의학석사 학위논문

Change in bladder wall thickness and detrusor wall thickness after surgical treatment of benign prostatic enlargement in patients with lower urinary tract symptoms

하부요로증상 환자들에서 전립선의 수술적 치료 후 발생하는 방광벽 및 배뇨근의 두께 변화에 관한 연구

2014년 2월

서울대학교 대학원

임상의과학과

이 학 민

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지도 교수 손 환 철

이 논문을 의학석사 학위논문으로 제출함

2013년 10월

서울대학교 대학원

임상의과학과

이 학 민

이학민의 의학석사 학위논문을 인준함

2014년 02월

위 원 장 _____ (인)

부위원장 _____ (인)

위 원 _____ (인)

학위논문 원문제공 서비스에 대한 동의서

본인의 학위논문에 대하여 서울대학교가 아래와 같이 학위논문 제공하는 것에 동의합니다.

1. 동의사항

① 본인의 논문을 보존이나 인터넷 등을 통한 온라인 서비스 목적으로 복제할 경우 저작물의 내용을 변경하지 않는 범위 내에서의 복제를 허용합니다.

② 본인의 논문을 디지털화하여 인터넷 등 정보통신망을 통한 논문의 일부 또는 전부의 복제.**배포** 및 전송 시 무료로 제공하는 것에 동의합니다.

2. 개인(저작자)의 의무

본 논문의 저작권을 타인에게 양도하거나 또는 출판을 허락하는 등 동의 내용을 변경하고자 할 때는 소속대학(원)에 공개의 유보 또는 해지를 즉시 통보하겠습니다.

3. 서울대학교의 의무

① 서울대학교는 본 논문을 외부에 제공할 경우 저작권 보호장치(DRM)를 사용하여야 합니다.

② 서울대학교는 본 논문에 대한 공개의 유보나 해지 신청 시 즉시 처리해야 합니다.

논문제목 : Change in bladder wall thickness and detrusor wall thickness after surgical treatment of benign prostatic enlargement in patients with lower urinary tract symptoms: A preliminary report

학위구분 : **석사 ■ · 박사 □**
학 과 : 임상의과학과
학 번 : 2012-22721
연 락 처 :
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제 출 일 : 2013 년 10 월 22 일

서울대학교총장 귀하

Abstract (English)

Introduction:

The purpose of the present study was to evaluate the perioperative changes in bladder wall thickness and detrusor wall thickness after transurethral prostatectomy.

Methods:

Fifty-one men who were treated for benign prostatic hyperplasia/lower urinary tract symptoms with transurethral prostatectomy were prospectively analyzed from May 2012 to July 2013. Prostate size, detrusor wall thickness, and bladder wall thickness were assessed by transrectal and transabdominal ultrasonography perioperatively. All postoperative evaluations were performed 1 month after the surgery.

Results:

The mean age was 69.0 years, the mean prostate-specific antigen was 8.1 ng/mL, and the mean prostate volume was 63.2 mL. The mean bladder wall thickness was 5.1(±1.6,SD) mm, 5.1(±1.6,SD) mm, and 5.0(±1.4,SD) mm preoperatively and 4.5(±1.5,SD) mm, 4.5(±1.3,SD) mm, and 4.6(±1.2,SD) mm postoperatively (anterior wall, dome, and trigone, respectively; p = 0.178, 0.086, and 0.339, respectively). The mean detrusor wall thickness was 0.9(±0.4,SD) mm preoperatively and 0.7(±0.3,SD) mm postoperatively (p = 0.001). A subgroup analysis stratifying patients into a large prostate group (weight, ≥45 g) and a high Abrams-Griffiths number group (>30) showed a significant decrease in detrusor wall thickness (p = 0.002, p = 0.018).

Conclusions:

There was a decrease in detrusor wall thickness after transurethral prostatectomy. The large prostate group and the high Abrams-Griffiths number group showed a significant decrease in detrusor wall thickness after surgery.

