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Original Article: Clinical Investigation

Differentiation of lower urinary tract dysfunctions: The role of ambulatory urodynamic monitoring

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Abbreviations & Acronyms
CISC = clean intermitting self-catheterization
DO = detrusor overactivity
IDC = involuntary detrusor contraction
LUTS = lower urinary tract symptoms
OAB = overactive bladder
SD = standard deviation
UDS = urodynamic study/ studies
UI = urinary incontinence
UTI = urinary tract infection

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Objectives: To determine the value of ambulatory urodynamic monitoring in the assessment of patients with lower urinary tract symptoms.

Methods: This was a cross-sectional study including patients who underwent both conventional urodynamic and ambulatory urodynamic assessment at our Center between December 2002 and February 2013. The ambulatory urodynamic studies were interpreted in a standardized way by a resident experienced with urodynamic measurements, and one staff member who specialized in incontinence and urodynamics.

Results: A total of 239 patients (71 male and 168 female) were included in the present study. The largest subgroup of patients, 79 (33%), underwent ambulatory urodynamic monitoring based on suspicion of an acontractile bladder. However, 66 of these patients (83.5%) still showed contractions on ambulatory urodynamics. Other groups that were analyzed were patients with suspected storage dysfunction (47 patients), inconclusive conventional urodynamic studies (68 patients) and incontinence of unclear origin (45 patients). Particularly in this last group, ambulatory urodynamics appeared to be useful for discrimination between different causes of incontinence.

Conclusions: Ambulatory urodynamic monitoring is a valuable discriminating diagnostic tool in patients with lower urinary tract symptoms who have already undergone conventional urodynamics, particularly in the case of patients with suspected bladder acontractility and incontinence of unclear origin during ambulatory urodynamics. Further study is required to determine the clinical implications of the findings and their relationship with treatment outcome.

Key words: acontractile bladder, ambulatory urodynamics, detrusor overactivity, lower urinary tract dysfunction, lower urinary tract symptoms.

Introduction

Urodynamic investigations are an important tool in the diagnostic route of patients with lower urinary tract dysfunction. Apart from the generally used conventional-UDS, certain centers carry out ambulatory-UDS additionally for specific indications.

In contrast to conventional-UDS, in which artificial filling is used, ambulatory urodynamic monitoring is based on diuresis-induced natural filling of the bladder.[1] Natural (orthograde) fill cystometry was described for the first time in 1957 by Comarr[2] and the technique has evolved ever since.[1,3,4] At present, ambulatory-UDS is a reliable and well tolerated cystometry tool overcoming certain arguments that exist against conventional-UDS, such as inadequate representation of normal filling.[5] In addition, ambulatory-UDS is particularly valuable in recording the bladder filling and voiding phase, combined with the amount and timing of UI in a near-normal situation.[6–10] This makes it a useful tool in patients with troublesome urinary tract symptoms.[1] Despite the advantages of ambulatory-UDS, conventional-UDS is the "gold standard" for investigation of lower urinary tract symptoms, as it is a highly standardized and validated measurement tool.[11] Validation of the ambulatory urodynamic monitoring to its gold standard has proven to be difficult, and studies comparing ambulatory urodynamics with patients' treatment outcomes have not been described yet.

Several studies already showed that ambulatory-UDS results in a more frequent detection of storage dysfunctions, such as DO, compared with conventional-UDS.[4,12,13] However, the additional value of ambulatory-UDS with respect to other storage dysfunctions (e.g. mixed UI) and voiding dysfunctions (e.g. suspected acontractile bladder) is less clear. Therefore, the primary objective of the present study was to determine the diagnostic value of ambulatory-UDS in different

lower urinary tract dysfunctions using a large cohort of patients who underwent both conventional- and ambulatory-UDS.

Methods

The present study was designed as a cross-sectional study. Between December 2002 and February 2013, a total of 239 patients with urinary tract complaints were included consecutively in the ambulatory-UDS database. In all patients, a conventional- and ambulatory-UDS was carried out during diagnostic work-up. Conventional urodynamic studies were carried out in line with the ICS-Good Urodynamic Practices standards.[11] Ambulatory urodynamic monitoring was carried out for different reasons. First, in case of OAB complaints without DO on conventional-UDS. Second, in case patients were suspected to suffer from bladder acontractility based on history and conventional-UDS. Third, in case of a history of stress or urge incontinence without additional clinical or urodynamic evidence and in patients, with mixed UI in which the timing of urine loss and/or the predominant cause of incontinence was not clear. Repeatedly inconclusive or poor quality (as a result of artifacts) conventional-UDS was a fourth reason for carrying out ambulatory-UDS.

