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Özgün araştırma / Original research

BPH ile eşzamanlı detrüsör aşırı aktivitesi (DAA) sıklığının değerlendirilmesi: Karakteristik klinik BPH parametrelerinin eşzamanlı DAA mevcudiyeti ile ilişkisi var mı?

The evaluation of the prevalence of DOA concomitant to BPH: May the characteristic parameters of clinical DOA have any relationships with the presence of concomitant DOA?

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Özet

Amaç: Benign prostat hiperplazisine (BPH) eşlik eden detrüsör aşırı aktivitesinin (DAA) prevalansını araştırmak ve karakteristik BPH parametreleri ile eşzamanlı DAA varlığı arasındaki olası ilişkiyi değerlendirmek.

Gereç ve yöntem: Bu çalışmada DOA olduğu bilinmeyen klinik BPH'lı 100 hasta prospektif olarak değerlendirildi. Tüm hastalar operasyon öncesi dönemde ürodinami ile değerlendirildi. Hastalar ürodinami sonuçlarına göre iki gruba ayrıldı (Grup 1: Pür BPH, Grup 2: BPH+DAA). İki grup arasında bazı klinik BPH parametreleri istatistiksel olarak karşılaştırıldı.

Bulgular: Dolum sistometri sonuçları 52 (%52) hastada DAA varlığını gösterdi. Basınç akım çalışmasında tüm hastalarda obstruktif işeme bulguları belirlendi. Tek değişkenli analizde, DAA' lı hastalar daha yaşlı idi ve anlamlı biçimde daha düşük Q max, daha yüksek kreatinin düzeyi, daha yüksek IPSS ve AAM V-8 skoruna sahipti. Diğer yandan çok değişkenli analizde sadece yaş, IPSS ve AAM V-8 skorları bağımsız olarak eşzamanlı DAA varlığı ile ilişkili bulundu.

Sonuç: Klinik BPH hastalarında eşzamanlı DAA varlığı bağımsız olarak sadece yaş, IPSS ve AAM V-8 skorları ile ilişkilidir. Daha önceden koyulmuş klinik BPH tanısı olan ve uzun süredir buna yönelik tedavi almasına karşın LUTS semptomları devam eden hastalarda eşzamanlı DAA aktivitesini her zaman dikkate almak ve bu tür hastalara yaklaşımda AAM V-8 sorgulamasını rutin olarak kullanmak oldukça mantıklı ve isabetli bir yaklaşım olacaktır.

Anahtar kelimeler: Benign prostat hiperplazisi, detrüsör aşırı aktivitesi, alt üriner sistem semptomları, ürodinamik inceleme.

Abstract

Objective: To investigate the prevalence of detrusor overactivity (DOA) concomitant to clinical benign prostate hyperplasia (BPH) and the relationship between some of the characteristic parameters of BPH and the presence of concomitant DOA.

Materials and methods: This is a prospective analysis of 100 patients with a previous diagnosis of clinical BPH and no previous diagnosis of DOA. All patients were urodynamically evaluated and divided in two groups (Group 1: Pure BPH, Group 2: BPH with DOA). Some characteristic parameters of BPH were statistically compared between two groups.

Results: Filling cystometry results showed that 52 men (%52) had detrusor overactivity. In pressure-flow studies, obstructive voiding findings were determined in all patients. In univariate analysis, patients with DOA were significantly older, had lower Q max, higher creatinine, higher IPSS and OAB V-8 scores. On the other hand, multivariate analysis revealed that only age, IPSS, and OAB V-8 scores were independently associated with the presence of DOA.

Conclusion: In BPH patients, the presence of concomitant DOA is independently associated with only age, IPSS, and OAB-V8 scores. It will be very logical to consider concomitant DOA and especially to routinely use OAB questionnaire in the management of patients with previous diagnosis of clinical BPH and ongoing LUTS despite receiving prolonged medical treatment.

Key words: Benign prostate hyperplasia, detrusor overactivity, lower urinary tract symptoms, urodynamic testing.

