Efficacy and Safety of Augmentation Ileocystoplasty for the Treatment of Interstitial Cystitis

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Aims of Study: Bladder pain syndrome/interstitial cystitis (BPS/IC) is a chronic condition that characterized by irritative bladder symptoms and suprapubic pain. Although a number of nonsurgical treatment modalities have been used, some patients have refractory conditions that do not respond at all to symptomatic treatment. Augmentation ileocystoplasty is one of the last options for BPS/IC refractory to conservative treatments. Reported long-term success rates of ileocystoplasty have varied from 25 to 90%. The aims of this study were to evaluate the long term efficacy and safety of augmentation ileocystoplasty for severe symptomatic patients with BPS/IC.

Materials and Methods: We prospectively evaluated 26 patients, who had undergone augmentation ileocystoplasty by single surgeon from July 2006 to February 2010 for severe BPS/IC refractory to conservative treatments. We analyzed the patients by pain visual analogue scale (VAS), 3-days micturition time chart, O'Leary-Sant IC symptom (ICSI) and O'Leary-Sant IC problem (ICPI) indexes before and after the operation. We performed voiding cystourethrography (V.C.U.G) at 3 months follow-up and urodynamic study at 6 months follow-up of the operation. Patients were interviewed for the improvement of symptoms by using global response assessment (GRA) and for interaction between the degree of symptoms and limitation of activities by using patient global assessment (PGA) questionnaires. We evaluated the responsiveness of the ICSI according to reference standards of mean change in the ICSI scores; 2.3 in those who worsened, -1.5 in stable respondents, and -5.4 in those who improved.

Result: Twenty six (mean age 58.69±10.03 years, 25 women and 1 man) patients were evaluated. The follow-up range was 4 to 34 months. The mean symptom duration was 3.9±2.0 years. Pain VAS, voiding frequency, ICSI and ICPI have improved significantly after the operation ($p<0.05$). Functional bladder capacity and maximal cystometric capacity have increase significantly after treatment (Table 1). According to the responsiveness of the ICSI, 73% of patients were improved and 19% were stable respondents. There was no patient who was worsened. Eighty-eight percents (24/26) of patients improved their symptoms after treatment according to GRA questionnaires. With PGA questionnaire, 67% (17/26) of patients had no limitation of normal activities and five patients noted that there was limitation of some normal activities. Perioperatively, there was no complication such as gastrointestinal problem like ileus. Four patients showed vesicoureteral reflux without upper urinary tract damage according to V.C.U.G. at 3 months after operation. Five patients had urinary tract infection that had resolved with antibiotic treatment. One patient showed urothelial carcinoma. Four patients were needed to perform clean intermittent self-catheterization. Of them, 3 patients had answered that their symptoms were moderately improved by global response assessment. There was no severe complication with surgery at long-term follow-up.

Conclusions: Our results showed augmentation ileocystoplasty has good outcomes that pain and frequency had decreased and bladder capacity has increased significantly. There's no severe complication with surgery for short term and long term follow up. The finding that in some clean intermittent self-catheterization is required after surgical reconstruction is in accordance with previous experience. It had known that clean intermittent self-catheterization is well accepted by patients because the overall situation is so markedly improved after surgery. We recommend augmentation ileocystoplasty is effective and safe treatment method for severe symptomatic interstitial cystitis.

Table 1. The change of pain visual analogue scale, urodynamic parameters, and O'Leary-Sant IC symptom (ICSI) and problem (ICPI) index before and after augmentation ileocystoplasty

	Baseline	Post-op (6 months)	p-value
Pain visual analogue scale	8.73±1.75	0.96±1.28	<0.05
Micturition frequency	21.55±2.05	10.74±5.35	<0.05
Maximum flow rate (mL/sec)	13.84±8.45	18.16±10.49	0.148
Maximum voided volume (cc)	130.53±27.10	283.16±63.43	<0.05
Maximal cystometric capacity (cc)	206.48±17.91	377.38±90.50	<0.05
Post voiding residual urine (cc)	31.88±30.51	150.06±190.27	0.004
O'Leary-Sant IC-Q questionnaires			
IC-Symptom index (0-20)	17.36±2.84	8.56±5.41	<0.05
IC-Problem index (0-16)	15.00±1.52	6.12±4.40	<0.05

