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Original Article
Clinical Investigation

Clinical manifestations of interstitial cystitis and bladder pain syndrome: Analysis of a patient registry in Japan

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Abbreviations & Acronyms
BPS = bladder pain syndrome
ESSIC = European Society for the Study of Interstitial Cystitis
IC = interstitial cystitis
IPSS = International Prostate Symptom Score
LSCS = lumbar spinal canal stenosis
LUTS = lower urinary tract symptoms
NRS = Numerical Rating Scale for pain
OSPI = O'Leary and Sant's Problem Index
OSSI = O'Leary and Sant's Symptom Index
QOL = quality of life

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Objective: To describe clinical manifestations of patients with interstitial cystitis and bladder pain syndrome (IC/BPS) using a patient registry in Japan.

Methods: This retrospective cohort study utilized a patient registry supported by the Japanese Ministry of Health, Labor, and Welfare. Patients were classified as IC or BPS based on cystoscopic findings. Data on demographics, comorbidities, symptom severity, pain intensity, and bladder function were collected and we evaluated the differences in clinical characteristics between IC and BPS, and used multivariate analysis to search for additional factors that might contribute to pain.

Result: A data set comprising 529 patients was obtained from 14 university hospitals. 66.5% of the cases were classified as IC and 33.5% as BPS. IC patients were significantly aged and female-dominant. Comorbidities such as autoimmune diseases were more prevalent in IC patients.

All of the symptom severity, quality of life impairment, and bladder function were significantly worse in patients with IC. Urinary frequency and maximum voided volume on the Frequency-volume chart were 18.8 times and 15.0 times, and 160.9 and 214.1 mL, respectively. Bladder capacity under anesthesia was 293.8 and 472.6 mL, respectively. Maximum voided volume and the number of Hunner lesions were significant predictors of pain in IC patients.

Conclusion: The analysis revealed clinical manifestations of IC/BPS using the largest cohort in Japan. The results indicated higher age, higher female proportion, and higher symptomatic and functional severity in IC patients compared to BPS.

Key words: bladder pain syndrome, Hunner lesion, interstitial cystitis, patient registry.

INTRODUCTION

Interstitial cystitis/bladder pain syndrome (IC/BPS) primarily affects women, with unremarkable findings on blood tests, urinalysis, and imaging; however, it causes intractable lower urinary tract symptoms (LUTS) and severe bladder pain, resulting in deteriorated quality of life

(QOL).[1,2] Due to the small patient population and unknown etiology, the clinical manifestations remain poorly understood.

Recent studies on the pathology and genetics have revealed two distinct clinical entities of IC/BPS. The first entity is a condition with Hunner lesions (Hunner type IC or shortly IC), also known as the European Society for the Study of Interstitial Cystitis (ESSIC) BPS type 3.[3] Histopathology of IC is characterized by extensive infiltration of lympho-plasma cells and epithelial denudation. The infiltrating B cells often show clonal expansion, suggesting immunogenic inflammation as the etiology.[4] The contention has been further supported by the recent finding that genetic linkage of HLA-DQb1 in IC, with an odd ratio of 2.35.[5] The other entity that lacks Hunner lesions is designated as BPS, corresponding to ESSIC BPS types 1 and 2.[3] BPS lacks inflammatory changes in the bladder and frequently presents with somatic and/or psychological symptoms thus urothelial dysfunction and/or neurophysiological abnormalities would be the potential etiology.[6] The latest clinical guidelines advocated this classification for the proper clinical management of patients. However, most of the past reports collected the data as a single cohort, in other words, mixture of IC and BPS.[7–9] In this report, we analyzed clinical data of IC/BPS patients accumulated at a multicenter patient registry in Japan to clarify the difference in clinical manifestations of IC and BPS.

METHODS

This study is a retrospective cohort study using a patient registry supported by the Ministry of Health, Labor, and Welfare (MHLW) Research Grant on rare and intractable diseases. In a series of studies, the present study analyzed baseline medical information at the time of the initial transurethral surgery and all the patients were to be classified at registry either IC or BPS based on cystoscopic observation.

