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Original Article

Questionnaire survey assessing seasonal changes in lower urinary tract symptoms in men with benign prostate hyperplasia

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ABSTRACT

Objective: A prospective questionnaire survey was conducted for patients with benign prostatic hyperplasia (BPH) to clarify seasonal changes in the lower urinary tract symptoms (LUTS).

Material and methods: Male patients receiving α1-adrenoreceptor antagonists for BPH were enrolled. They answered the International Prostate Symptom Score (IPSS) questionnaire, and an unvalidated questionnaire that consisted of 10 questions assessing variations in the urinary stream (voiding symptoms) and urinary frequency (storage symptoms), depending upon the seasons or the patients' subjective sensations of warm and cold in last one year.

Results: A total of 412 participants answered IPSS and our unvalidated questionnaire. Of the 412 participants, 36.7% and 59.0% realized seasonal variations in urinary stream and frequency, respectively. Among patients perceiving seasonal urinary stream and urinary frequency changes (n=151 and n=243, respectively), significantly more patients realized weaker urinary stream, 59.8% (107/179) in winter compared with 26.2% (47/179) in summer, and increased urinary frequency, 69.8% (199/285) in winter compared with 20.7% (59/285) in summer ($p<0.0001$ and $p<0.0001$, respectively). Even in summer, when feeling cold, 34.7% and 56.3% realized a weaker urinary stream and an increased urinary frequency, and even in winter, when feeling warm, 53.4% and 69.4% realized a stronger urinary stream and a decreased urinary frequency. Those with seasonal stream changes showed a significantly higher IPSS total, voiding and post-voiding scores than those without, and those with seasonal frequency changes showed significantly higher IPSS total, storage, voiding, and post-voiding scores.

Conclusion: Our results revealed seasonal changes and feeling of hot and cold were associated with subjective changes of LUTS in BPH patients.

Keywords: Hyperplasia; lower urinary tract symptoms; prostate; seasons; surveys and questionnaire.

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Introduction

Previous studies have reported that the lower urinary tract symptoms (LUTS) are influenced by the patients' sensation of temperature.[1-4] In one study, a total of 2,280 residents randomly selected in three Japanese towns answered two questionnaires: the International Prostate Symptom Score (IPSS) questionnaire and the International Consultations on Incontinence Questionnaire-Short Form (ICIQ-SF). These questionnaires were administered during the summer and winter. The storage symptoms (frequency, urgency, and nocturia) were significantly worse in winter.[1] Another investigation revealed that the severity of nocturia in men with LUTS differed significantly with seasons.[2] Previous studies have focused on recording seasonal changes in scores regarding bladder capacity and temperature on validated questionnaires; however, the association between the subjective perception of warmth and cold and LUTS has not been described precisely. Thus, in this study, we administered both IPSS and an unvalidated questionnaire of our making to evaluate the seasonal changes in LUTS in men with benign prostate hyperplasia (BPH) undergoing treatment with α1-adrenoreceptor antagonists.

Material and methods

A prospective questionnaire-based study was conducted for men with BPH in our institute from April to September 2016. The participants answered IPSS and an unvalidated questionnaire of our making to assess whether the urinary stream and frequency changed with seasonal changes or the perception of hot and cold in the past one year under the supervision of urologists. Each participant answered the questionnaire once, but not in every season during the study periods, looking back on their symptoms in last one year. Patients older than 50 years old, having an estimated prostate volume exceeding 20 mL (as determined by ultrasonography), and undergoing treatment with α1-adrenoreceptor antagonists for more than a year were included. Patients with histories of complete urinary retention, prostate cancer, prostatitis or urethral stricture, cardiac or cerebral vascular disorders, hepatic disorders, renal dysfunction, or orthostatic hypertension were excluded from the study, as were those taking anticholinergics, β3-adrenoceptor agonists, and Phosphodiesterase type-5 (PDE5) inhibitor or 5-α reductase inhibitor to avoid the effects of concomitant drugs. All patients in the study provided written informed consent and the study was approved by the ethical committee of our institute (IRB 2711). The study was conducted in accordance with the Declaration of Helsinki.

A non-universal and unvalidated questionnaire consists of 10 questions assessing variations in urinary stream (voiding symptoms) and urinary frequency (storage symptoms) depending upon the seasons or the patients' subjective sensations of warm and cold in last one year (Table 1). We also evaluated the total IPSS and quality-of-life (QOL) scores and the scores of the individual IPSS items. The scores for each symptom of the IPSS includes three voiding symptoms (the item number 3: intermittency, 5: weak urinary stream, and 6: abdominal straining to void), three storage symptoms (the item number 2: frequency, 4: urgency, and 7: nocturia) and one post-voiding symptom (the item number 1: sensation of incomplete voiding).