Increased Expression of TRPA1, TRPV2, ASIC1 and CXCL9 mRNA in Bladder Tissue from Patients with Ulcer-type Interstitial Cystitis

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Aims of Study: Interstitial cystitis (IC) is a chronic inflammatory disease of the bladder with unknown etiology. The quantitative real-time polymerase chain reaction (qRT-PCR) approach offers the opportunity to discover differential gene expression independently of any prior hypothesis of etiology, providing ideas for new therapeutic strategies. In

the present study, we assessed the differential expression of the human transient receptor potential (TRP) channel gene transcripts, acid sensing ion channel (ASIC), nerve growth factor (NGF), uroplakin 3A (UPK3A) and chemokine (C-X-C motif) ligand 9 (CXCL9) in bladder tissue in IC patients and controls.

Materials and Methods: Patients with IC scheduled for hydrodistension or with non-invasive bladder cancer (as controls) undergoing transurethral resection were enrolled under informed consent. Diagnosis of IC was based on the clinical guidelines for IC and hypersensitive bladder syndrome. Cystoscopy was performed with a rigid 9-mm cystoscope under spinal anaesthesia and bladder specimens were obtained from (1) retrotrigonal portions in non-ulcer- type IC patients, (2) non-ulcerative retrotrigonal portions in ulcer-type IC patients, (3) ulcerative portions in ulcer-type IC patients, and (4) non-cancerous retrotrigonal portions in bladder cancer patients (non-IC bladder, BT) with cold-cup biopsy forceps, and placed immediately in ice-cold RNA later and stored at -80˚C. Total RNA was extracted from bladder samples, and reverse transcribed into cDNA with reverse transcriptase. The mRNA expression levels of several TRP channels (TRPA1, TRPV1, TRPV2, TRPV4, TRPM2, TRPM7 and TRPM8), ASIC1, NGF, UPK3A and CXCL9 were compared among the three groups by qRT-PCR. The mRNA levels were expressed as the fold change in the average value for non-IC bladder tissue. The protocol of the study was approved by our Institutional Review Board.

Results: After optimization of the protocol, a total of 43 specimens (non-ulcerative lesions and ulcerative lesions from ulcer type, 14; non-ulcer type, 9; bladder cancer, 6) were analyzed between October 2009 and January 2011. The subjects' background is shown in Table 1 and the qRT-PCR results are shown in Table 2.

Among the TRP channels, TRPA1 and TRPV2 showed significantly increased mRNA expression in non-ulcerative portions of ulcer-type IC compared with controls. In the same portions, a significant increase in the mRNA expression of ASIC1 and CXCL9 and a decrease in the mRNA expression of UPK3A were observed. Also, in ulcerative portions of ulcer-type IC, a significant increase in TRPV2 and CXCL9 and a significant decrease in UPK3A were found as compared with controls. However, no significant difference in any of these mRNA expressions was observed between non-ulcer-type IC tissue and controls (Fig. 1).

Conclusions: This study demonstrates increased expression of TRPA1, TRPV2, ASIC1 and CXCL9 mRNA and decreased expression of UPK3A mRNA in ulcer-type IC but no significant changes in non-ulcer-type IC. These findings suggest that there is a distinct difference in pathophysiology and disease entity between these two types of IC and also that TRPA1, TRPV2, ASIC1 and CXCL9 may be potential targets to novel therapy for ulcer type IC.