Clinical data of patients visiting our institutions were consecutively uploaded to an online cloud-based registry between September 2017 and October 2020. The definition of IC/BPS was based on the latest East Asian guidelines as "the condition with chronic pelvic pain, pressure or discomfort perceived to be related to the urinary bladder accompanied by other urinary symptoms, such as a persistent urge to void or urinary frequency in the absence of confusable diseases". The patients had to undergo cystoscopy prior to the registry to confirm the presence or absence of Hunner lesions. Those with Hunner lesions were classified to IC and those without Hunner lesions were to BPS. The participating institutions (n = 14) were university hospitals and their affiliated hospitals in Japan.

General background information consisted of gender, age, comorbidities, and family history. Symptoms were assessed by the O'Leary and Sant's Symptom Index (OSSI; the maximum or worst score of 20 points) and the O'Leary and Sant's Problem Index (OSPI; the maximum or worst score of 16 points). Intensity of pain was measured by The Numerical Rating Scale (NRS; the maximum or worst score of 10 points). The International Prostate Symptom Score (IPSS) QOL questionnaire (the maximum or worst score of 6 points) was used to assess QOL. The duration of symptoms and episodes of exacerbation by specific foods were also recorded. The urinary frequency and the amount of voided volume were counted by a frequency-volume chart.

The patients received transurethral surgery under either general or spinal anesthesia; hydrodistension of the bladder by hydropressure up to 80 cmH_2O for BPS, and hydrodistension with concomitant transurethral electrofulguration of Hunner lesions for IC. During the surgery, the surgeon evaluated the number and location of Hunner lesions.

All statistical analyses were performed with commercially available software (JMP pro ver. 11). For continuous variables, mean ± standard deviation is given alongside. One-way ANOVA and the Tukey–Kramer test were applied for comparisons of each factor. A p-value less than 0.01 was considered statistically significant and less than 0.05 was considered potentially significant. The factors associated with pain (NRS >4, equivalent to moderate to severe pain) were examined by multivariate logistic regression models. This study was conducted with the approval of the institutional review board of the University of Tokyo (Approval Number: 11523), and written informed consent was obtained from each patient.

RESULTS

Baseline characteristics of the patients

A data set of 529 patients including IC (n = 352, 65.6%) and BPS (n = 177, 34.4%) was obtained (Table 1). The mean age was higher in the IC group (64.7 ± 12.8 years) than in the BPS group (56.9 ± 16.8, $p < 0.001$). The age distribution was unimodal, with a peak in the 70s in the IC group, while it lacked an evident peak and extended to younger ages in the BPS group (Figure 1). Female dominance tended to be higher in the IC group than in the BPS group (82.7% vs. 69.9%; $p \leq 0.017$). There was no significant difference in the duration of illness at the time of diagnosis (approximately 142 months) and the duration required for definitive

TABLE 1 Patient characteristics.

	IC (n = 352)	BPS (n = 177)	p
Age	64.7 ± 12.8	56.9 ± 16.8	<0.001*
Gender (male:female) (% female)	52:300 (82.7)	41:136 (69.9)	0.017
Duration of illness at the time of diagnosis (month)	141.9 ± 84.8	142.3 ± 7.2	0.958
Duration required for definitive diagnosis of IC/BPS (month)	36.7 ± 51.6	36.1 ± 44.5	0.912
Number of clinics/hospitals visited before diagnosis	2.0 ± 1.3	1.7 ± 1.2	0.061
Past surgical history of pelvic organs/spinal canal	26	12	0.592
Familial history of IC	1	2	0.110

Note: The differences between the two groups were analyzed using the Mann–Whitney U-test. Values are the mean ± SD. Abbreviations: BPS, bladder pain syndrome; IC, interstitial cystitis. *Statistically significant ($p < 0.01$).