Main Points:

- The novelty of this study lies in the fact that it focuses not only on the seasonal changes but also on the perception of warmth and cold (during the hot and cold seasons) as the effects of climatic parameters on LUTS.
- This questionnaire survey shows that seasonal changes and the perception of hot and cold are associated with subjective changes in the LUTS in men with BPH receiving α1-adrenoreceptor antagonists.
- Seasonal symptom changes and the awareness of warmth should be considered when treating LUTS in BPH patients.

According to reports from the regional meteorological stations in Japan, the highest and lowest atmospheric temperatures in the patients' residential area (longitude 139°E and latitude 36°N, in a temperate zone) during the study were 35.9°C (96.2°F) and -1.1°C (30°F), respectively; the range of daily average atmospheric temperature was 7.3°C to 29.0°C (45.1–84.2°F); and the mean temperature was 20.2°C (68.4°F).

Statistical analyses

All data were expressed as mean±standard deviations (SD), and the differences between the participants' responses to the questionnaires were evaluated by the Chi-square test. The differences in the symptom scores for clinical characteristics were analyzed with the Mann-Whitney U test. All tests were two-sided, and $p<0.05$ was considered statistically significant. All statistical analyses were performed using the JMP 14 software (SAS Institute, Cary, NC, USA).

Results

Seasonal variations in the lower urinary tract symptoms

In total, 412 patients were enrolled in the study. The mean age, body mass index (BMI), total IPSS score, and QOL index were 71.7±8.0 years old, 22.8±3.6 kg/m^2, 12.4±7.8, and 3.0±1.5, re-

Table 1. Non-validated questionnaire for a seasonal change of LUTS

Please circle the answers that apply and fill out the questionnaire.
1. Did you realize the changes in your urinary stream depending on seasons? (Yes / No)
2. If you answered "Yes", then when was it? (spring, summer, autumn, winter)
3. Comparing summer and winter, in which season did you realize weaker urinary stream? (summer, winter, no change)
4. Did you realize the changes in the urinary frequency depending on seasons? (Yes / No)
5. If you answered "Yes", then when was it? (spring, summer, autumn, winter)
6. Comparing summer and winter, in which season did you realize increased urinary frequency? (summer, winter, no change)
7. Did you realize weaker urinary stream when you feel cold, even in summer? (Yes / No)
8. Did you realize stronger urinary stream when you feel warm, even in winter? (Yes / No)
9. Did you realize increased urinary frequency when you feel cold, even in summer? (Yes / No)
10. Did you realize decreased urinary frequency when you feel warm, even in winter? (Yes / No)

LUTS: lower urinary tract symptoms

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spectively. Patients with hypertension, diabetes mellitus, and hyperlipidemia were 164, 50, and 86, respectively, and no patients had thyroid dysfunction (Table 2). Of the 412 men, 354 (85.9%) answered all 10 questions (7 men did not answer in question 1, and 12 men did not answer in question 4). Around 151 patients (36.7%) experienced seasonal variations in the urinary stream (question 1; Figure 1); of these, around 7.3% (13/179) experienced changes in the spring, 26.2% (47/179) in the summer, 6.7% (12/179) in the autumn, and 59.8% (107/179) in the winter (question 2: multiple answers allowed). Significantly, more patients chose winter as the season of realizing a weaker urinary stream as compared with summer (26.5% versus 5.1%, p<0.0001; question 3).

Of the 412 subjects, 243 (59.0%) also experienced seasonal changes in the urinary frequency (question 4; Figure 2), with

Table 2. Clinical variables with and without seasonal changes of LUTS

	Total (n=412)	Patients with seasonal change of urinary stream: Yes in Q1 (n=151)	Patients without seasonal change of urinary stream: No in Q1 (n=254)	p	Patients with seasonal change of urinary frequency: Yes in Q4 (n=243)	Patients without seasonal change of urinary frequency: No in Q4 (n=157)	p
Age (mean±S.D.)	71.7±8.0	71.6±8.5	71.8±7.7	0.760	71.7±8.0	72.1±8.0	0.653
BMI (mean±S.D.)	22.8±3.6	23.0±2.7	22.8±3.0	0.611	22.9±4.0	23.0±2.6	0.691
Hypertension, n (%)	164 (39.8%)	62 (41.1%)	102 (40.2%)	0.858	100 (41.2%)	64 (40.8%)	0.939
Diabetes Mellitus, n (%)	50 (11.9%)	16 (10.6%)	34 (13.5%)	0.393	26 (10.7%)	24 (15.5%)	0.160
Hyperlipidemia, n (%)	86 (20.9%)	32 (21.2%)	54 (21.3%)	0.987	55 (22.6%)	31 (19.8%)	0.492
Thyroid dysfunction, n (%)	0 (0%)	0 (0%)	0 (0%)		0 (0%)	0 (0%)	

Q1: question 1; Q4: question 4; BMI: body mass index (kg/m^2).

