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Evaluation of urodynamic pattern in short and long-standing diabetic patients

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Summary

Purpose: To address the pattern of urodynamic findings in diabetic patients with lower urinary tract symptoms (LUTS), comparing short-standing and long-standing type 2 diabetes mellitus (T2DM).

Methods: A prospective study was conducted on 50 patients presenting with LUTS and a concurrent diagnosis of T2DM, between February 2016 and May 2018. Patients were classified and evaluated according to the duration of diabetes into two groups: short-standing DM (< 15 years, n = 31), and long-standing DM (≥ 15 years, n = 19) groups. The impact of LUTS and quality of life were assessed in female patients using ICIQ-FLUTS and male patients using ICIQ-MLUTS.

Results: A total of 50 patients were included in the study. The mean duration of T2DM was 10 ± 0.7 years. The mean age was 56.3 ± 1.2 years, and the mean HbA1c was 7.5 ± 1.2%.

Urodynamic evaluation detected significantly higher detrusor overactivity (DO) and increased bladder sensation with the short-standing DM group (35.5 vs. 15.8%, $p = 0.01$ and 32.3 vs. 5.3%, $p = 0.01$, respectively). Comparatively, weak, or absent detrusor contractility were more frequent in patients with long-standing DM (52% and 26% respectively $p = 0.01$). As expected, overflow incontinence and straining during voiding were significantly higher in the long-standing DM group ($p = 0.04$ and $p = 0.03$, respectively). Surprisingly, there was no significant correlation between patients presenting with urgency in their voiding diary (subjective) and urodynamic detection of DO ($p = 0.07$).

Conclusions: There are different patterns in urodynamic characterizations of T2DM. Patients with short-standing DM present more commonly with storage symptoms and detrusor overactivity on urodynamics. Contrastingly, patients with long-standing DM present more frequently with voiding symptoms and detrusor underactivity on urodynamics. Thus, screening for an underactive bladder is advisable in patients with long-standing T2DM.

KEY WORDS: Urodynamic study; Diabetes mellitus; LUTS; Urinary bladder; Urinary incontinence; Detrusor underactivity; Detrusor overactivity.

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INTRODUCTION

Diabetes mellitus (DM) is a prevalent major health condition associated with lower urinary tract symptoms (LUTS)

and bladder dysfunction (1). The impact and pathophysiology of diabetes on the urinary bladder could be multifactorial including the osmolarity diuresis effect, metabolic perturbation, microvascular damage, and diabetic neuropathy, consequently resulting in detrusor smooth muscle and urinary bladder urothelial dysfunction (2). Historically, LUTS associated with DM were reported as a triad of symptoms; impaired bladder sensation, increased bladder capacity, and decreased detrusor contractility (3). However, more recently, DM was reported to cause a variety of LUTS, including *detrusor overactivity* (DO), impaired detrusor contractility and urethral dysfunction (4-6). These symptoms culminate in diabetic cystopathy and asymptomatic bacteriuria, which is reported to be between 25% and 90% in the literature (3).

Despite the main focus of DM associated LUTS being referred to as diabetic cystopathy for many years, recent evidence has demonstrated the impact of diabetes on the lower urinary tract to be multifactorial (1, 2, 7).

Furthermore, the pathogenesis of LUTS in diabetic patients is under-investigated, remaining elusive.

Osmolarity diuresis effect, metabolic abnormalities, microvascular damage, and neuropathy of diabetes may result in dysfunctions of smooth muscle, urothelium, and neuronal components of the bladder (6, 8). Previous studies have reported several urodynamic findings in diabetic patients (1, 8). However, there is a paucity in the literature addressing the urodynamic changes concerning the duration of DM.

Therefore, the study aimed to address the pattern of urodynamic findings in diabetic patients presenting with LUTS, comparing short and long-standing DM.

PATIENTS AND METHODS

Study design

After obtaining ethical approval, a prospective study was conducted on patients who presented with LUTS symptoms and had a concurrent diagnosis of type 2 DM between February 2016 and May 2018. All subjects signed informed consent to participate in the study. Patients with

previous pelvic surgery, coexisting neurologic disorders, or any other medical condition that interferes with bladder or sphincter function were excluded from the study. Patients were classified and evaluated according to the duration of diabetes into short-standing: > 15 years (group I), and long-standing: \geq 15 years (group II).