Results of the ambulatory-UDS were interpreted by a resident experienced in judging urodynamic measurements, and one staff member who specialized in incontinence and urodynamics from Maastricht University Medical Center, Maastricht, The Netherlands. Bladder acontractility was defined as a bladder filling and micturition phase without detrusor pressure rise. Patients were only indicated as "suspected for bladder acontractility" in case they were unable to void during free uroflowmetry, or voided with significant post-void residual urine. Hypocontractility was defined as a low detrusor contraction pressure (less than 10 cm H_2O) during the voiding phase, relative to the degree of obstruction, not resulting in (efficient) micturition during urodynamic assessment. For the present study, urodynamic results were not solely analyzed, but medical history data (i.e. previous surgery, comorbidity and current medication) of these patients were also taken into consideration.

Ambulatory urodynamic monitoring

At our urological referral university clinic, ambulatory-UDS is only used as a second-line diagnostic tool. In addition, it is only carried out if indicated based on a previously carried out conventional pressure-flow analysis and clinical necessity. Typically, an ambulatory urodynamic monitoring study takes on average approximately 5–7 h, during which patients are assumed to take part in normal daily activities.[8] In patients with nocturia, a 12-h ambulatory-UDS during night-time can be used to determine the underlying condition.

Patients discontinue anticholinergic medication at least 5 days before the urodynamic assessment. Ten days before ambulatory-UDS, the patients' urine is cultured. In case of bacteriuria, focused antibiotic treatment is implemented after which the recovery of the bacteriuria is confirmed before the ambulatory-UDS is started. To start ambulatory urodynamic monitoring, two Uni-sensor micro-tip catheters are inserted (Medical Measurement Systems, Enschede, The Netherlands). One catheter is inserted in the rectum to record abdominal pressure differences. The other catheter containing a double-pressure sensor, combined with a conductance sensor, is inserted through the urethra. The distal pressure sensor lies in the bladder, close to the bladder neck, and the proximal measurement sensor is located in the region with the highest urethral pressure. This way the bladder and urethral pressure are measured accurately, and leakage is registered using a conductance sensor.

The ambulatory recording device contains several event buttons. Patients are instructed to use these buttons at specific events; that is, in case of urgency, a toilet visit, drinking or involuntary leakage of urine. These events are registered at the ambulatory-UDS timeline in parallel. Registration of events, together with the voiding diary and pad test are essential for interpretation of the ambulatory-UDS. If the patient carries out CISC, an additional 8-Fr catheter is inserted in the urethra during the assessment. Post-voiding residual urine is drained after every voiding attempt in case of incomplete voiding.

Statistical analysis

Quantitative data are given as a mean with SD. Other results are presented in frequency tables. The data were collected in an Excel spread sheet, and statistical analyses were performed using IBM SPSS statistics software, version 20 (IBM, Armonk, NY, USA).

Results

The mean age for the 239 patients was 58 years (SD 13.1) in men and 51 years (SD 12.7) in women. Other patient characteristics are shown in Table 1. The mean duration of the ambulatory-UDS was 5.6 h (SD 2.2). During ambulatory urodynamic monitoring, the mean drinking volume was 1371 mL (SD 610). The mean urine production was 827 mL (SD 559) with a micturition frequency of 4 (SD 2.9) times during the measurement. The frequency of UI episodes was 2.9 (2.8), with a mean volume of leakage of 97 g (SD 254.6), based on the pad test. In the next sections, the specific storage and voiding LUTS indications for ambulatory-UDS are highlighted.