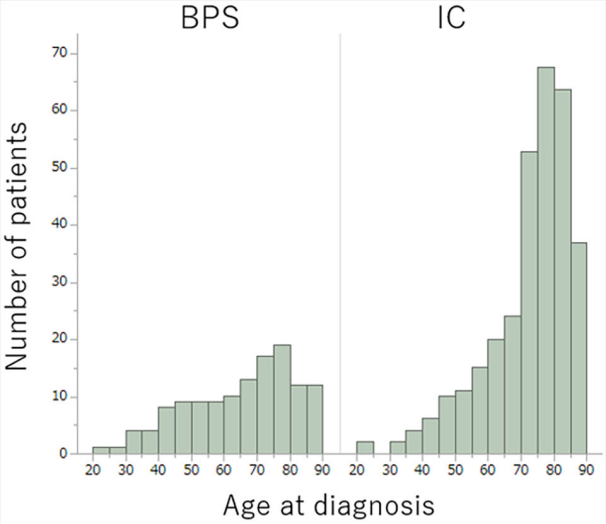

FIGURE 1 Histogram showing the difference in age distribution between IC and bladder pain syndrome (BPS). The age distribution was unimodal, with a peak in the 70s in the interstitial cystitis (IC) group, while it lacked an evident peak and extended to younger ages in the BPS group.

TABLE 2 Comorbidities.

	IC (n = 352)	BPS (n = 177)	p
Allergy	29	16	0.742
Autoimmune disease	44	8	0.002*
Sjögren's syndrome	22	6	0.154
Rheumatoid arthritis	11	1	0.038
Benign prostatic hyperplagia	13	7	0.877
Cancer	28	10	0.332
Chronic fatigue syndrome	0	0	-
Depression	17	13	0.241
Fibromyalgia	2	0	0.157
Inflammatory bowel disease	2	0	0.157
Irritable bowel syndrome	4	4	0.329
Lumbar spinal canal stenosis	27	14	0.915
Neurodegenerative disease	27	6	0.045
Pelvic organ prolapse	12	8	0.528
Stress urinary incontinence	2	0	0.157
Urethral stricture	7	7	0.195
Urolithiasis	3	2	0.756

Note: Multiple responses were allowed for this question. The differences between the two groups were analyzed using the Mann–Whitney *U*-test. Values are the mean ± SD. Abbreviations: BPS, bladder pain syndrome; IC, interstitial cystitis. *Statistically significant (p < 0.01).

diagnosis (approximately 36 months) between IC and BPS groups. Family history of IC/BPS was extremely rare. An IC patient reported her mother had been diagnosed with IC/BPS, and a female twin had BPS. Common comorbidities were autoimmune diseases, lumbar spinal canal stenosis (LSCS), neurogenerative diseases, allergy, and cancer (Table 2). IC is more often associated with autoimmune diseases (p = 0.002).

Symptoms

Overall IC patients were more symptomatic than BPS (Table 3). The OSSI total score was significantly higher in the IC group (14.6 ± 4.0 points) than the BPS group (11.9 ± 4.1; p < 0.0001). The OSPI was also higher in the IC group (12.6 ± 3.5 vs. 10.9 ± 3.7; p = 0.001) (Table 3). When divided for each question item, the difference in nighttime frequency scores (OSSI Q3 and OSPI Q2) were most evident. NRS was worse in the IC group (7.3 ± 2.3 points vs. 6.5 ± 2.2; p = 0.001). IPSS QOL scores was slightly higher in IC group (5.6 ± 0.9 vs. 5.1 ± 1.4; p = 0.005). The frequency of pain episodes was reported from 173 patients, and it was less than once daily (n = 48) or daily (n = 125). The frequency was not significantly different between IC and BPS. Food-related pain exacerbation was reported in 5.1% of IC and 4.5% of BPS cases, respectively. The trigger food was spices (n = 5), citrus fruits (4), coffee (3), and soy products (2).

TABLE 3 Symptoms.