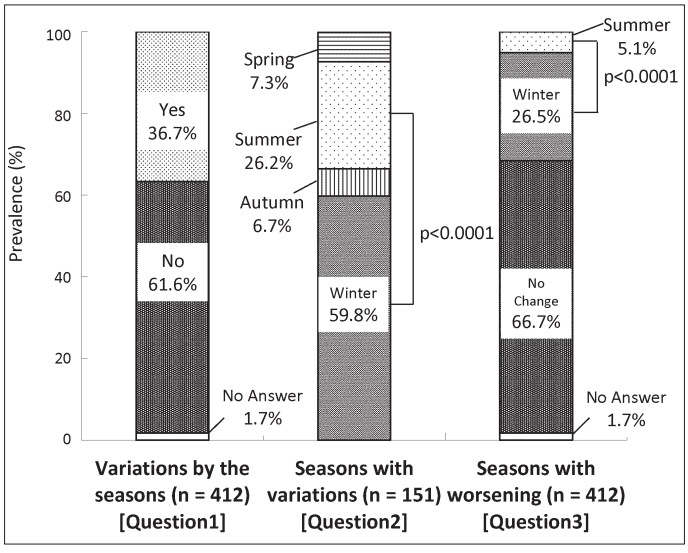

Figure 1. Seasonal variations of urinary stream. 151 patients of 412 (36.7%) had seasonal variations of urinary stream (Question 1). The number of patients realizing seasonal change of urinary stream in spring was 13 (7.3%), in summer was 47 (26.2%), in autumn was 12 (6.7%), and in winter was 107 (59.8%) (Question 2: multiple answers allowed). Significantly more patients realized decreased urinary stream in winter compared with summer (26.5% versus 5.1%, p<0.0001) (Question 3)

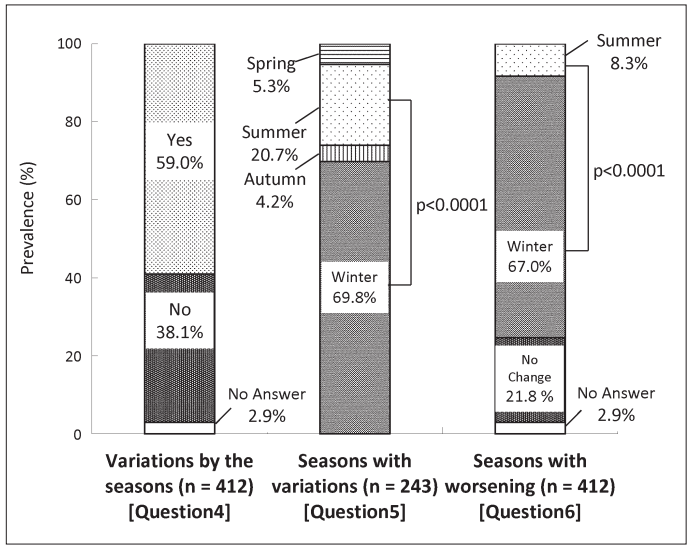

Figure 2. Seasonal variations of urinary frequency. 243 patients of 412 (59.0%) realized seasonal change of urinary frequency (Question 4). The number of patients realizing the change of urinary frequency in spring was 15 (5.3%), in summer was 59 (20.7%), in autumn was 12 (4.2%), and in winter was 199 (69.8%) (Question 5: multiple answers allowed). Urinary frequency was significantly increased in winter compared with summer (67.0% versus 8.3%, p<0.0001) (Question 6)

5.3% (15/285) patients realizing these changes in the spring, 20.7% (59/285) in the summer, 4.2% (12/285) in the autumn, and 69.8% (199/285) in the winter (question 5: multiple answers allowed). Significantly, more patients chose winter as the season of increased urinary frequency as compared with summer (67.0% versus 8.3%, p<0.0001; question 6).

There were no significant differences in any patients' characteristics between those with and without seasonal symptom changes (Table 2).