Table 1 Characteristics of patients undergoing ambulatory urodynamic study

Patient characteristics	No. patients
Sex (male/female)	71/168
Previous history of	
Hysterectomy	49
Urethral suspension operation for UI	42
Prostate operation	24
Hernia nuclei pulposi	14
Diabetes	10
Cerebrovascular accident	1
Medication before conventional-/ambulatory-UDS	
5- α Reductase inhibitors	3
α-Blockage	10
Anticholinergics	26
Para-sympathicomimetics	4
Prostaglandin E_1 inhibitors	7
Antidepressives	15

Storage dysfunction as an indication for ambulatory-UDS

Suspected detrusor overactivity

A total of 47 patients (19.7%) included in the present study suffered OAB, as defined by the ICS. To objectify their complaints, they underwent a conventional-UDS and a consecutive ambulatory-UDS. In 29 (61.7%) patients, IDC during the filling phase were confirmed, where conventional-UDS did not show any IDC, as shown in Table 2. The mean IDC frequency was 7 (6.1), with a mean (SD) maximum contraction amplitude of 129 cm H_2O (66.6 cm H_2O).

Seven patients suspected for DO showed mixed UI on ambulatory-UDS, with dominant stress UI in two of these patients. In one patient, solely stress UI was objectified. In 10 (21.2%) patients with OAB complaints, ambulatory-UDS showed a normal micturition without confirmation of IDC.

Voiding dysfunction as an indication for ambulatory-UDS

Suspected bladder acontractility

In this heterogeneous patient group, the largest subgroup of patients underwent an ambulatory-UDS with the suspicion of bladder acontractility based on conventional urodynamics. In 79 patients (33.0%), an ambulatory-UDS was carried out for this indication. In 13 (16.5%) patients, the diagnosis of acontractile bladder was confirmed (Table 2). The other 66 (83.5%) patients with suspected bladder acontractility showed contractions on ambulatory-UDS. The largest group, 34 (43.0%) patients, had multiple IDC during the filling phase on ambulatory-UDS, with a mean (SD) amplitude of 112 cm H_2O (47.0 cm H_2O) and mean (SD) frequency of 8 (6.8).

Based on the maximum detrusor pressure combined with the initial symptom presentation, a small portion of the patients (12 patients, 15%) was defined as having a hypocontractile rather than acontractile bladder. These patients had a mean (SD) maximum detrusor pressure amplitude of 52 cm H_2O (35.8 cm H_2O). A total of 16 of the 79 patients in this group showed a normal micturition contractile response on ambulatory-UDS without IDC.

In three of the four patients remaining in this group, patients' ambulatory-UDS showed mixed incontinence, of which two patients had predominant stress UI and one had primarily filling phase contractions with subsequent loss of urine. In one relatively young patient, ambulatory urodynamic monitoring showed high urethral pressures throughout the assessment, suspicious of Fowler's syndrome.

Incontinence as an indication for ambulatory-UDS

A total of 26 patients with alleged mixed incontinence were included in this database. In 16 of these patients, only IDC were seen on ambulatory-UDS, with a mean (SD) amplitude of 103 cm H_2O (35.1 cm H_2O) and mean (SD) frequency of 9 (5.8). In three patients, only stress UI was objectified. MUI with predominantly IDC was found in two patients, and MUI with predominant stress UI in one patient. The remaining four patients showed no IDC or stress-induced UI on ambulatory-UDS.

A total of seven patients with potentially isolated stress IO underwent an ambulatory urodynamic assessment. In four (57.1%) of the patients, stress UI was confirmed in the absence of IDC. In the other three patients, ambulatory-UDS showed a normal filling and micturition phase.

Additional ambulatory-UDS was carried out in 12 patients with urgency, suspicious for urge incontinence. Seven (58.3%) of these patients had IDC during ambulatory urodynamics. The other five (41.7%) patients showed no abnormalities on their ambulatory-UDS recordings.

Inconclusive conventional-UDS as an indication for ambulatory-UDS

The second largest group (28.5%) undergoing ambulatory-UDS consisted of patients with an inconclusive conventional-UDS or one of poor quality. In 68 of these cases ambulatory urodynamics was carried out and data were included in the present study. Involuntary detrusor contractions during the filling phase were found in the majority of these patients (63.2%), with a mean (SD) maximum amplitude of 106 cm H_2O (57.6 cm H_2O) and a mean (SD) contraction frequency of 6 (5.1).