	IC (n = 352)	BPS (n = 177)	p
OSSI Q1 (urge)	3.0 ± 1.8	2.7 ± 1.7	0.269
OSSI Q2 (daytime frequency)	4.1 ± 1.4	3.6 ± 1.4	0.006*
OSSI Q3 (nighttime frequency)	4.0 ± 1.1	2.6 ± 1.5	<0.001*
OSSI Q4 (pain)	3.4 ± 1.4	3.1 ± 1.5	0.072
OSSI total score	14.6 ± 4.0	11.9 ± 4.1	<0.001*
OSPI Q1 (daytime frequency)	3.2 ± 1.1	2.8 ± 1.2	0.054
OSPI Q2 (nighttime frequency)	3.3 ± 1.0	2.6 ± 1.4	<0.001*
OSPI Q3 (urge)	3.0 ± 1.2	2.5 ± 1.4	0.009*
OSPI Q4 (pain)	3.2 ± 1.2	3.0 ± 1.2	0.151
OSPI total score	12.6 ± 3.5	10.9 ± 3.7	0.001*
NRS	7.3 ± 2.3	6.5 ± 2.2	0.001*
IPSS QOL score	5.6 ± 0.9	5.1 ± 1.4	0.005*
Frequency of pain (n = 173)			
Several times per week (no. of pts)	35	13	0.147
Times per week	4.75 ± 2.0	3.2 ± 0.4	
Everyday (no. of pts)	93	32	0.816
Times per day	9.8 ± 8.3	9.4 ± 8.7	
Presence of specific foods that exacerbate symptoms (n, %)	18 (5.1)	8 (4.5)	0.018

Note: The differences between the two groups were analyzed using the Mann–Whitney *U*-test. Values are the mean ± SD. Abbreviations: BPS, bladder pain syndrome; IC, interstitial cystitis; IPSS, International Prostate Symptom Score; NRS, Numerical Rating Scale for pain; OSSI, O'Leary and Sant's Symptom Index; OSPI, O'Leary and Sant's Problem Index; QOL, quality of life. *Statistically significant (p < 0.01).

Frequency-volume chart variables

A frequency-volume chart was recorded in 529 patients (Table 4). The 24-h frequency was significantly higher in the IC group (18.8 ± 8.4 times) than in the BPS group (15.0 ± 7.8; p < 0.001). Nighttime frequency was also significantly higher in IC. (4.9 ± 2.9 vs. 3.0 ± 2.8; p < 0.0001). The average voided volume was significantly lower in the IC group (98.0 ± 48.9 mL) than in the BPS group (112.3 ± 65.2 mL; $p \leq 0.009$). The maximum voided volume was also significantly lower in the IC group (160.9 ± 76.3 mL vs. 214.1 ± 105.9 mL; p < 0.001). The nighttime urinary amount was significantly larger in the IC group (452.4 ± 271.2 mL vs. 293.8 ± 260.0 mL; p = 0.001).

TABLE 4 Frequency-volume chart variables.

	IC (n = 352)	BPS (n = 177)	p
24 h frequency	18.8 ± 8.4	15.0 ± 7.8	<0.001*
Nighttime frequency	4.9 ± 2.9	3.0 ± 2.8	<0.001*
Daytime frequency	13.7 ± 0.6	11.0 ± 5.3	0.012
Average voided volume (mL)	98.0 ± 48.9	112.3 ± 65.2	0.009*
Maximum voided volume (mL)	160.9 ± 76.3	214.1 ± 105.9	<0.001*
24 h amount of urine (mL)	1552.0 ± 672.2	1384.6 ± 668.4	0.060
Nighttime urinary amount (mL)	452.4 ± 271.2	293.8 ± 260.0	0.001*
Daytime urinary amount (mL)	1073.8 ± 505.7	881.5 ± 513.7	0.024

Note: The differences between the two groups were analyzed using the Mann–Whitney *U*-test. Values are the mean ± SD. Abbreviations: BPS, bladder pain syndrome; IC, interstitial cystitis. *Statistically significant ($p < 0.01$).