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Introduction

Detrusor overactivity (DOA) is a frequent cause of lower urinary tract symptoms (LUTS) and incontinence. DOA is characterized by frequency, urgency, nocturia, and/or urge incontinence, and also involuntary contractions in filling cystometry (1). Although the mechanism is not well known, benign prostate hyperplasia (BPH) is known among the etiologic factors of benign prostatic enlargement (BPE), bladder outlet obstruction (BOO), lower urinary tract symptoms (LUTS), or a combination of these components. The term of BPH is a histopathological diagnosis, but this term is commonly used to mean clinical BPH in current practice.

It has been determined that some morphological and functional alterations occur in detrusor muscle, which has some potential effects on the occurrence of LUTS (2). The frequencies of BPH and DOA comparatively increase with aging (3). Although DOA is commonly appeared with storage symptoms, benign prostatic obstruction (BPO) is a frequent diagnose that is commonly characterized by voiding LUTS (4). Many of pressure-flow studies in patients with clinical BPH commonly show BOO that is characterized by decreased urine flow and increased detrusor pressure (Pdet). The continuous obstruction distal to bladder may cause DOA by some mechanisms not well known, such as decreased blood flow and ischemia, cholinergic denervation, consequent supersensitivity of muscarinic receptors to acetylcholine and increased detrusor collagen content (2, 5, 6). It has been reported that DOA is commonly concomitant to BPH, and the frequency of this association significantly increases with aging (7, 8). In clinical practice, such patients are commonly treated by medications directed to BPH without determining the concomitant DOA, which is resulting in treatment failure and patient displeasure.

In this report, we aimed to investigate the prevalence of DOA concomitant BPH and the relationship between some of the characteristic parameters of clinical BPH and the presence of concomitant DOA in men, who were with bothersome LUTS and could not be adequately improved

Table 1. The comparison of the parameters between two groups (by using independent sample t test).

DETRUSOR OVERACTIVITY					
Parameters	**Pure BPH (without DOA) (Group 1, n=48)**		**BPH+ DOA (Group 2, n=52)**		**p values***
	Median	**Std. D.**	**Median**	**Std. D.**	
AGE	60,958	5,140	68,346	8,718	<0,001*
PROSTATE SIZE	49,580	14,112	51,880	11,914	0,383 √
Q MAX	13,700	5,133	7,758	3,560	<0,001*
CREATININE	0,888	0,084	1,152	0,205	<0,001*
IPSS SCORE	13,063	5,583	21,596	6,518	<0,001*
OAB-V8 SCORE	8,125	2,951	19,192	6,692	<0,001*
THE DURATION OF EVIDENT LUTS(MONTH)	27,333	14,371	27,423	15,057	0,738 √

* Statistically significant value
√ Statistically insignificant value

Table 2. The demonstration of independently significant parameters with the results of logistic regression analysis.

Parameters	Significant p values	The probability rates (%95 GA)
AGE	<0,001	0,941 (0,911-0,972)
IPSS SCORE	0,003	0,575 (0,398-0,829)
OAB- V8 SCORE	<0,001	2,873 (1,681-4,912)

by prolonged medical treatment yet.

Materials and methods

This is a prospective analysis of 100 patients with a previous diagnosis of clinical BPH who were on follow-up with medical treatment in our outpatient clinic, could not be adequately improved by this treatment yet, and were interned in our clinic for prostate surgery between April 2008 and May 2009. The sample had bothersome LUTS despite receiving medical treatment (alpha-blocker, 5-alpha reductase inhibitor, or combination) and no previous diagnosis of DOA. All patients were exhaustively informed about the study. A detailed history was taken, and a detailed physical examination including neurological check-up was performed to exclude the patients with other urological or nonurological causes of LUTS and DOA. International Prostate Symptom Score (IPSS) and Overactive Bladder V-8 (OAB V-8) questionnaires were completed, and the results were recorded in our database. At initial presentation, PSA, creatinine, prostate volume on suprapubic ultrasound (USG), Qmax, and postvoid residual urine measurements were done. Patients with a suspicious PSA value (> 4 μg/l) were scheduled for a prostate biopsy and excluded from the study. Urine culture was routinely done as a part of the preoperative examinations to exclude patients with urinary infection.