Subjects' evaluation

All patients were subjected to entire medical history. The impact of LUTS and quality of life was assessed in female patients utilizing ICIQ-FLUTS (*International Consultation on Incontinence Modular Questionnaire on Female Lower Urinary Tract Symptoms*) and in male patients using ICIQ-MLUTS (*International Consultation on Incontinence Modular Questionnaire on Male Lower Urinary Tract Symptoms*). These questionnaires provide rigorous validity and reliability, both of which are frequently used worldwide (9, 10). Patients underwent a clinical examination (including focused neurological examination). Furthermore, all patients underwent routine laboratory investigations, which included: urine analysis, urine culture and sensitivity, HbA1c, fasting and postprandial blood sugar, and serum creatinine. imaging studies (KUB, abdominopelvic US), and urodynamic evaluation. The urodynamic machine used was the Ellipse-4 Andromeda (*GmbH, Wallbergstraße 5. D-82024 Taufkirchen/Potzham - Germany*).

Statistical analysis

Statistical analysis was carried out using SPSS software package version 28.0. Numerical values were presented as means and *standard deviation* (SD). Categorical values were presented as frequency and percentages. Comparison between different categorical variables was made using Fisher's exact test. Additionally, a Student's t-test was used to compare the means of the continuous variables among different groups. Two-tailed P values less than 0.05 were considered statistically significant.

RESULTS

A total of 50 patients were included in the study: 40 women (80%) and 10 men (20%). The mean age was 56.28 ± 1.14 years (range 45 to 73 years), the mean HbA1c was $7.5 \pm 1.2\%$, and the mean *fasting blood sugar* (FBS) was 199.88 ± 9.24 mg%. The mean duration of DM was 10 ± 0.77 years (Table 1).

Clinical presentation

Storage symptoms were the predominant class of LUTS reported by the participants. In particular, 88% described nocturia (44 subjects) followed by 86% noting daytime frequency (43 subjects), urgency 78% (39 subjects), urge incontinence 54% (27 subjects), and nocturnal enuresis 28% (14 subjects). Comparatively, voiding LUTS were reported less frequently: 40% complained of straining during voiding, 38% reported a weak urine stream and 34% of an interrupted stream. Overflow incontinence was the main complaint in 20% of the study cohort (Table 1).

Voiding diary

Charts were reported as the mean of variable per patient as follows: mean diurnal voids/day was 7.78 ± 0.45 and mean

Table 1.

Patients demographics, clinical presentation, questionnaires evaluation and voiding diary profile.

Variable	Value
Patients demographics:	
vMean age (SE, range), year	56.28 ± 1.14 (45 to 73)
Male/female ratio, n (%)	10 (20%)/40 (80%)
Mean duration of DM (SE, range), year	10 ± 0.77 (5 to 29)
Mean FBS (SE, range), mg %	199.88 ± 9.24 (102 to 392)
HbA1c	7.5 ± 1.2
Mean serum Creatinine (SE, range), mg %	$1.09 \pm .04$ (0.5 to 1.5)
Clinical presentation:	
Nocturia, n (%)	44 (88%)
Daytime frequency, n (%)	43(86%)
Urgency, n (%)	39 (78%)
Urgency incontinence, n (%)	27 (54%)
Nocturnal enuresis, n (%)	14 (28%)
Weak stream, n (%)	19 (38%)
Interrupted stream, n (%)	17 (34%)
Straining during voiding, n (%)	20 (40%)
Continuous dripping of urine, n (%)	10 (20%)
Questionnaires evaluation:	
ICIQ-FLUTS	28.5 ± 7
ICIQ-MLUTS	30.3 ± 5.8
Voiding diary profile:	
Diurnal voids/day (SE, range)	7.78 ± 0.45 (2 to 15)
Nocturnal voids/night (SE, range)	3.78 ± 0.29 (0 to 8)
Urgency episodes/day (SE, range)	4.54 ± 0.48 (0 to 14)
Urgency incontinence episodes/day (SE, range)	2.17 ± 0.51 (0 to 14)
Voided volume/void (SE, range)	268.47 ± 14.86 (90 to 500)

nocturnal voids/night was 3.78 ± 0.29 ; mean of urgency episodes/day was 4.54 ± 0.48 , and mean of urge incontinence episodes/day was 2.17 ± 0.51 . Finally, the mean voided volume/void was 268.47 ± 14.86 mL (Table 1).