Keywords: Prostate, Bladder, Low urinary tract

Student Number: 2012-22721

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Introduction

Benign prostatic hyperplasia (BPH) and lower urinary tract symptoms (LUTS) have become very common among middle-aged men in Korea. The overall prevalence of BPH/LUTS is approximately 40% among men aged >65 years [1]. However, the relationship between benign prostatic enlargement, LUTS, and bladder outlet obstruction (BOO) is unknown. Therefore, there has been much effort to understand this conundrum in the last decade. The gold standard diagnostic tool for BOO traditionally has been the pressure-flow study (PFS), but it is an invasive, expensive, and time-consuming procedure [2]. Moreover, the increasing number of PFSs is not clinically favorable [3].

Bladder wall thickness (BWT) and detrusor wall thickness (DWT) assessments have been shown to be promising substitutes for PFSs to diagnose BOO [4-8]. They are noninvasive, easy to perform, and less time-consuming than PFSs. Another strong point is that it can be performed in combination with transrectal prostate ultrasonography. There are already commercially available instruments that can measure BWT and automatically estimate bladder weight using transabdominal ultrasonography [9].

Studies have shown that the relief of obstruction by surgery reduces secondary bladder hypertrophy caused by BOO [10,11]. However, the change in BWT and DWT after surgery for BPH is poorly investigated thus far. Accordingly, the present study aimed to evaluate the perioperative changes in these parameters and to investigate whether a change in these parameters differ depending on patients' baseline characteristics.

Materials and Methods

Between May 2012 and July 2013, 56 patients were surgically treated for LUTS/BPH. Patients with a history of neurologic disease, urologic surgery, urinary stones, or urethral stricture, any malignancy in pelvic cavity were excluded. One patient who had prostate cancer after the surgery was excluded from the study. Thus, a total of 51 men were analyzed for this study. This study was designed as a prospective observation study. Data were collected during the preoperative assessment and postoperative follow-up examination. Preoperative workup includes trans-rectal prostate ultrasonography, free uroflowmetry, and the International Prostate Symptom Score (IPSS). BWT and DWT were simultaneously assessed with transrectal ultrasonography (7.5 MHz, SA-8000, Medison, Seoul, Korea).

The surgery was performed by 2 experienced urologists. All patients were treated by transurethral prostatectomy. At the postoperative follow-up examination 1 month after the surgery, transabdominal and transrectal ultrasounds were performed. DWT was assessed after uroflowmetry in the suprapubic area (Figure 1). BWT was checked at 3 locations (i.e., the anterior wall, dome, and trigone) using transrectal prostate sonography after uroflowmetry. All these sonographic examinations were performed by a single experienced radiologist during the postmicturition state after uroflowmetry [12].

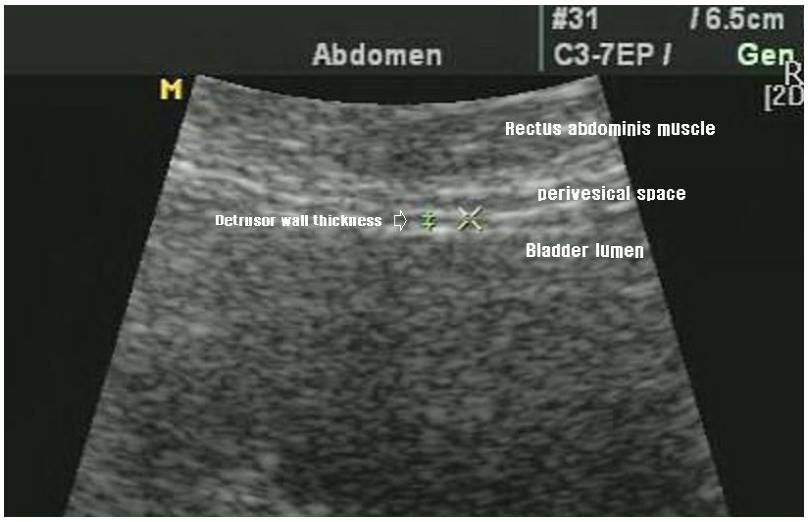

Figure 1. Measurement of detrusor wall thickness by transabdominal approach

Subgroup analysis was performed by stratifying patients according to prostate size, response after surgery, and the Abrams-Griffiths (AG) number. The response after surgery was determined to be good when the change in IPSS was >4. The paired samples t-test and Wilcoxon signed-rank test were used to analyze the differences after the surgery. A p value 0.05 was considered significant. All statistical analyses were performed using commercially available software (SPSS 19.0, Chicago, IL, USA).