Inclusion Criteria

1. The patients who were with a previous diagnosis of clinical BPH and had prolonged medical treatment
2. The patients who were with bothersome LUTS despite receiving prolonged medical treatment and interned for prostate surgery
3. The patients with no previous urological surgery
4. The patients with no previous diagnosis of DOA and anticholinergic treatment
5. The patients with no other urological pathologies that may cause LUTS and DOA except BPH

Exclusion Criteria

1. The history of previous urological surgery
2. The presence of previously diagnosed DOA or the history of anticholinergic treatment
3. The presence of simultaneous diagnosis of urinary stone disease, urinary malignancy, urinary tract infection etc. with BPH and LUTS
4. The presence of extraurological malignancies
5. The presence of a possible disorder that may simultaneously occurs with DOA or causes DOA (such as Diabetes Mellitus, Parkinson's disease, Spinal cord pathologies, Central Nervous System disease, Multiple Sclerosis etc.)
6. The history of previous neurological surgery
7. The patients with increased PSA value requiring prostate biopsy (PSA value > 4 μg/l)

After an initial evaluation, a pressure flow study was routinely performed to demonstrate the presence of possible DOA and BOO in all patients. The same experienced investigator performed the urodynamic investigations that were in line with the suggested good urodynamics practice standards of the International Continence Society (ICS) (9). All patients were measured in the sitting position after a sterile urine culture. Urodynamic examination was performed by using a 6-Fr double-lumen transurethral catheter, a 10-Fr single lumen rectal catheter, and superficial EMG electrodes. Sterile physiological saline solution at a temperature of 37.8 C was infused through the transurethral catheter with an infusion speed of 25–50 ml/min. DOA was defined according to the 2002 classification of ICS as spontaneous or provoked involuntary detrusor contractions during the bladder-filling phase regardless of amplitude. Furthermore, BOO was characterized by decreased urine flow with simultaneously increased detrusor pressure (Pdet) during voiding phase (10).

After the elimination of measurement artefacts, the urodynamic traces were analysed by an experienced urologist. As a result of this evaluation, the frequency of DOA concomitant to BPH was exhibited in our sample. On the other hand, the presence of any relationships between the presence of DOA concomitant to BPH and the characteristic parameters of BPH, such as prostate volume, Q max, age, creatinine, the duration of evident LUTS, IPSS and OAB V-8 scores were evaluated.

For statistical analysis, SPSS version 11.0 (SPSS, Inc, Chicago, IL, USA) was used, and a p-value of 0.05 was considered significant. The groups of pure BPH (Group1) and BPH with DOA (Group 2) were compared by using parametric tests. Because, the data was measurable; and the sample size had adequate capacity. Free sample t-test was used to compare the numeric data. Logistic regres-

sion analysis was performed for the multivariate analysis, and the probability rates were separately measured for all parameters.

Results

The mean age was 64.8± 6.74 (49- 81). It was found that the mean prostate volume was 50.78± 12.51 ml, the mean value of Qmax was 10.61± 4.28 ml/s, the mean value of creatinine level was 1.025 ± 0.13 mg/dl, and the mean value of the duration of evident LUTS was 27.38± 14.83 months. However, the mean values of IPSS and OAB V-8 scores were 17.50± 5.98 and 13.88± 4.75, respectively. Four men (%4) had an IPSS of 7 or less, whereas 96 men (%96) had an IPSS of more than 7. Furthermore, two (%2) patients had OAB V-8 score < 8, and 98 (%98) had scores ≥ 8.

Filling cystometry showed spontaneous or provoked uninhibited contractions in 52 of 100 patients. In pressure-flow studies, obstructive voiding findings (BOO) were determined in all patients (n: 100). It has been found that the prevalence of DOA concomitant to BPH was 52% in our sample. Group 1 included the patients (n= 48) who had obstructive findings with no uninhibited contractions (BPH without DOA), and group 2 included the patients (n= 52) with uninhibited contractions and obstructive findings (BPH+ DOA).

