Central European Journal of Urology

ORIGINAL PAPER

FUNCTIONAL UROLOGY

Detrusor underactivity in symptomatic anterior pelvic organ prolapse

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Citation: Rubilotta E, Gubbiotti M, Herms A, Goldman H, Antonelli A, Balzarro M. Detrusor underactivity in symptomatic anterior pelvic organ prolapse. Cent European J Urol. 2024; 77: 77-81.

Article history
Submitted: Oct. 22, 2023
Accepted: Dec. 28, 2023
Published online: Jan. 31, 2024

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Introduction The aim of this study was to assess the detrusor underactivity (DUA) prevalence of females with symptomatic anterior pelvic organ prolapse (POP) and to evaluate the relationship between DUA and POP stage.

Material and methods This was a prospective study recruiting women with symptomatic anterior POP. Patients with symptomatic stage 2–4 POP quantification system (POP-Q) who underwent urodynamics (UD) between January 2018 and April 2021 were included.

Results Data on 330 women (mean age 63.7 ±18.4 years old) with anterior vaginal wall defect were enrolled. Concomitant apical defect (uterine/vaginal vault) requiring surgical correction was diagnosed in 38 women (11.5%). DUA was found in 166 females (50.3%). In DUA women, POP-Q stage 2 was found in 45.2%, stage 3 in 50.9% and stage 4 in 76.5%. Only stage POP-Q stage 4 showed a statistically significant difference between DUA and non-DUA females (p 0.006).

Conclusions In women with symptomatic POP, regardless of the POP-Q stage, the chance of DUA occurrence was high. DUA was diagnosed in approximately half of the women undergoing UD for symptomatic POP, and it was three-fold higher in cases of POP-Q stage 4. Due to the high incidence of DUA in POP-Q 4 stage, it may be advantageous to identify and treat prolapse before they progress to stage 4.

Key Words: pelvic organ prolapse ‹› anterior vaginal wall defect ‹› urodynamics ‹› detrusor underactivity

INTRODUCTION

Diagnosis of female detrusor underactivity (DUA) is challenging due to the lack of specific criteria [1]. The ICS definition of DUA – a contraction of reduced strength and/or duration, resulting in prolonged bladder emptying and/or failure to achieve complete bladder emptying within a normal time span – does not report any urodynamic (UD) thresholds, and has no numerical cut-offs [2]. How strong a 'normal' detrusor contraction should be and how long it should last are not stated. The prevalence of female DUA ranges from 15 to 53.9%, but these numbers are impacted by the use of non-homogeneous criteria [3]. Little high-quality information is available on DUA rates in women with symptomatic pelvic organ prolapse (POP) and in these patients DUA ranges from 13.3% to 40.9% but, again, this great variability is probably due to the different criteria utilized [4, 5, 6]. Therefore, the actual clinical relevance of female DUA in the general population, and even more so in women with POP, has yet to be defined with certainty. Also, no findings are available on the relation between detrusor impairment and POP stages. Therefore, epidemiological data on the relationship of DUA to POP stages is needed, as investigation into

the relationship between POP with associated DUA and its interaction with lower urinary tract symptoms. This study explored these under researched topics to provide missing epidemiological data.
The aim of the study was to assess DUA prevalence in females with symptomatic POP in a large cohort of candidates for POP surgery, using the four most recognized UD criteria. A second aim was to evaluate the relationship between DUA and POP stage.

MATERIAL AND METHODS

This was a prospective study recruiting women with symptomatic anterior POP, assessed by POP quantification system (POP-Q), undergoing UD between January 2018 and April 2021 in one Tertiary referral Centre [7]. Inclusion criteria were: any symptomatic anterior POP stage ≥2 according to POP-Q system, with or without associated apical/uterus descensus. For symptomatic POP we included all the symptoms related to pop as pelvic discomfort or pain, bulge of tissue or organs, protruding to or past the vaginal opening, sexual difficulties, dyspareunia related to POP, fulness of pressure in vagina, vaginal spotting. Medical and urogynecological history, and UD data were recorded. POP evaluation and staging were performed by 3 specialized urologists (MB, ER, AD).
Due to the lack of standardized UD parameters for female DUA, we classified patients as having DUA if they met at least one of the main criteria reported in the literature: 1) Pdet@Qmax ≤10 cmH_2O and Qmax ≤12 mL/s (Jeong et al, 2012); 2) Pdet@Qmax <30 cm H2O and Qmax <10 mL/s (Abarbanel and Marcus, 2007); 3) Pdet@Qmax <20 cm H_2O and Qmax <15 mL/s and BVE <90% (BVE criteria); 4) Pdet@Qmax + Qmax (Griffiths, 2004) [8–13]. For the above mentioned reasons patients could be included in multiple DUA groups according to the criteria used. The control group (CG) consisted of women with symptomatic POP and non-DUA UD criteria. Primary lower urinary tract symptoms (LUTS) such slow stream, straining, hesitancy, urgency and frequency were recorded. The association between DUA and POP stages was assessed. The concomitance of lower urinary tract dysfunctions (LUTD) such as urinary retention was also evaluated.
Ethical standards were performed according to the 1964 Declaration of Helsinki and its later amendments. Informed consent was obtained before enrollment in the study. Local Ethics Committee for Clinical Trials (University of Verona) determined that the approval for this investigation was unnecessary since it only involved standard clinical practice. This research was registered in the clinical audit in our hospital.