Around 143 patients (34.7%) realized a weaker urinary stream when feeling cold even during summer (question 7; Figure 3),

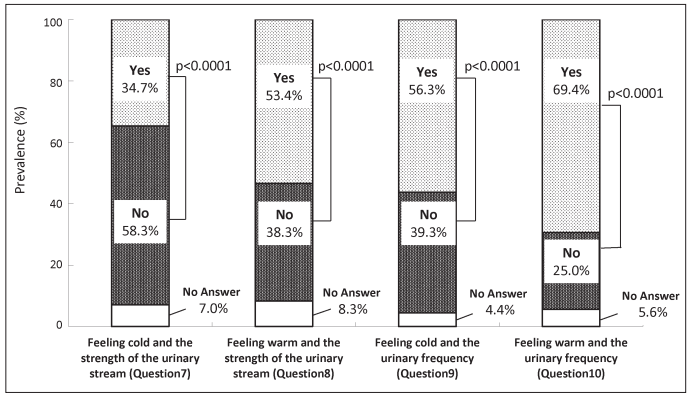

Figure 3. The changes of urinary stream and frequency when feeling cold or worm. When feeling cold, 143 of 412 (34.7%) men perceived small urinary stream (question 7), whereas 232 (53.4%) men felt increase urinary stream when warm (question 8). Urinary frequency was also deteriorated in 232 patients (56.3%) when cold (question9) but improved in 286 patients (69.4%) when warm (question 10)

while 220 (53.4%) experienced an increased urinary stream when warm even during winter (question 8). In 232 patients (56.3%), the urinary frequency deteriorated when cold during summer (question 9), while it improved in 286 (69.4%) patients when they felt warm during winter (question 10).

Association of IPSS and QOL Scores with seasonal variations in LUTS

Table 3 compares the IPSS and QOL indexes between the patients with and without seasonal symptom changes. The total IPSS score was significantly higher in patients with seasonal changes in the urinary stream than in those without (p=0.0068). Patients with seasonal changes in the urine stream also showed significantly higher IPSS voiding and post-voiding symptom scores (p=0.0057 and 0.028, respectively). In contrast, there were no significant differences in the IPSS storage symptom and QOL scores between those with and without seasonal urinary stream changes.

Those with seasonal changes in the urinary frequency also demonstrated significantly higher total IPSS scores, and higher IPSS storage, voiding, and post-voiding symptom scores (p=0.0064, 0.034, 0.014 and 0.042, respectively). However, there were no significant differences in the QOL scores between those with and without seasonal urinary stream changes.

Discussion

All patients in this study were receiving α1-adrenoreceptor antagonist monotherapy for more than a year in order to minimize the changes of drug effects for last one year. That is because α1-adrenoreceptor antagonists improves LUTS within a few months and keeps a plateau for a long time.[5] In contrast, it is

Table 3. IPSS and QOL score in patients with and without seasonal changes of LUTS

	Patients with seasonal change of urinary stream: Yes in Q1 (n=151)	Patients without seasonal change of urinary stream: No in Q1 (n=254)	p	Patients with seasonal change of urinary frequency: Yes in Q4 (n=243)	Patients without seasonal change of urinary frequency: No in Q4 (n=157)	p
Total IPSS score	13.6±8.1	11.8±8.3	0.0068	13.1±7.8	11.5±7.3	0.0064
IPSS storage symptom score (IPSS item 2, 4, 7)	6.3±3.8	5.7±3.8	0.080	6.2±4.0	5.6±3.7	0.034
IPSS voiding symptom score (IPSS item 3, 5, 6)	5.6±4.5	4.7±4.2	0.0057	5.3±4.5	4.6±4.1	0.014
IPSS post-voiding symptom score (IPSS item 1)	1.7±1.6	1.4±1.4	0.028	1.6±1.6	1.4±1.4	0.042
QOL Index	3.0±1.7	3.0±1.4	0.698	3.1±1.6	2.9±1.3	0.132

IPSS: International prostate symptom score; QOL: Quality of life.
Storage symptom, (the item numbers of the IPSS: 2 frequency, 4 urgency, and 7 nocturia); Voiding symptom, (the item numbers of the IPSS: 3 intermittency, 5 weak urinary stream, and 6 abdominal straining to void); Post-voiding symptom, (the item number of the IPSS: 1 sensation of incomplete voiding).