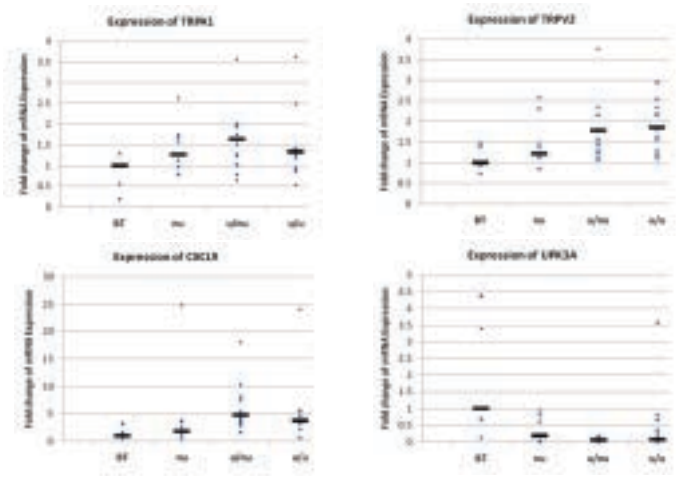
Table 1. Subjects' background

Variables	BT (control)	Non-ulcer-type IC	Ulcer-type IC
Number of patients (male/female)	6 (4/2)	9 (4/5)	14 (2/12)
Mean age (range)	74.0±9.63 (61-88)	52.3±20.5 (20-73)	70.4 ±12.2 (36-83)
BMI	22.4±2.89	23.5±4.43	22.0±2.26

Table 2. mRNA expression in the bladder tissue with interstitial cystitis (fold change of control)

	Non-ulcer type IC		Ulcer-type IC			
Gene symbol			Non-ulcerative lesion		Ulcerative lesion	
	Fold change	p-value (n=9)	Fold change	p-value (n=14)	Fold change	p-value (n=14)
ACTB	0.87	0.272	1.39	0.179	1.38	0.179
TRPA1	1.27	0.388	1.64	0.041*	1.34	0.353
TRPV1	1.32	0.145	1.47	0.076	0.61	0.779
TRPV2	1.23	0.456	1.79	0.005**	1.86	0.009**
TRPV4	1.08	0.776	0.83	0.274	0.79	0.153
TRPM2	0.40	0.328	1.17	0.968	1.02	0.841
TRPM7	0.95	0.955	1.02	0.779	0.96	0.779
TRPM8	2.39	0.224	1.45	0.091	1.51	0.109
NGF	2.45	0.181	1.57	0.207	0.61	0.659
ASIC1	1.22	0.272	1.57	0.009**	0.91	0.779
UPK3A	0.19	0.224	0.07	0.009**	0.08	0.033**
CXCL9	1.82	0.224	4.78	0.000**	3.78	0.006**

GAPDH mRNA levels were used as an internal normalization control
The p-values were determined by the Wilcoxon rank-sum test (*p<0.05, **p<0.01)



BT: bladder tumor (control); nu: non-ulcer type IC; u/nu: non-ulcerative lesion of ulcer type IC; u/u: ulcerative lesion of ulcer type IC

Fig. 1. mRNA expression of TRPA1, TRPV2, CXCL9 and UPK3A in the bladder tissue.

Bladder Damage Induced by Ketamine Abuse in a Rat Animal Model

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Aims of Study: Clinically, ketamine abuse is associated with severe lower urinary tract dysfunction. Reduced bladder capacity and hemorrhagic cystitis with irreversible pathological changes may develop in some cases of long-term drug abuse. Up to now, the mechanisms that cause these severe side effects are still not clear. Herein, we will determine the pathological changes and explore the pathological mechanisms of urinary bladders destruction in a novel ketamine addiction rat model.
Materials and Methods: Thirty-six rats were divided into three groups, including the control, 14 days and 28 days of ketamine injection. Ketamine administration (25 mg/kg) was given as intra-peritoneal (IP) daily injection, while the controls were administered of normal saline. In vivo isovolumetric cystometrography studies were performed. The bladder tissues were then collected for Western blotting and immunohistochemical studies.
Results: Ketamine treatment significantly increased micturition pressure, but decreased bladder capacity compared to control rats, especially after 28 days ketamine injection. Ketamine treatment also markedly decreased bladder compliance and increased the frequency of bladder non-voiding contraction. Immunofluorescence studies confirmed the neurotoxicity of ketamine. Neurofilament staining was significantly decreased after 28 days ketamine treatment. TUNEL staining showed multiple degenerated cells diffusely distributed in the urothelium, sub-urothelium, and smooth muscle layers in the ketamine treated rats. Western blotting demonstrated ketamine injection increased bladder iNOS, eNOS and COX-2 expressions in protein level.
Conclusions: Chronic exposure to low, subanesthetic concentrations of ketamine could affect cell survival and impair neuronal morphology. Impaired neuronal structure and increased inflammatory process might lead to neural networks dysfunction and altered bladder micturation reflex.