Statistical analysis

Statistical analysis was performed with IBM-SPSS ver. 17 for Windows (IBM Corp, Armonk, NY). Continuous variables were reported as mean and standard deviation. Categorical variables were expressed as numbers and percentages. Student t-test and the Mann-Whitney U test were performed to compare continuous variables, as appropriate. Categorical variables were tested with the χ^2 test. Statistical significance was set at $p \leq 0.05$.

RESULTS

Data was collected on 330 women, with mean age (years) 63.7 ±18.4, all of whom had anterior vaginal wall defect. A concomitant apical defect (uterine/vaginal vault) requiring surgical correction was diagnosed in 38 women (11.5%). According to any of the 4 UD criteria for DUA, this condition was found in 166 females (50.3%), while normal detrusor contractility in the voiding phase was demonstrated in the remaining 164 women (49.7%). Table 1 reports the stratification of women according to POP-Q stages in the overall group, in the DUA group and in the non-DUA group. In all groups, POP-Q stage 2 was the most represented, while POP-Q stage 4 was the least. Comparison of DUA and non-DUA females

Table 1. *Detrusor underactivity and normal detrusor contractility (No- DUA) incidence in women with pelvic organ prolapse staged by Pelvic Organ Prolapse Quantification system*

	Overall population	DUA women	No- DUA women	p
# of patients	330	50.3% (166/330)	49.7% (164/330)	
POP-Q stage				
2	56.4% (186/330)	45.2% (84/186)	54.8% (102/186)	0.3
3	33.3% (110/330)	50.9% (56/110)	49.1 (54/110)	1
4	10.3% (34/330)	76.5% (26/34)	23.5% (8/34)	0.006

DUA – detrusor underactivity; No- DUA – normal detrusor contractility; POP-Q – Pelvic Organ Prolapse Quantification

Table 2. *Rates of lower urinary tract symptoms in women with pelvic organ prolapse: comparison between patients with detrusor underactivity and control group (no detrusor impairment)*

Symptoms	DUA (n = 166)	Control group (n = 164)	p
Slow stream: n (%)	130 (78.3%)	78/164 (57.3%)	0.1
Straining: n (%)	81 (48.8%)	65 (39.6%)	0.008
Hesitancy: n (%)	69 (41.6%)	56 (34.1%)	0.004
Urgency: n (%)	129 (77.7%)	107 (65.2%)	0.05
Frequency: n (%)	117 (70.5%)	75 (45.7%)	0.08

DUA – detrusor underactivity; n – number of patients

Table 3. *Main urodynamic comparison between patients with detrusor underactivity and control group (no detrusor impairment)*

UD data (median)	DUA (n = 166)	Control group (n = 164)	p
Pdet/Qmax (cmH_2O)	11	20	0.01
Qmax (ml/sec)	10	15	0.01
PVR (ml)	190	20	0.00

UD – underactivity; Pdet/Qmax – detrusor pressure at peak flow; Qmax – peak flow; PVR – post void residual

according to the POP-Q stages showed that in DUA women POP-Q stage 4 was significantly higher. In contrast, POP-Q stage 2 and 3 were not statistically different between females with detrusor underactivity and normocontractility. LUTS were more common in those with DUA, with statistical significance for each symptom except for slow stream (Table 2). In women with POP and DUA, we found low rates of urinary retention: 5.4%. In table 3 are reported the main different urodynamic data between the two groups.

DISCUSSION

We found a higher prevalence of DUA in women undergoing UD for symptomatic POP (>50%) than previously reported [4, 5, 6]. However, data on DUA frequency in this population is poorly comparable due the different UD criteria used. In a recent study on 518 women with POP, DUA rate was reported as 40.9% [4]. However, the author's used a diagnostic parameter validated only for males (Bladder Contractility Index) [14–17]. This questionable choice was likely impacted their outcomes. In another study, using PIP-1 Griffith parameter, the pre-operative DUA prevalence was only 19%, but with a very low sample size (63 women; 6). For these reasons, the evaluation of the actual occurrence of DUA in women with POP is still challenging, and the few data available are not really comparable. In our study, we followed the main internationally recognized UD criteria for female DUA diagnosis in a large cohort [8–12]. The aim of our choice was to reduce bias in identifying women with DUA. Indeed, DUA diagnosis related to UD characteristics that met at least one of these criteria may have improved the accuracy of our findings.

Detrusor impairment in women with POP is likely a consequence of bladder outlet obstruction (BOO). In general, detrusor underactivity may be caused by either neural or muscular factors. The latter may be due to detrusor muscle damage or reduced excitability by neural stimuli. The former is represented by impairments at any level of the neural pathways of control of micturition, which may lead to an inappropriate transmission of contractile stimuli. They comprise impaired synaptic transmission, denervation, nerve damage, and reduced input from the pontine micturition center. Thus, the consequences of POP on detrusor function have to be considered in this perspective.