RESULTS

The baseline characteristics are presented in Table 1. The mean prostatic volume was 63.2 mL. The mean preoperative and postoperative IPSS was 24.5 and 18.5, respectively.

Variable	Mean value ± SD (range)
No. of patients	51
Age (years)	69.0 ± 7.6 (49–83)
BMI (kg/m^2)	16.4 ± 3.8 (9.2–24.5)
PSA (ng/dL)	7.4 ± 9.3 (0.1–41.4)
Preoperative IPSS	24.6 ± 10.2 (3–41)
Preoperative Qmax (mL/s)	7.7 ± 4.3 (1.3–19.0)
Preoperative BWT (mm)	
Anterior	5.1 ± 1.6 (2.5–10.8)
Dome	5.1 ± 1.6 (2.6–10.8)
Posterior	5.0 ± 1.4 (2.6–9.6)
Preoperative DWT (mm)	0.9 ± 4.0 (0.3–2.1)

TABLE 1. Patient demographics

The change in the parameters after the surgery is shown in Table 2. IPSS and DWT significantly decreased after the surgery, but no significant change in DWT and the maximal urinary flow rate (Qmax) was noted.

Variables (mean)	Preoperative	Postoperative	
IPSS	24.6 ± 10.2	18.5 ± 10.4	p = 0.003
DWT (mm)	0.9 ± 0.4	0.7 ± 0.3	p = 0.001
BWT (mm)			
Anterior	5.1 ± 1.6	4.5 ± 1.5	p = 0.178
Dome	5.1 ± 1.6	4.5 ± 1.3	p = 0.086
Trigone	5.0 ± 1.4	4.6 ± 1.2	p = 0.339
Qmax (mL/s)	7.7	9.4	p = 0.085

TABLE 2. Changes in parameters after surgery

A subgroup analysis was performed by stratifying patients according to prostate size, response after surgery, and the AG number from their preoperative PFS (Table 3). DWT significantly decreased after surgery in the high AG number group (≥30). The subgroup analysis of prostate size revealed that there was a significant decrease in DWT in the large prostate group (≥45g). In the small prostate group, the decrease in BWT was significant. Good responders after surgery showed significant Qmax improvement compared with that of the nonresponder group, whereas both BWT and DWT decreased in the nonresponder group.