Urodynamic evaluation

The free flowmetry of the cohort revealed that the mean voided volume was 235 ± 17.05 mL. The mean maximum flow rate was 15.21 ± 1.12 mL/s and the mean of post-void residual (PVR) urine was 114.94 ± 22.76 mL. Of note, 30% of participants had a PVR greater than 100 mL. Bladder sensation was normal in 54% (26 patients), increased in 22% (11 patients), reduced in 12% (6 patients) and absent in 14% (7 patients). The mean first sensation volume (FSV) was 159 ± 10.88 mL. The mean first desire volume (FDV) was 255.97 ± 11.36 mL, and the mean strong desire volume (SDV) was 334.68 ± 11.56 mL (Table 2).

The mean value of bladder compliance was 81.70 ± 9.84 mL/cm H₂O. The latter was normal in 88% (44 subjects), reduced in 10% (5 subjects), and increased in 2% (1 subject).

The mean *maximum cystometric capacity* (MCC) was 383.56 ± 15.7 mL of which, was valid for 74% of subjects. The MCC could not be assessed in 26% (13 subjects) due to either absent sensation, urine leakage, or reduced sensation (Table 2). Of the subjects whom the MCC was successfully calculated, 58% had a normal MCC; it was reduced in 14% and increased in 2% of the study cohort. Amongst the studied participants, 28% (14 subjects) had DO. The DO was phasic in 20% (10 subjects) and termi-

Table 2.
Urodynamic evaluation of the study' cohort.

1. Free flowmetry:	
Mean voided volume (SE, range), mL	235 ± 17.05 mL. (12 to 468)
Mean maximum flow rate (SE, range), mL/s	15.21 ± 1.12 mL/s. (1 to 40)
Mean amount of post voiding residual urine (SE, range), mL	114.94 ± 22.76 mL. (0 to 500)
2. Filling cystometry:	
a. Bladder sensation:	
Absent bladder sensation, n (%)	7 (14%)
Reduced, increased, normal bladder sensation, n (%)	6 (12%), 11(22%), 26(54%)
Mean first sensation volume (FSV) (SE, range) mL	159 ± 10.88 (31 to 352)
Mean first desire volume (FDV) (SE, range) mL	255.97 ± 11.36 (129 to 430)
Mean strong desire volume (SDV) (SE, range) mL	334.68 ± 11.56 (206 to 474)
b. Bladder compliance:	
Normal, reduced, increased bladder compliance, n (%)	35 (70%), 5 (10%), 10(20%)
Mean value of bladder compliance (SE, range) mL/cm H ₂ O	81.70 ± 9.84 (5.7 to 455)
c. Maximum cystometric capacity:	
Normal, increased, reduced n (%)	29 (58%), 7(14%), 1(2%)
Mean maximum cystometric capacity (SE, range) mL	383.56 ± 15.7 mL (225 to 657)
d. Parameters of detrusor overactivity:	
Detrusor overactivity number (SE, range)	3.46 ± 0.82 (1 to 12)
Detrusor overactivity duration (SE, range)	45.85 ± 10.75 (10 to 149)
Detrusor overactivity amplitude (SE, range)	41.4 ± 6.02 (7.4 to 75)
First contraction volume (SE, range)	141 ± 26.63 (31 to 347)
e. Parameters of leakage with detrusor overactivity:	
Amount of leakage (SE, range)	125.62 ± 28.19 (30-258)
First leakage volume (SE, range)	172.75 ± 32.78 (73-324)
Leak detrusor pressure (SE, range)	56.34 ± 3.77 (43-75)
f. Pressure flow study:	
Detrusor contractility: normal, weak, absent n (%)	30 (60%), 13 (26%), 7 (14%)
g. Flow	
Obstructed, not obstructed, could not be assessed n (%)	1 (2%), 42 (84%), 7 (14%)

nal in 8% (4 subjects) with regards to DO; the mean value of wave numbers was 3.64 ± 0.82 waves (range 1 to 12 waves), the mean duration was 45.85 ± 10.75 seconds (range 10 to 149 seconds), the mean amplitude was 41.4 ± 6.02 cm H₂O, and the mean value of the first contraction volume (FCV) was 141 ± 26.63. The detrusor contractility was normal in 60 % (30 subjects), weak in 26% (13 subjects), and absent in 14 % (7 subjects) (Table 2). With regards to the duration of DM, the cohort was classified into group I (short-standing DM, < 15 years) included 31 patients (62%), and group II (long-standing DM, ≥ 15 years) included 19 patients (38%). The mean score of ICIQ-FLUTS was significantly lower in group I when compared with group II (24.67 ± 5.4 vs. 34.25 ± 4.9; p < 0.001). Likewise, the mean score of ICIQ-MLUTS was significantly lower for group I when compared with group II (28.7 ± 5.9 vs. 34 ± 2.3; p = 0.048) (Table 3).