The characteristic parameters of clinical BPH were separately determined in each groups and statistically compared in each other. The mean ages were 60.95 in group 1 and 68.34 in group 2. The mean prostate volume and Q max were 49.58 ml and 13.70 ml/s in group 1, and these were 51.88 ml and 7.75 ml/s in group 2; respectively. In addition, the duration of evident LUTS was found 27.33 months in group 1 and 27.42 months in group 2. It was determined that IPSS and OAB V-8 scores were 13.06 and 8.12 in group 1, and these were 21.59 and 19.19 in group 2; respectively (table 1). The statistical analysis of the data showed that the patients in group 2 were significantly older and had significantly lower Qmax, higher creatinine level, higher IPSS and OAB V-8 scores (p< 0.001). On the other hand, there were no statistically significant differences between the parameters of prostate volume and the duration of evident LUTS of two groups (p: 0,383, p: 0,738; respectively).

Furthermore, multivariate analysis revealed that only age (p< 0.001), IPSS (P: 0.003) and OAB V-8 (p< 0.001) scores were independently associated with DOA concomitant to BPH. The probability rates as the results of logistic regression analysis were shown in table 2 (table 2).

Discussion

Benign Prostate Hyperplasia is a common disorder in aging men with increasing frequency (3, 11). For a long time, BOO related to BPH has been accepted as the main factor in the mechanism of LUTS, and the treatment of this obstruction has been the main target of most of the treatment regimens (12, 13). Nevertheless, recent studies showed that BPH did not always progress as a separate disease, and it was commonly together with DOA (14-19). This cooperation had a real significance in changing the classical management of such patients, and many studies were conducted to show how frequently DOA together with BOO in BPH patients was.

In this sense, we aimed to investigate the prevalence of DOA concomitant BPH and the relationships between some of the characteristic parameters of clinical BPH and the presence of concomitant DOA in men who were with bothersome LUTS and could not be adequately improved by prolonged medical treatment yet. Therefore, we created a sample that included 100 BPH patients who had different degrees of ongoing LUTS despite receiving prolonged medical treatment, and were interned to our clinic for prostate surgery. According filling cystometry, the frequency of DOA concomitant to BPH was found %52. In addition, pressure-flow study results showed that all patients had obstructive voiding findings (BOO). While in one study, the evaluation of 162 BPH patients manifested that the frequency of DOA was %45 (14), other two independent studies showed that the frequency was %50 (15, 16). Hyman et al. had also similar results (17), and a metaanalysis of 1418 patients with LUTS showed that 864 patients (%60.9) had DOA concomitant to BPH (18, 19). Our results were similar with these studies above.

In a previous study, the prevalence of DOA before TUR-P was found %68, and it decreased to %31 after 5 years from the prostate surgery showing that DOA did not completely disappear in every patient after the surgery of BPO (20). It is known that aging and other not clearly proven parameters have significant roles in the

pathophysiology of DOA, and it has been shown that it was not possible to treat DOA by only treating BOO related to BPH (21). Therefore, we thought that it would be more effective and helpful if the clinicians separately consider this frequent disorder, which commonly affects the classical diagnosis and treatment modalities of BPH.

Some reports showed that the characteristic parameters of BPH, such as prostate volume, Qmax, residual urine did not have significant correlations with the severity of LUTS (11, 22- 24). LUTS related with storage may also continue after a successful removal of the prostate (25, 26). May the diagnostic parameters of clinical BPH have any relationships with the presence of concomitant DOA? If yes, which parameters have any relations? Hence, we analysed the parameters of prostate volume, Qmax, age, creatinine level, the duration of evident LUTS, IPSS and OAB V-8 scores by parametric tests, and the results were statistically compared between two groups. We have seen that although age, Qmax, creatinine level, IPSS and OAB V-8 scores had significant differences (P<0.001), prostate volume and the duration of evident LUTS had no significant correlations with the presence of concomitant DOA (P: 0.383, P: 0.738). As a result of this comparison, it has been found that the patients with BPH and DOA were older and had lower Qmax, higher creatinine, higher IPSS, and OAB V8 scores. Nevertheless, the logistic regression analysis showed that just the parameters of age, IPSS and OAB V8 scores had independently significant relations with the presence of concomitant DOA (P<0.001, P: 0.003).