The main pathophysiological mechanism leading to development of DUA in women with POP is likely traction caused by prolapse which leads to an obstructive kinking and compression of the urethra. This may exert detrimental direct effects on other structures which may contribute to the development of DUA. Increasing postvoid residual may lead to bladder overdistension, and thus add further damage to the detrusor due to muscle tissue ischemia. Behavioral factors or functional alterations of the cerebral centers involved in the control of micturition are conceivable, but evidence is lacking.

BOO provokes numerous compensatory pathophysiological changes of the detrusor muscle tissue, which ultimately compromise efficacy of contraction [18, 19]. Not surprisingly obstruction has also been shown to lead to reduced receptor density and innervation of the detrusor muscle [20, 21, 22]. While the effects of obstruction on detrusor function have been extensively investigated, consequences of direct effects of traction are less clear. Currently available literature only shows a correlation between POP and nerve damage, but a possible relationship between them and DUA has not yet been addressed [23]. Detrusor underactivity may arise from chronic detrusor ischemia, which in turn may be the result of hypertrophy due to BOO [24, 25, 26]. Whether tractional forces in POP may further contribute to bladder ischemia has not been investigated. It is known that for every muscle fiber an optimal stretch length exists, at which the fiber develops its maximum contraction [27]. Assuming that a healthy, non-prolapsed bladder allows the optimal contraction of all its muscular components, it is conceivable, that at least parts of a prolapsed, deformed bladder are not able to develop their maximum contractional force. Interestingly, the rate of detrusor impairment increased dramatically in women with POP-Q stage 4 and DUA was significantly associated with the highest grade of POP. This finding may be explained by the more obstructive effect of high-stage prolapse, and by the prolonged time of bladder outlet obstruction and mechanical traction and ischemia. In POP-Q stage 4, muscle fibers may have lost their contraction strength showing that the exposure over time to a worsening POP-Q stage might create a no turning back bladder condition whereby even

with prolapse reduction the contractile ability will not return. According to this theory it may be advisable to identify patients with POP before their prolapse progresses to POP-Q stage 4. DUA occurred approximately in half of the patients with symptomatic POP-Q stage 2 and 3, and was three-fold higher in females with stage 4. Surprisingly, DUA was approximately equally distributed in the lower POP-Q stages (2 and 3), with a ratio of almost 1:1 between DUA and no-DUA patients. This points to the significant prevalence of DUA in older women with even lower stages of POP. In the subgroup of women with POP-Q stage 4, a detrusor impairment should be highly supposed and preoperative invasive urodynamics may be considered to allow appropriate counselling and avoid patient disappointment in cases of persistent voiding symptoms after surgery [28].

A consequence of detrusor failure can be represented by voiding symptoms. Usually, in women with POP these LUTS are supposed to be related to the obstructive mechanism of the vaginal wall defect. However, the high rate of DUA even in low stages indicates that those voiding symptoms may not be due solely to the obstructive effect of POP, but also to the development of an underlying DUA condition. This latter disorder could partially or completely explain some of the preoperative voiding symptoms of these women and the lack of improvement after surgery that sometimes occurs. Our data showed higher rates of voiding symptoms in women with DUA. This finding confirmed that emptying disorders may be only partially due to POP-related BOO, while in a non-negligible percent of women they may depend on detrusor impairment.

DUA showed a high prevalence in all POP stages, especially in stage 4. Voiding symptoms may be due to chronic bladder outlet obstruction but also to detrusor failure. Hence, in the case of symptomatic POP, preoperative UD may give additional functional data that may be useful to better tailor surgical counselling.

Strengths of our study are the large sample size and the choice of the most commonly used and internationally recognized UD criteria existing for the diagnosis of female DUA to provide robust epidemiological data on this under researched topic.

One limitation of our study was the lack of post-operative urodynamics; nevertheless, this epidemiological study was focused on the assessment of DUA prevalence and relation to the POP stages as its primary endpoint, and not on the POP surgery and outcomes of surgical treatments. A second limitation was the lack of a standardized and worldwide accepted UD parameter for the diagnosis of female DUA, however this is an intrinsic limit related to this topic per se. The control group consisted of women attended our office for symptoms related to POP but not claiming LUTS as a problem. At our analysis they showed some LUTS, although significantly lower than in DUA women. An ideal CG should have included asymptomatic patients for LUTS, but this is very rare in female population with POP. This could be a limitation of our study, but it represents also a picture of real practice.

CONCLUSIONS

DUA is highly prevalent in women with symptomatic anterior prolapse. DUA was diagnosed in approximately half of the women undergoing UD for symptomatic POP, and it was three-fold higher in those with POP-Q stage 4. LUTS were more common in DUA patients, and clinicians should be aware that urinary symptoms in women with POP may also result from the development of detrusor impairment.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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