DO and increased bladder sensation were more common in patients with short-standing DM (35.5% vs. 15.8%, p = 0.01) and (32.3 vs. 5.3%, p = 0.01), respectively. In contrast, weak or absent detrusor contractility was more frequent in patients with long-standing DM (52% and 26% respectively p = 0.01). As expected, overflow incontinence and straining during voiding were significantly higher in the long-standing DM group (p = 0.04 and p = 0.03), respectively (Table 4). There was no significant correlation between patients presenting with urgency on voiding diary (subjective) and urodynamic detection of DO (p = 0.07).

Table 3.
Comparison between the study groups regarding clinical presentation.

LUTS evaluation	Short-standing DM N = 31 (%)	Long-standing DM N = 19 (%)	P value
Day time frequency	28 (90.3%)	15 (78.9%)	0.4
Nocturia	28 (90.3%)	16 (84.2)	0.66
Urgency	26 (83.9%)	13 (68.4%)	0.29
Urgency incontinence	18 (58.1%)	9 (47.4)	0.56
Nocturnal enuresis	5 (16.1%)	9 (47.4)	0.25
Weak stream	7 (22.6%)	12 (63.2)	0.07
Interrupted stream	6 (19.4%)	11 (57.9%)	0.12
Overflow incontinence	2 (6.5%)	8 (42.1%)	0.04
Straining during voiding	7 (22.6%)	13 (68.4%)	0.03
ICIQ-FLUTS	24.67 ± 5.4	34.25 ± 4.9	< 0.001
ICIQ-MLUTS	28.7 ± 5.9	34 ± 2.3	0.048

Table 4.
Comparison between the study groups regarding urodynamic findings.

Bladder sensation N (%)	Short-standing DM N=31	Long-standing DM N=19	P value
Normal	17 (54.8%)	9 (47.4%)	0.01
Increased	10 (32.3%)	1 (5.3%)	
Reduced	1 (3.2%)	5 (26.3%)	
Absent	3 (9.7%)	4 (21.4%)	
Bladder compliance			
Normal	26 (83.8%)	9 (47.4%)	0.1
Increased	2 (6.4%)	8 (42.1%)	
Reduced	3 (9.7%)	2 (10.5%)	
Maximum cystometric capacity			
Normal	17 (54.8%)	12 (63.2%)	0.42
Increased	1 (3.2%)	0	
Reduced	6 (19.4%)	1 (5.3%)	
Cannot be assessed	7 (22.6%)	6 (31.6)	
Parameters of detrusor overactivity			
Phasic	9 (29%)	1 (5.3)	0.01
Terminal	2 (6.5%)	2 (10.5%)	
With leak	6 (19.4%)	2 (10.5%)	
Without leak	5 (16.1%)	1 (5.3%)	
Detrusor contractility			
Normal	26 (83.9%)	4 (21.1%)	0.01
Weak	3 (9.7%)	10 (52.6%)	
Absent	2 (6.5%)	5 (26.3%)	
Flowmetry			
Non obstructed	28 (90.3%)	14 (73.7%)	0.12
Obstructed	1 (3.2%)	0	
Could not be assessed	2 (6.5%)	5 (26.3%)	

DISCUSSION

Diabetic bladder dysfunction can present with a broad spectrum of LUTS (10). Clinically, LUTS in diabetic patients range from storage symptoms to voiding symptoms. Common storage LUTS experienced by diabetic patients include nocturia, increased daytime frequency, urgency, and urge incontinence. On the other hand, frequently experienced voiding LUTS in diabetic patients encompass weak flow of urine, interrupted stream, straining during voiding, and eventually urine retention or overflow incontinence. The pathology shows a diverse and progressive evolution from an overactive bladder to a

poor non-contractile bladder. Diabetic urinary symptoms manifest alongside the progression of diabetes. As such, we evaluated diabetic patients presenting with LUTS to specifically address the urodynamic pattern in such cohort over the course of the disease. Therefore, the study was conducted to characterize the specific urodynamic findings associated with the diabetic population in both short and long disease duration.

As previously reported, in the early course of diabetes, the main pathological factor is related to polyuria, causing detrusor muscle remodeling, hypertrophy and overactivity. Over time, there is an accumulation of toxic metabolites and oxidative stress leading to a decline in detrusor smooth muscles contractility, and bladder urothelium and neuronal alteration. Collectively, this results in significant bladder sensation degradation and altered filling response (12).