In three patients, solely stress UI was found during ambulatory-UDS, and in four patients mixed UI with predominantly stress UI was seen. Two patients appeared to have a hypocontractile bladder during ambulatory urodynamic monitoring, which was not seen on conventional-UDS. In 23.5% of the cases with inconclusive conventional-UDS, ambulatory-UDS showed a normal bladder filling and micturition phase.

Table 2 Diagnosis after ambulatory urodynamic assessment given for each indication

	Diagnosis after ambulatory-UDS					
	Acontractile bladder	Hypocontractile bladder	IDC	Other	Normal ambulatory-UDS	Total no. patients (% of total)
Indication ambulatory-UDS						
Suspected DO	0	0	29	8	10	47 (19.7)
Suspected acontractile bladder	13	12	34	4	16	79 (33.0)
Inconclusive conventional-UDS	0	2	43	7	16	68 (28.5)
Incontinence	0	0	23	10	12	45 (18.8)
Total no. patients (% of total)	13 (5.4)	14 (5.9)	129 (54.0)	29 (12.1)	54 (22.6)	239 (100)

Bladder acontractility: bladder filling and micturition phase without detrusor pressure rise. Bladder hypocontractility: a low detrusor contraction pressure not resulting efficient micturition during urodynamic assessment.

Discussion

Although relatively elaborate to carry out and to analyze, ambulatory-UDS is thought to be a more accurate tool for diagnosing LUT dysfunctions in both children and adults.[14,15] In case of DO, ambulatory-UDS is reported to have a higher sensitivity compared with conventional-UDS.[6] After conventional-UDS, 47 (19.7%) patients were thought to have involuntary detrusor contractions during the filling phase. However, ambulatory-UDS showed involuntary contractions in 129 (54.0%) patients. Therefore, the results from the present study are in line with present literature. The difference in observations between both assessment types could be explained by the technique used. The retrograde, rapid bladder filling and the shorter timespan of conventional urodynamics could very well lead to an underestimation of IDC. However, it cannot be excluded that the vesical catheter itself is a non-physiological trigger resulting in a higher incidence of detrusor overactivity during ambulatory urodynamics.[16] In addition, a previous study in healthy female volunteers showed IDC on ambulatory-UDS in 68% of the cases, compared with 18% after conventional-UDS.[17] In healthy male volunteers, IDC were also found during ambulatory urodynamics.[18]

There still remains a great deal of controversy regarding the clinical implications of using urodynamics in OAB patients.[19] Giarenis *et al.* recently showed that women with OAB and additional DO on conventional- or ambulatory-UDS experience more significant impairment to their quality of life and have a greater degree of bladder dysfunction compared with OAB patients without DO on urodynamics.[20] A study of OAB patients treated with sacral neuromodulation described a correlation between reduction in IDC and clinical outcome after treatment.[21] Comparable findings were found in neurogenic DO patients after treatment with onabotulinumtoxinA.[22] However, the result after intradetrusor injections of onabotulinumtoxinA is not predicted by the presence of detrusor overactivity on pretreatment conventional-UDS in idiopathic OAB patients.[23]

Ambulatory-UDS is used in our center in the specific group of treatment refractory OAB patients without DO on conventional-UDS. The fact that the bladder produces involuntary detrusor contractions in response to the small flexible catheters during an ambulatory urodynamic measurement itself might indicate a higher excitability of the bladder sensory function or a decreased central inhibition of the urethra-detrusor facilitative reflex contractions in the filling phase.[24] This might even serve as a biomarker of pathology. To accomplish this, quantification and characterization of IDC on ambulatory-UDS is necessary. At present, there is an ongoing study from our center regarding the use of ambulatory-UDS in these patients and the effect of treatment with sacral neuromodulation. In the near future, this might support the use of ambulatory-UDS in differentiation of OAB patients into responders and non-responders to treatment.

Based on the small data sample of patients with incontinence of unclear origin in the present study, we see a slight trend that ambulatory-UDS might be a useful tool in patients with mixed UI and unclear predominant origin of the incontinence. This is a small subgroup of patients, which, at present has not been described in the literature in relation to ambulatory urodynamics. The role of ambulatory-UDS in this subgroup of patients requires further investigation in a prospective setting in which ambulatory-UDS results are related to treatment choice, treatment success rate and the patient's satisfaction.

