this cross-sectional collected data

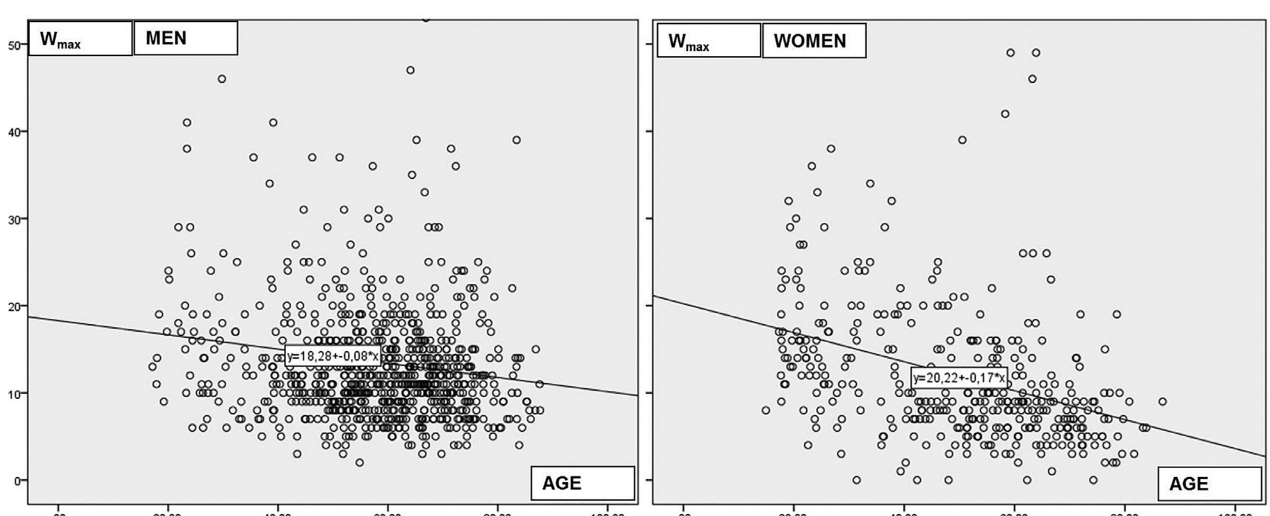


**Figure 1.** Scatter graph: $W_{max}$ vs age MEN; Pearson $R^2 = -0.191$; WOMEN; Pearson $R^2 = -0.305$.

**Table 2.** Mean $W_{max}$ per patient age decade

| Decade Age | $W_{max}$ Female | | | $W_{max}$ Male | | | F<>M |
|---|---|---|---|---|---|---|---|
| | N | Mean | Sd | N | Mean | Sd | *t* test |
| 20-30 | 72 | 16.7 | 8.9 | 45 | 18.7 | 13.1 | 0.386 |
| 30-40 | 37 | 15.5 | 8.3 | 44 | 14.2 | 8.2 | 0.470 |
| 40-50 | 55 | 10.7 | 6.0 | 109 | 13.9 | 8.6 | 0.016 |
| 50-60 | 82 | 11.4 | 9.7 | 210 | 13.4 | 8.2 | 0.082 |
| 60-70 | 73 | 10.1 | 8.3 | 227 | 13.4 | 9.3 | 0.008 |
| 70-80 | 45 | 7.2 | 4.2 | 125 | 12.4 | 5.9 | <0.001 |
| 80-90 | 5 | 6.6 | 2.5 | 28 | 11.2 | 6.7 | Too low N |
| *ANOVA* | | *<0.001* | | | *0.002* | | |
| Mean All | 369 | 11.9 | 8.6 | 788 | 13.6 | 8.7 | 0.003 |

may suggest that men lose around 12% of their maximum detrusor contraction power in the 30 years after their fiftieth birthday and that women lose around 30% in this period.

The persons reported here were all symptomatic, referred, and able to void almost as usual after cystometry. Therefore this sample is a clinical epidemiology sample that should not be confused with a population based or longitudinally followed cohort. This clinical cohort may however, be considered representative for the persons referred to specialist care with LUT symptoms. Of further note; patients unable to void because of urinary retention, or unable to void because of the situation (during urodynamic testing) are potentially within the clinical spectrum of DU but—understandably—not included in this cohort.

The male bladder outlet, with higher outflow resistance, is associated with a somewhat stronger contraction than women, already in the decades from 20 to 50 years of age (Table 2). The gender differences become however most obvious in the group over 50 years of age (see Tables and Fig. 2). Presumably, the clinical association with (continuing growth and) enlargement of the prostate and therefore increasing prevalence of bladder outflow obstruction with age becomes relevant here.[25] $W_{max}$ is similar in men and women in the first 4 decades of adulthood and starts to be significantly less from the 5th decade on, specifically in women. Figure 2 suggests, again when the data is interpreted in a longitudinal manner, that the diminishing of maximum contraction power is prevented or delayed by the challenge that the prostate poses to the detrusor muscle. The slowly growing prostate may cause a training effect with every voiding and may induce compensatory muscle strength and or hypertrophy, as demonstrable in clinical P-Q studies[10] and well demonstrated in laboratory animal studies[26-28] that were also used to confirm the clinical observations.[28] The association of URA with age and gender in this cohort is also shown in Figure 2 demonstrating that average outflow resistance is not significantly different throughout the course of life in women and that it is a relevant phenomenon in men.