Next Surgical Management of Female Stress Urinary Incontinence after Failed Midurethral Sling: Tape Tightening or Tepeat Sling?

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Aims of Study: At present there are no guideline regarding the management of patients who fail sling procedures. We therefore compared outcomes and factors associated with cure in patients with recurrent or persistent stress urinary incontinence (SUI) after initial midurethral sling (MUS) who undergo repeat MUS or shortening of pre-implanted tape.
Materials and Methods: We enrolled all patients who underwent repeat MUS or tape shortening as a second surgical procedure due to recurrent or persistent SUI between January 2006 and June 2009. Persistent SUI was defined as leakage within 6 weeks after initial MUS in response to stress events causing increased intra-abdominal pressure, and recurrent SUI was defined as leakage occurring more than 6 weeks after initial successful MUS. The choice of treatment method was based on a joint decision by the patient and the surgeon, and all patients were theoretically suitable for either approach. Of the total of 66 women, 36 underwent repeat MUS and 30 underwent tape shortening.

All patients were followed-up for at least 12 months after second surgery. Efficacy was measured by cure and success rates on stress cough test. Safety was evaluated by assessing maximal urine flow rate (MFR), postvoid residual urine volume (PVR) and procedure- related complications.

Cure of SUI was defined as the absence of any episodes of involuntary urine leakage during stressful activities and by the results of the stress cough test. Improvement was defined as a significant decrease in urine leakage without further treatment. Failure was defined as persistent SUI after surgery or recurrent SUI during postoperative follow-up. Cure or improvement of SUI was regarded as surgical success.

Outcomes and cure rate were assessed relative to the reasons for the secondary procedure (i.e. persistent or recurrent SUI) and intrinsic sphincter deficiency (ISD). We also assessed factors associated with cure, changes in uroflowmetry parameters and procedure-related complications.
Results: There were no significant between-group differences in patients age at operation, body mass index, MFR, PVR and urodynamic parameters (valsalva leak point pressure, maximal urethral closing pressure, and maximal detrusor pressure). In contrast, there were significant differences between the two groups in SUI symptom grade, mean interval from initial surgery to secondary procedure, types of first MUS (retropubic or transobturator approach) and the reason for secondary procedure (persistent/recurrent SUI).

Although the success rates of repeat MUS and tape shortening did not differ significantly (83.3% vs 70.0%, p=0.198), the cure rate was significantly higher in patients who underwent repeat MUS (72.2% vs 46.7%, p=0.034). Among patients with ISD, the cure rate was significantly higher in patients who underwent repeat MUS than tape shortening (76.5% vs 40.0%, p=0.048). Among the patients who underwent repeat MUS, those who were cured had a significantly shorter mean interval from initial surgery to secondary procedure than those who failed the secondary procedure (14.2±21.7 vs 23.0±20.7 months, p=0.031). In patients who underwent tape shortening, only the presence of urgency incontinence was associated with cure rate (p=0.032).