One study that analysed 162 BPH patients and compared the parameters between two groups (BPH alone and DOA with BPH) reported that the patients with BPH and DOA were significantly older, had lower voided volume at uroflowmetry, higher PSA levels and more severe obstruction. Besides, prostate volume, IPSS score, Qmax, and postvoid residual urine volume had no significant differences between two groups (14). In a metanalysis, it has been shown that men with DOA were significantly older, commonly had irritative IPSS subscores, higher prostate volume, lower voided volume at uroflowmetry and lower maximal cystometric bladder capacity. Most of the parameters had significant relations in univariate analysis. Nevertheless, the logistic regression analysis showed that just age and obstruction grade had independently significant relations with DOA (18).

The relationship between increasing age and the presence of DOA was the evident significant parameter in the literature. In our study, it has been shown that IPSS and OAB V8 scores were also independently related to the presence of concomitant DOA. Moreover, according to the multivariate analysis results of our study, the patients with clinical BPH and concomitant DOA were significantly older, higher IPSS and OAB V8 scores. We thought that it might be a very helpful management style routinely using the OAB questionnaire especially in elderly patients with evident LUTS despite receiving prolonged medical treatment, because of its potential effect on the treatment and the quality of life (QoL).

While it was known that the bladder outlet obstruction in BPH patient was related to the infravesical obstruction secondary to BPH, but now the focus to understand the storage LUTS and DOA concomitant to BPH shifted from prostate to the bladder(11, 27). Some potential mechanisms such as myogenic, epithelial, neurogenic or a combination have been shown to explain the occurrence of concomitant DOA (27-30). Bladder outlet obstruction due to BPH caused some morphological(increased collagen deposit and bladder wall thickness, neurological hypertrophy, the increase and alteration of adrenoreceptors) and functional alterations (ischemia, the imbalance of neurotransmitters, the electrical changes in bladder smooth muscle cells, remodelling of spinal micturition reflex) in the bladder wall (27- 30). The microscopic analysis of detrusor muscle showed some abnormal gap junctions, responsible from the spread of the spontaneous depolarisation and the occurrence of synchronized uninhibited contractions in some sections (29, 30).

Clinical BPH and concomitant DOA were two different combined pathologies in men. Therefore, it will be very logical to consider possible concomitant DOA and especially to routinely use OAB questionnaire in the management of patients with previous diagnosis of clinical BPH and ongoing LUTS despite

receiving prolonged medical treatment. The limitations of this study were including a limited sample and only the patients who had obstructive findings in pressure-flow studies, and not having any of non-obstructive cases. The determination of BOO in all sample was attributed to small size of the sample and the patient selection that was performed in patients who were with previous diagnosis of clinical BPH and bothered with evident LUTS despite receiving prolonged medical treatment, and were interned for prostate surgery. In conclusion, neither causes nor processes of concomitant DOA are clearly known yet. DOA is a very common pathology in BPH patients. Age, IPSS, and OAB- V8 scores were independently associated with the presence of concomitant DOA. The presence of DOA concomitant to BPH was more common in older patients and patients with higher IPSS and OAB- V8 scores. Nevertheless, prostate volume, Qmax and other characteristic parameters had no independently relations with the presence of concomitant DOA. We thought that it might be a very effective and helpful strategy to consider possible concomitant DOA and especially to routinely use OAB questionnaire in the management of patients with previous diagnosis of clinical BPH and ongoing LUTS despite receiving prolonged medical treatment. According to our opinion, well planned, more detailed and comprehensive studies are required about these common and bothersome concomitant disorders.

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