Variables	Prostate size ≥ 45 (n = 31) (mean)			Prostate size < 45 (n = 20) (mean)		
	Preoperative	Postoperative		Preoperative	Postoperative	
DWT (mm)	0.97 ± 0.46	0.74 ± 0.32	p = 0.001	0.75 ± 0.26	0.66 ± 0.23	p = 0.232
BWT (mm)						
Anterior	5.42 ± 1.70	4.92 ± 1.62	p = 0.194	4.74 ± 1.36	3.97 ± 0.93	p = 0.011
Dome	5.40 ± 1.71	4.92 ± 1.53	p = 0.262	4.76 ± 1.42	3.94 ± 0.69	p = 0.014
Posterior	5.27 ± 1.45	4.96 ± 1.36	p = 0.345	4.66 ± 1.15	4.11 ± 0.70	p = 0.036
Qmax (mL/s)	7.67 ± 4.54	9.82 ± 7.47	p = 0.245	7.80 ± 3.91	8.87 ± 5.37	p = 0.575
Variables	Change of IPSS ≥ 4 (n = 24)			Change of IPSS < 4 (n = 20)		
	Preoperative	Postoperative		Preoperative	Postoperative	
DWT (mm)	0.91 ± 0.50	0.75 ± 0.38	p = 0.056	0.84 ± 0.29	0.66 ± 0.19	p = 0.022
BWT (mm)						
Anterior	4.88 ± 1.31	4.56 ± 1.46	p = 0.203	5.23 ± 1.50	4.13 ± 0.96	p = 0.006
Dome	4.88 ± 1.42	4.57 ± 1.34	p = 0.287	5.26 ± 1.42	4.09 ± 0.79	p = 0.002
Posterior	4.84 ± 1.29	4.60 ± 1.20	p = 0.335	5.13 ± 1.13	4.31 ± 0.76	p = 0.009
Qmax (mL/s)	7.24 ± 3.93	12.35 ± 7.64	p = 0.002	9.05 ± 4.36	8.26 ± 3.71	p = 0.438
Variables	AG number ≥ 30 (n = 18)			AG number < 30 (n = 18)		
	Preoperative	Postoperative		Preoperative	Postoperative	
DWT (mm)	0.944 ± 0.43	0.749 ± 0.38	p=0.018	0.87±0.35	0.70 ± 0.17	p = 0.059
BWT (mm)						
Anterior	4.92 ± 1.66	4.72 ± 1.66	p=0.461	5.52 ± 2.15	4.64 ± 1.29	p = 0.177
Dome	5.04 ± 1.26	4.61 ± 1.58	p=0.222	5.35 ± 2.16	4.61 ± 1.23	p = 0.286
Posterior	4.94 ± 1.09	4.82 ± 1.54	p=0.653	5.16 ± 1.76	4.66 ± 0.96	p = 0.355
Qmax (mL/s)	8.84 ± 3.45	12.74 ± 7.85	p=0.122	8.51 ± 4.60	7.12 ± 4.21	p = 0.286

TABLE 3. Subgroup analysis

Discussion

In the last decade, a number of studies have shown the effectiveness of various diagnostic parameters such as BWT and DWT, but there are still several limitations associated with their clinical use as diagnostic tools because normative data, a standardized procedure, and unified bladder filling are still lacking. Nevertheless, many studies have found a relevant relationship between BOO and these parameters [3,5-8,12].

Vincenzo et al described "bladder wall hypertrophy as first line anatomic change after BOO" in their review [14]. Oelke et al assessed DWT in patients with BOO and found a positive correlation between the degree of BOO and DWT [5]. DWT was 1.33, 1.62, 2.4, and >3 mm in the unobstructed, equivocal, obstructed, and severely obstructed groups, respectively. Oelke et al also reported DWT to be a sensitive parameter to predict BOO compared with other parameters such as Qmax and postvoid residual urine (PVR) [7]. DWT 2 mm showed a high positive predictive value of 94%. Kessler et al assessed 102 patients with LUTS and found that DWT was significantly higher in the obstructed group than in the unobstructed and equivocal groups [6]. DWT >2.9 mm showed a strong predictive value of BOO (positive predictive value = 100%, specificity = 100%, and sensitivity = 43%).

Several studies showed that bladder hypertrophy was reversible after the resolution of BOO. Nielsen et al reported a 6-fold increase in bladder weight, a 3-fold increase in the muscle cell number, an 8-fold increase in collagen content after the creation of BOO, and a partial reversal after recovery in an animal study [15]. Kojima et al analyzed the estimated bladder weight before and after surgical treatment of BPH (open prostatectomy and transurethral prostatectomy), and bladder hypertrophy was markedly reduced after the surgery. The mean estimated bladder weight was 52.9 g preoperatively and 31.6 g after 3 months, and that of the control group was 26.5 g [16-18].

Based on previous studies, the present study showed that DWT decreased after surgery for BPH ($p = 0.001$). In addition, the change in DWT after surgery was associated with the preoperative prostate size and AG number (Table 3). In a subgroup analysis of the AG number, both groups showed a decrease in BWT and DWT, but the decrease in DWT was significant only in the high AG number group. DWT is related to smooth muscle hypertrophy, which can result from BOO. This finding suggests that DWT can be a more sensitive indicator of BOO than BWT. This

result corroborates findings from other studies that showed a decrease in bladder weight after resolving BOO [10].