The MFR decreased significantly in the repeat MUS (from 27.1 mL/s to 19.0 mL/s) but not in tape shortening (from 25.3 mL/s to 21.4 mL/s). The PVR increased significantly after repeat MUS (from 33 mL to 49.7 mL) but not after tape shortening (from 25.1 mL to 17.5 mL). One patient who underwent repeat MUS required tape cutting and one who underwent tape shortening experienced mesh erosion.
Conclusions: Repeat MUS has a higher cure rate than tape shortening in the surgical treatment of patient with persistent or recurrent SUI, especially in patients with ISD.
Keywords: midurethral sling, reoperation, urinary incontinence, stress

Evaluation of the Usefulness of the Japanese Version of Nocturia Quality of Life through a Cross-sectional Survey of Nocturia in Tochigi, Japan

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Aims of Study: To evaluate the usefulness of the Japanese version of Nocturia Quality-of-Life questionnaire (N-QoL) through a cross-sectional survey of nocturia in Tochigi, Japan.
Materials and Methods: A joint urologic survey designed to investigate the epidemiologic aspects of nocturia. A prospective questionnaire survey was conducted from October 2008 to June 2009 using outpatients in urology, orthopedics, internal medicine, surgery, gynecology, etc at 95 sites in Tochigi, Japan. Participants were surveyed with the Japanese version of N-QoL, the overactive bladder symptom score (OABSS) and self-administered questionnaires about nighttime voiding including nighttime awakening, nocturia, nighttime incontinence, falling. Since overactive bladder (OAB) is one of the main factors of nocturia, the relationship between the Japanese version of N-QoL and the OABSS as an out-standard were evaluated by the correlation coefficient (Spearman rank sum test). We considered that the absolute value of number was judged to be 0.400 or greater validity. The Jonckheerre-Terpstra test was performed to evaluate the relationship between the N-QoL and the frequency of nighttime voiding, falling, and nighttime incontinence.
Results: Overall, 2,494 subjects (male:1,154, female:1,208; with a mean age of 63.2±15.1) joined this survey and the underlying diseases were diabetes, hypertension, cardiovascular disease and benign prostatic hyperplasia. N-QoL score was 86.8±16.9 at average in 2,494 patients. Overall, 27% of subjects (625 out of 2,494 patients) were diagnosed with an OAB. Overall score of N-QoL was correlated with the OABSS (r=0.5966) and nighttime frequency score in OABSS (r=0.5389). Both Sleep/Energy domain and Bother/Concern domain in N-QoL were also well correlated with OABSS (r=0.4898, r=0.5361, respectively) and with nighttime frequency score in OABSS (r=0.4455, r=0.5361, respectively). N-QoL score was lower in the patients with nighttime awakening compared to without nighttime awakening ($p<0.0001$). Moreover, the decreasing N-QoL overall score correlate with the increasing nighttime frequency, nighttime incontinence and falling number respectively ($p<0.0001$).
Conclusions: The results of this study confirmed that the Japanese version of N-QoL was useful to evaluate nocturia. Moreover, this study represents the first report that the decreasing N-QoL overall score correlate with the increasing falling number associated with nocturnal episodes. Further interventional studies are needed for this tool.

Urinary Bladder as One of the Target Organs of Desmopressin in Nocturnal Enuresis

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Aims of Study: Nocturnal enuresis had been successfully treated by pediatric specialists with desmopressin. However, recent studies revealed that there decreasing urine amount may not be the only reason for PNE improvements. We evaluated a rat model of additional desmopressin to evaluate if bladder is affected by the use of desmopressin.
Materials and Methods: Diurnal voiding patterns of rats were monitored with metabolic cages. Desmopressin were given in half of the rats to monitor voiding pattern, cystometrography, and urine/serum biochemistry changes. Aquaporin 1, 2, and 3, along with Rho kinase and Transient receptor potential cation channel subfamily V member 4 (TRPV4) mRNA expression in bladder were evaluated for the effect of desmopressin on bladder. Urine nerve growth factor (NGF) was measured to correlate with bladder function.
Results: Voiding interval was significant different between desmopressin treated rats and control. Detrusor contractility significantly increased after desmopressin treatment, which is demonstrated in cystometrography and bladder muscle strips contractility under electric field stimulation. The overall amount of bladder aquaporin 1, 2, and 3 generally increased in experiment group at the end of the study. There were no difference in Rho kinase mRNA expression and urine NGF between the two, but TRPV4 expression is increased in desmopressin rats.
Conclusions: Desmopressin may help increase bladder contractility and decrease voiding interval, and thus improve bladder voiding efficacy. It may work through increase of aquaporin or TRPV4 expression, but may not be associated with NGF or Rho kinase.