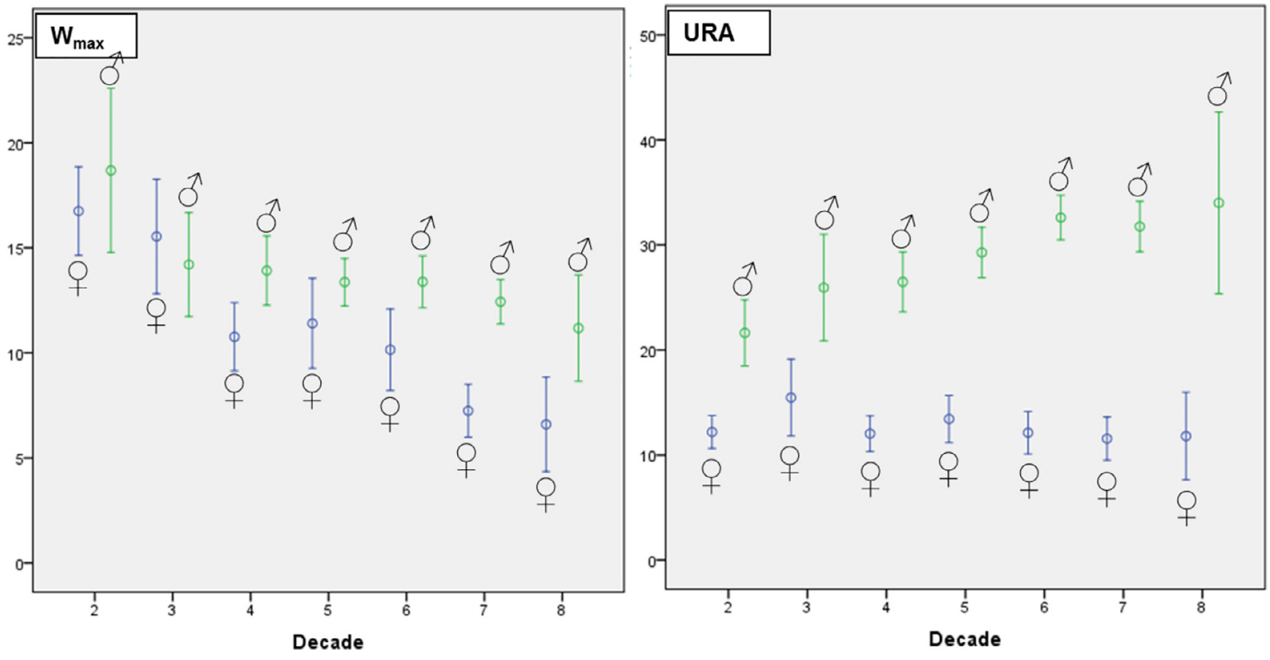


**Figure 2.** $W_{max}$ and URA per age-decade and gender: mean and standard error. (Color version available online.)

The hypothesis that the presumably intrinsic (advancing age) decline of detrusor muscle contraction function, as is observed in this cohort of women, is delayed in men by the training effect that the prostate causes, can be postulated on the basis of these clinical epidemiologic observations. Oestrogens may affect the detrusor muscle and menopause may associate with DU[29] and testosterone may affect smooth muscle function[30] but we consider the specific preclinical evidence for this too immature and or conflicting, to conclude that gender differences in hormone level are the direct and principal cause of our observations.

Although quantification of detrusor contraction with the here used parameters is in general expert accepted, no parameter is a perfect reflection of the genuine smooth muscle contractility or contraction.[14] Whereas the voiding of male persons with a relatively large prostate, acting as a fixed nozzle is usually fairly stable, with regard to the balance of contraction vs outflow, the female bladder and outlet are much less in balance throughout the course of voiding. This includes the fact that—as observable in this manuscript also—the outflow resistance is much lower in women, plus the outflow tract has a much shorter intra-abdominal part (not as the prostate, in men). The influence of intra-abdominal content weight and or abdominal muscle straining on flowrate is therefore potentially more significant in women than in men.[15] The results here presented are only from micturitions almost as usual, overall this has excluded significant straining. Also the $P_{det\ at\ Qmax}$ has been corrected for artefact peaks before this analysis. The graphs show however that there have been outliers in the database, especially in $W_{max}$; but a specific age-related confounder, because of straining or other peak artefacts is unlikely. Outlier $W_{max}$ values were observed without (see Fig. 1) an association with age and or gender. $W_{max}$ is normally observed, before $P_{det\ at\ Qmax}$. $W_{max}$ can be affected by small intravesical volume at the end of voiding however this was, in our practice, systematically corrected. Although $W_{max}$ is claimed to be more precise,[13] the results are similar to BCI (see correlations in Table 1). At present it is undetermined whether one of the parameters to quantify detrusor voiding contraction is more robust than the others, especially since to scarce information on responsiveness and or test retest variation of these parameters is available. The number of observations (except for the cohort >80 years) gives our analysis sufficient statistical power for epidemiologic analysis, and prevents too much effect of outliers.

These cross-sectional observations regarding detrusor contraction maximum power, especially in women over the age of 50 years may be another confirmation of smooth muscle function decline. Ideally however these observations should be challenged in longitudinal follow-up cohort studies, independent of the presence of patient-perceived signs or symptoms. In reality and ethically such studies, requiring invasive testing, will be difficult to initiate.

## CONCLUSION

The association of detrusor maximum contraction power during a subjectively representative micturition of referred (clinical) patients with lower urinary tract symptoms was analyzed in relation with age and gender in a cross-sectional study. We found lowered detrusor maximum contraction power in higher-age cohorts, both for women as for men. In elderly women the maximum detrusor power showed, in association with age advancing, more declining than in males over similar age range.

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