The present results show that lower urinary tract dysfunctions that are missed or misdiagnosed in a conventional-UDS could be diagnosed accurately in ambulatory-UDS. However, because of the complexity of the ambulatory-UDS, the time-consuming interpretation of the results and the expertise required, ambulatory-UDS is usually not the first choice to diagnose any LUT dysfunctions. Therefore, it should be considered only for certain indications where conventional-UDS has been carried out and has not been able to show the correct diagnosis.

Bladder acontractility is characterized by an inability to empty the bladder completely, without a visible contraction on cystometry. Clinically these patients present themselves with the inability to void to completion and/or with recurrent UTI or urinary retention. Bladder acontractility can be caused by dysfunction at various levels in the brain–bladder axis, from damage to the detrusor muscle itself, its autonomic nerve supply to dysfunction at the spinal level. In addition, the pontine micturition center can be damaged or even a defect in cortical functions leading to an inability to relax adequately can cause an inhibition of a (persistent) bladder contraction.

Bladder acontractility represents a heterogeneous urological entity and the etiological variety forces us to search for different therapeutic approaches. However, a first step in this process is finding the most optimal diagnostic tool in diagnosing true bladder acontractility. The present study, consisting of a cohort of patients undergoing ambulatory-UDS, showed that just 16.5% of the patients with suspected bladder acontractility indeed showed no contraction on ambulatory-UDS. In all other cases, either a minimal or normal micturition contraction was seen, with or without simultaneous storage dysfunction present on ambulatory-UDS (Table 2). The group marked as having a hypocontractile, instead of an acontractile, bladder showed a mean maximum detrusor pressure amplitude of 52 cm H_2O. Although this seems acceptable, in these cases the detrusor pressures appeared to be too low to overcome the urethral resistance, resulting in inefficient voiding in these cases. Possibly, a bladder outlet obstruction component was involved in at least some of these patients. The present study confirms earlier preliminary results from a retrospective study carried out in our center, pointing out the value of ambulatory-UDS in differentiating LUTS etiology.[8]

Current treatment options for restoring voiding effectiveness in patients with complete ambulatory-UDS confirmed bladder acontractility are limited. Bladder and sphincter reflex modulation techniques, such as sacral neuromodulation, can only be used in case there is little or no damage to the brain–bladder axis in combination with intact function of the detrusor contractile apparatus. Therefore, in the right selection of patients (with at least some contractile function present on ambulatory-UDS), this therapeutic option can be effective.[25,26] Furthermore, a reconstructive surgical procedure, such as latissimus dorsi detrusor myoplasty, is only feasible in a highly selected group of patients with an acontractile bladder.[27] This means that the

majority of patients are left with no other options than carrying out life-long CISC.[28]

In order to increase the success rate of the invasive, limited and expensive therapeutic options, such as sacral neuromodulation, there is a need for a valid diagnostic tool in patients with suspected bladder acontractility. The present data show that conventional-UDS is not an accurate test in confirming true bladder acontractility. In fact, in over 80% of the cases, ambulatory-UDS led to a different conclusion compared with conventional-UDS. Therefore, in case of no detrusor contractions on conventional-UDS, an ambulatory urodynamic assessment should be carried out to confirm or exclude true bladder acontractility.

In the near future, several novel treatment options are expected, for treatment of either decreased contractile strength or inadequate coordination between urethral relaxation and detrusor contraction.[29] Hence, ambulatory-UDS is expected to gain a more prominent role in the diagnostic algorithm for detrusor underactivity and the differentiation of this entity from true bladder acontractility.[30]

The present results show that ambulatory urodynamic monitoring is a valuable discriminating diagnostic tool in patients with various lower urinary tract complaints, particularly in patients with suspected bladder acontractility. In addition, ambulatory-UDS might be a useful tool to distinguish the predominant cause of incontinence in patients with an unclear origin of incontinence. In order to confirm the clinical significance of these findings during the ambulatory urodynamic measurement, a future study is required to relate these results to treatment outcome and to further validate the technique.

Conflict of interest

GA van Koeveringe is a consultant, speaker and trial participant for Astellas.

M.S. Rahnama'i has won the Eugen- Rehfish Preis of the Forum Urodynamicum Germany for the presentation of this study.

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