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well known that 5-α reductase inhibitor improves LUTS for long term by reducing prostate volume and mechanical obstruction induced by apoptosis of prostate epithelial cells.[5] It is possible that PDE-5 inhibitor also improves LUTS for long-term periods and difficult to define when their effects reach a plateau. Therefore, in this study, patients with these drugs were excluded.[6]

It is reported that cold temperatures can influence lower urinary tract function in healthy individuals and in patients with LUT disorders, and worsen their symptoms[7,8]; this is consistent with our results. Lower environmental temperature is associated with more frequent urination in healthy individuals. Around 46% of overactive bladder patients reported that cold weather aggravated urgency symptoms.[7] Conversely, another investigation considered subjective or objective seasonal changes in 31 men with BPH.[9] That study showed that the IPSS and QOL scores did not change with seasons and that the maximum flow rate in the uroflowmetry was significantly lower in the summer. While that study contradicts our findings, the number of patients enrolled in it was too small to conclude whether hot temperatures improved or aggravated urine stream in men with BPH.

The certain reason for what affected the seasonal variation in LUTS was unclear from our results, because there were no significant differences in the patients' characteristics between those with and without seasonal changes in LUTS. To our best knowledge, there was few studies evaluating the characteristics affecting seasonal changes in LUTS, but a previous study speculated that the difference may be derived from the individual adaptation responses to cold stress or the improvement of air conditioner reducing the difference between room and outer temperature.[2] These factors also may affect the existence of seasonal changes in LUTS in our study, but further investigation will be needed.

Yoshimura examined seasonal (summer versus winter) variations in LUTS, including nocturia, in three different climatic regions of Japan: the subarctic (Hokkaido), temperate (Kyoto), and subtropical (Okinawa) regions.[1] During the hottest and the coldest seasons, approximately 6,000 men and women aged between 41 and 70 years took a questionnaire survey. This study revealed that the IPSS parameters for each storage symptom and residual urine were significantly higher in the coldest season. These results are consistent with our finding that the urinary frequency increased during the winter and decreased during the summer in men with BPH.

Subjective sensations of warmth and cold may depend on various factors such as temperature, moisture, and air stream; they differ even within a season. Patients might occasionally feel warm even in winter or cold even in summer. It is well known that blood pressure and symptoms of heart diseases change with seasons or temperature.[10-12] Therefore, we hypothesized that not only the seasons, but also the subjective sensations of warmth and cold would be associated with the severity of LUTS.

We found that when the patients felt cold, the urinary stream was weaker, and the urinary frequency increased, and when they felt warm, these symptoms improved. Depending on the subjective warm and cold sensations, more patients realized changes in the urinary frequency than in the urinary stream.

Bladder storage and voiding function depend on a complex neural control system to coordinate the activities of the urinary bladder, urethra, and urethral sphincters. Several transient receptor potential (TRP) channels are thought to modulate the mechanosensory functions of the urothelium and sensory neurons.[13] TRP ankyrin 1 (TRPA1) and TRP melastin 8 (TRPM8) respond to cold stress or nociceptive stimulation, and these are expressed in the human bladder urothelium and sensory nerve fibers[14,15]; TRPM8 is considered the predominant thermoreceptor to cold temperatures.[16] TRPM8 expression was found to be upregulated in the bladder of overactive bladder patients and a previous study reported that TRPM8 modulated the storage function of rat bladder.[17,18] Our results were consistent with these findings that TRPM8, a cold thermoreceptor, modulated bladder storage function.

Several limitations existed in the present study. First, we obtained the answers of these questionnaires at only once but not every season by looking back over the last one year, and the survey period is from spring to autumn, not in winter. We cannot deny the possibility that their answer was affected by the season answering questionnaires and lack of winter assessment reduce the reliability of the data in this study. Second, our self-reported questionnaire has not been validated in another institution or language. The internal validity of this Japanese questionnaire used in this study has not been evaluated, and it is unclear that our results can be applied in other countries. Third, the relatively small number of patients was enrolled. Finally, this study is a cross-sectional investigation on Japanese men with a clinical diagnosis rather than a urodynamic diagnosis.

In conclusion, our questionnaire survey showed that seasonal changes and the feeling of hot and cold were associated with subjective changes in LUTS in men with BPH receiving α1-adrenoreceptor antagonists. Seasonal symptom changes should be considered when treating LUTS patients.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Sano Kosei General Hospital [February 1, 2016 (IRB 2711)].

Informed Consent: All patients in the study provided written informed consent from the authors.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – S.K., J.K.; Design – S.K., J.K.; Supervision – K.S., T.S., A.F., S.A., T.T., T.M., T.F.; Data Collection and/or Processing – S.K., K.S., T.M.; Analysis and/or Interpretation - S.K., K.S., T.M.; Writing Manuscript – S.K., J.K.

Conflict of Interest: The authors have no conflicts of interest to declare.

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