The Impact of Overactive Bladder on Health-related Quality of Life, Sexual Life and Psychological Health in Korea

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Aims of Study: To estimate the prevalence of overactive bladder (OAB) in Korea, assess variation in prevalence by sex and age, and measure impact of OAB on quality of life regarding role limitation, sexual life, and psychological aspects.
Materials and Methods: Population-based cross-sectional telephone survey was conducted between April and June 2010 using questionnaire regarding prevalence of OAB, demographics and impact of OAB on quality of life. A geographically stratified random sample of men and women more than 30 years old were selected. To analyze differences in the prevalence by gender and age, subjects were stratified into 10 age categories, and a total of 2,000 subjects were targeted for the survey. Modified 2 items related to role limitations and personal relationships from The Korean version of the King's Health Questionnaire were used to survey the impact of OAB on job, daily life, and sexual life, and the Korean version of the Hospital Anxiety and Depression Scale was used to evaluate the impact of OAB on psychological aspects such as anxiety and depression.
Results: The overall prevalence of OAB was 22.9% (458/2,000) with 19% among male and 26.8% among female in Korean, more than 30 years old. The prevalence of OAB was more common in women than men in all ages, and increased with age in men. More than 37% of participants with OAB reported moderate (31.4%) or severe (6.2%) bothersome on their daily life due to OAB symptoms but about 5% of participants without OAB reported moderate (5.0%) or severe (0.6%) bothersome ($p<0.001$). About 19.9% of participants with OAB reported that voiding symptoms affected their sexual life but only 3.5% of participants without OAB reported about it ($p<0.001$). And About 22.7% and 39.3% of participants with OAB had anxiety and depression, but 9.7% and 22.8% of participants without OAB had those things ($p<0.001$). Only 19.7% of participants with OAB consulted a doctor for their voiding symptoms and 50.7% of respondents with OAB had willingness to visit hospital for the management of their OAB symptoms.
Conclusions: This study confirmed that OAB symptoms are highly prevalent in Korea, for which many sufferers appear to have actively sought medical help. And OAB has severe effects on daily life and sexual life as well as psychological health in Korea.

Increased Urine Nerve Growth Factor Associated with Lower Urinary Tract Symptoms and the Serum NOx Deficiency in the Men with Bladder Outlet Obstruction