There was a significant decrease in BWT and DWT in the nonresponder group (change of IPSS < 4). Although IPSS is a good representative of subjective symptoms of patients, it is difficult to establish a direct relationship between IPSS and BOO. Changes in BWT and DWT are considered associated with resolving BOO and not with symptoms. Therefore, the significant changes in BWT and DWT in the nonresponder group could have resulted from unconformity between subjective symptoms and structural alteration or the small number of samples.

However, compared with that measured in other studies, the DWT measured in the present study is relatively small. The mean DWT was 0.944, ranging from 0.901 to 1.37 even in the high AG number group. Unavoidable measurement error and personal error are known issues when measuring DWT. Considering that the approximate range of DWT is 1–2 mm, the impact of these errors can be more profound. Moreover, DWT is not uniform; it can vary depending on the site examiners choose to measure. To reduce these errors, ultrasonographic examination in the present study was performed by a single radiologist in a consistent manner. The discrepancy between the present study and previous studies might stem from racial differences; more research is needed in the future to bridge this gap.

The present study has several limitations. First, the study sample size is relative small, which might affect the robustness of our results. A follow-up study with a larger sample size and longer follow-up period are needed to confirm our outcomes. Second, bladder filling rate was not controlled in the present study. To avoid unnecessary invasive procedures, we assessed BWT and DWT during the post-micturition state. The bladder filling rate affects BWT and DWT and, thus, might have affected the results of the present study. To control this factor, an invasive procedure such as catheterization is needed. However, it is contradictory that measuring DWT, a noninvasive predictor of BOO, needs catheterization. Moreover, using a catheter to control the bladder filling rate is impractical for clinical use.

Finally, there is a possibility of bias because of the differences in PVR between the high and low AG number groups. The mean PVR was 75.2 mL and 31.1 mL for the high and low AG number groups, respectively. Considering the negative correlation between DWT and the bladder filling rate, DWT could have been underestimated in the high AG number group because of the high

PVR. Because the underestimation of DWT leads to underestimation of the change in DWT in the high AG number group, the direction of bias does not weaken our results.

Conclusion

DWT significantly decreased after transurethral resection of BPH, and patients in the large prostate and high AG number group showed a significant decrease in DWT after surgery in this preliminary study..

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초 록

서론:

경요도 전립선 절제술 이후에 발생하는 방광벽 및 배뇨근의 변화를 측정하여 하부 요로의 수술 전후의 구조적 변화 양상에 대하여 이해하고자 하였다.

방법:

2012년 5월에서부터 2013년 7월에 걸쳐 하부요로 증상으로 경요도 전립선 절제술을 시행받은 51명의 환자를 대상으로 전향적으로 분석하였다. 전립선의 크기, 배뇨근의 두께, 방광벽의 두께를 경직장, 경복부 초음파를 이용하여 수술 전 및 수술 후 1개월에 측정하였다.

결과:

환자의 평균 나이는 69세, 평균 전립선 특이 항원의 농도는 8.1ng/ml, 평균 전립선 크기는 63.2ml로 측정되었으며, 전벽, 천장, 삼각부에서 측정한 방광의 두께는 수술 전 5.1(±1.6,SD)mm, 5.1(±1.6,SD)mm, 5.0(±1.4,SD)mm로 측정되었고, 수술 후 4.5(±1.5,SD)mm, 4.5(±1.3,SD)mm, 4.6(±1.2,SD)mm 로 측정되었다. 배뇨근의 두께는 수술 전 0.9(±0.4,SD)mm, 수술 후 0.7(±0.3,SD)로 측정되었다. 전립선의 크기 및 Abrams-Griffiths number group으로 나누어 하위집단을 분석해보았을 때, 전립선 크기가 45g인 집단과, 30이상의 Abrams- Griffiths number집단에서 수술 전후로 유의한 배뇨근의 두께 변화를 보여주었다.

결론:

경요도 전립선 후에 배뇨근의 두께에 유의한 감소를 발견할 수 있었으며, 전립선의 크기가 큰 집단과 Abrams- Griffiths number 가 30 이상인 집단에서 수술 후에 배뇨근의 변화에 유의한 변화를 발견할 수 있었다.

주요어: 전립선, 방광, 하부 요로
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