Several reports demonstrate both urodynamic DO and poor bladder contractility could be present. Among 182 diabetic patients with a mean follow-up period of 5 years, *Kaplan et al.* found that DO was the main urodynamic pattern (55%), while detrusor contractility was impaired among 23% of patients (13).

Furthermore, *Kebapci et al.* found that decreased bladder sensation, weak bladder contractility, and increased bladder capacity with PVR < 100 mL were the most prominent urodynamic findings in diabetic patients (14). In their cohort, the duration of diabetes was less than nine years, and HbA1c was less than 7%. Additionally, *Yamaguchi et al.* reported trends of increased residual urine in long-standing diabetic patients (duration > 10 years) despite not being statistically significant (15).

Similarly, *Malik et al.* (16) conducted a prospective comparative study on 288 non-diabetic and 96 diabetic women. They detected delayed first sensation, higher cystometric capacity, and reduced detrusor pressure at maximum flow rate among the diabetic group. Those findings were more remarkable in long-standing DM (> 10 years). A significant relation between DM and a non-contractile bladder was not identified in their study. In contrast, in the present report, we included diabetic patients with a longer duration and reported weak detrusor contractility in 26% and 14%, respectively. Additionally, we detected a significant difference in detrusor contractility between long and short DM duration. 52% of patients had weak detrusor contractility and 26% had very weak detrusor contractility of long-standing T2DM, compared to 9% and 6% in short-standing, respectively ($p < 0.001$).

Furthermore, *Shin et al.* performed a retrospective review of a urodynamic study for 708 females who clinically presented with stress urinary incontinence, comparing the diabetic and non-diabetic groups. They found that Q_{max} and bladder contractility index is significantly reduced among the diabetic group (17).

The distinct finding of the present study recognises diabetes mellitus had a different impact on urinary bladder function; the pattern of dysfunction varies according to the duration of DM. Storage symptoms were more common amongst short-standing DM patients compared to long-standing T2DM patients. In particular, nocturia (90.3 vs. 84.2%), daytime frequency (90.3 vs. 78.9%), urgency (83.9 vs. 68.4%), and urge incontinence (58.1 vs. 47.4%). In contrast, voiding symptoms were more frequent in long-standing

DM, namely weak stream (63.2 vs. 22.6%), interrupted stream (57.9 vs. 19.4%), overflow incontinence (42.1 vs. 6.5%), and straining during voiding (68.4 vs. 22.6%).

Furthermore, the current study showed no significant correlation between urgency on voiding diary (subjective) and urodynamic detection of DO. We reported DO in 35.4% of patients who presented with storage LUTS. Such finding might reinforce the pathogenesis theory of diabetic LUTS as multifactorial (2). In such cohort, storage LUTS could be explained by the presence of glycosuria and osmolarity diuresis effect prior to detection of DO. Conversely, previous studies reported significant urodynamic findings in patients with mild voiding LUTS, specifically in the late stages of diabetic LUTS (8, 18). They explain that with the insidious onset of diabetic LUTS, patients may overlook the symptoms. In addition, health care workers tend not to consider bladder dysfunction complications while screening asymptomatic diabetic patients; they pay more attention to neuropathy, nephropathy, and retinopathy (19). Hence diabetic patients are liable to be diagnosed during the late stages of diabetic cystopathy.

Finally, the study is not without limitations. First, the MCC could not be assessed in 31% patients in the long-standing DM group due to absent bladder sensation. However, the filling was stopped after 600 mL to avoid post-procedural urine retention, which is considered high bladder capacity. Likewise, the MCC could not be assessed in 22% of the short-standing DM group primarily due to urine leakage. Therefore, the bladder filling was stopped earlier in those patients.

Second, the relatively small sample size of the present study. Nevertheless, the present study is prospective with strict and explicit inclusion and exclusion criteria in an attempt to eliminate any confounding factors which might affect bladder function. Additionally, the voiding diary provided a subjective evaluation that could not reflect the objective bladder dysfunction in the urodynamic study. Thus, we believe it is crucial to create a newly validated screening test for patients with diabetic cytopathy. Further prospective studies are still advisable.

CONCLUSIONS

There are different patterns in the urodynamic characterization of type 2 diabetic patients. Patients with short-standing DM often present with storage symptoms and detrusor overactivity on urodynamics. Comparatively, patients with long-standing DM present more frequently with voiding symptoms and detrusor underactivity on urodynamics. Screening for an underactive bladder is advisable in patients with a long-standing DM.

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