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Aims of Study: Urinary nerve growth factor (NGF) levels have been shown to increase in the patients with both bladder outlet obstruction (BOO) and overactive bladder (OAB) or detrusor overactivity (Urology 2008; 72:104). Recently, several clinical studies on the phosphodiesterase type 5 (PDE5) inhibitors for the treatment of lower urinary tract symptoms (LUTS) in men with benign prostate hyperplasia (BPH) have reported significant symptom improvement. On the other hand, we have revealed that the serum nitrite plus nitrate (NOx) in the women with OAB without urge urinary incontinence (OAB-Dry) was significantly lower than any other groups (Eur Urol 2010; 9 Suppl:251). Aims of this study are to assess whether the levels of urine NGF are related to LUTS and the serum NOx levels in community-dwelling men of 40 years or older in Japan.
Materials and Methods: All participants were recruited for the purpose of a mass-screening program of 2009 for general health in a community-based study in Japan. A total of 217 men (mean 66.6 years old, range 42 to 89) were asked to complete 3-day bladder diary and questionnaire to assess LUTS using International Prostate Symptom Score (IPSS). BOO was confirmed by transrectal ultrasonography. Urinary NGF levels were assayed by using a commercial ELISA kit (NGF Emax® ImmunoAssay System, Promega, Madison, WI, USA). All NGF values were standardized by urine creatinine (NGF/Cr). Serum NOx levels were measured using a commercial EIA kit (Nitrate/Nitrite Colorimetric Assay kit, Cayman Chemical, Ann Arbor, MI, USA).
Results: The urinary NGF/Cr levels of the men with BOO significantly increased more than those of the men without BOO (0.14 vs 0.056, $p=0.005$). On the other hand, the serum NOx levels of the men without BOO were greater than those of the men with BOO, however, there were no significant differences between the two groups (62.7 vs 57.4 ∝mol/L, $p=0.61$). In subgroup of the men with LUTS (total IPSS≥8) the urinary NGF/Cr levels of the men with BOO significantly increased when compared with those of the men without BOO (0.16 vs 0.025, $p=0.003$). The serum NOx levels of the men without BOO were greater than those of the men with BOO (80.7 vs 58.0 ∝mol/L, $p=0.20$). On the contrary, in subgroup of the men without LUTS (total IPSS<8) the urinary NGF/Cr levels did not change significantly between the men with and without BOO (0.12 vs 0.085, $p=0.18$). The serum NOx levels also did not change significantly between the men with and without BOO (57.0 vs 56.3 ∝mol/L, $p=0.72$). In linear regression analysis of all participants, a statistically significant positive correlation was observed between age and IPSS ($r=0.33$, $p<0.0001$) as well as prostate volume ($r=0.22$, $p=0.019$). The serum NOx levels also had a significant statistically positive correlation with age ($r=0.17$, $p=0.013$). Although, there was not a significantly statistical correlation between the urinary NGF/Cr levels and age ($r=-0.0056$, $p=0.93$). In contrast, a significant statistically negative correlation was observed between the urinary NGF/Cr levels and the serum NOx levels ($r=-0.20$, $p=0.004$). In particular, in subgroup of the men without BOO a highly significant statistically nega-

tive correlation was observed between the urinary NGF/Cr levels and the serum NOx levels (r=-0.65, p<0.0001), while there was no significant statistical correlation between the two levels in subgroup of the men with BOO (r=-0.005, p=0.71). In multiple regression analysis of all participants, the serum NOx levels were independently correlated with the urinary NGF/Cr levels (F=21.1, p<0.0001, R^2=0.19). Moreover, in the subgroup of the men without BOO the serum NOx levels were independently correlated with the urinary NGF/Cr levels (F=27.3, p< 0.0001, R^2=0.54).

Conclusions: This study demonstrates that the increased urinary NGF/Cr levels of the men with BOO associate with LUTS and the lower serum NOx levels. The results of this study suggest that the lower urinary NGF/Cr levels may be accompanied with the greater serum NOx levels in the men with BOO. It could provide important information on the clinical significance of the PDE5 inhibitors for the treatment of LUTS in men with BPH. The serum NOx levels could also contribute as a biomarker of BPH.

Involved Extrinsic Apoptotic Pathway from the Bladder Biopsy of Patients with Interstitial Cystitis

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Aims of Study: Previous studies have reported that the apoptosis is increased in patients with interstitial cystitis (IC). However, the real mechanism is not clear today. We studied the apoptosis-associated proteins by detecting Bcl-2/Bax ratio, cleaved caspase-9, Fas, cleaved caspase-8, and cleaved caspase-3 expressions from the bladder biopsy of patients with IC, for detecting the intrinsic or extrinsic pathway.

Methods and Materials: The study group consisted of 55 patients with IC, and the control group consisted of 8 volunteers. We obtained bladder biopsies from both groups and studied the expression of apoptosisassociated proteins by immunoblotting. Data were analyzed using the Mann-Whitney *U* test.

Results: Increased apoptotic protein (cleaved caspase-3) was found in the study group than in the control group (p<0.05). The expression of Fas and cleaved caspase-8 were also increased in the study group. There is no statistical difference in intrinsic apoptotic proteins including Bcl-2/Bax ratio and cleaved caspase-9 expression between the control and study groups.

Conclusions: Our findings showed that increased apoptosis through extrinsic pathway in the bladder tissues of patients with IC.