Findings at endoscopic surgery

The findings were recorded in 509 patients (Table 5). The capacity under anesthesia was significantly lower in the IC group (472.6 ± 189.1 mL) than in the BPS group (669.1 ± 218.5 mL; $p < 0.001$). Regarding the number of Hunner lesions, the average number was 2.4 ± 1.4. The location of the lesions was most common in the posterior wall (61.1%), followed by the lateral walls (43.1%) and the dome (26.7%). Lesions in the trigone and neck were rare, accounting for 1.4% and 0.6%, respectively.

Predictors of pain

One of the most notable symptoms of IC/BPS is pain. From the data obtained in this study, we performed an additional analysis to see if there were factors that could predict pain. Table 6 shows the logistic regression analysis of the association between moderate to severe pain and basic characteristics. Multivariate analysis of factors predicting moderate to severe pain showed the maximum voided volume and the number of Hunner lesions as the significantly influential factors in IC ($p = 0.006$, OR1.569, $p = 0.009$, OR 1.859, respectively). There were no relevant factors in BPS (Table 6).

DISCUSSION

This study described the clinical manifestations of IC/BPS patients attending a large registry in Japan. By comparing IC and BPS patients, we showed that IC patients were older, had a greater proportion of women, had more severe pain and more frequent urination, and had less bladder capacity.

The sample size of this study (n = 529)is the largest in Japan and would be one of the largest worldwide (Table 7). This may account for more than 10% of patients in Japan since the number of IC/BPS patients was estimated as approximately 4500 in Japan.[10] The study collected data separately for IC and BPS and analyzed them accordingly, while most of the past clinical studies collected data as a single group. A separate analysis would be essential because IC and BPS are symptomatically similar but a different disease based on histological features and gene expression profiles.[4,5]

The proportion of IC (66.5%) in this study was higher than the past values, for example, approximately 10% in the USA, 7.8% in Taiwan, and 41.8% in Korea.[11–13] A possible reason for the higher proportion of HIC than in the previously reported study is that all institutions participating in the study were tertiary care university hospitals, which have more severe cases and a higher proportion of refractory cases. Furthermore, All of the participating university hospitals use detailed cystoscopy rather than relying on symptom-based diagnosis, which may lead to more accurate typing. Logadottir et al. reported a high IC proportion (57%) by mandated use of cystoscopy at diagnosis.[14] A substantial portion of IC might have been overlooked by omitting cystoscopy in the most past studies. The age distribution showed a unimodal pattern with a peak in the 60–70 age group for IC, while the

TABLE 5 Findings at transurethral surgery.

	IC (n = 343)		BPS (n = 166)	p
Bladder capacity under anesthesia (mL)	472.6 ± 189.1		669.1 ± 218.5	<0.001*
Numbers of Hunner lesion	2.4 ± 1.4		N/A	
Location of Hunner lesion (n, %)				
Posterior wall	215	61.1%	N/A	
Right lateral wall	152	43.1%	N/A	
Left lateral wall	152	43.1%	N/A	
Dome	94	26.7%	N/A	
Anterior wall	41	11.6%	N/A	
Retrotrigone	15	4.3%	N/A	
Trigone	5	1.4%	N/A	
Neck	2	0.6%	N/A	
Whole bladder	14	3.97%	N/A	

Note: Multiple responses were allowed for this question. The total number of HIC patients differs from the total number of Hunner lesions because some cases have multiple lesions. The differences between the two groups were analyzed using the Mann–Whitney *U*-test. Values are the mean ± SD. Abbreviations: BPS, bladder pain syndrome; IC, interstitial cystitis. *Statistically significant ($p < 0.01$).

TABLE 6 Logistic regression analysis of the association between moderate to severe pain (NRS >4) and basic characteristics.

	IC (n = 352)			BPS (n = 177)	
	p	OR	95% CI	p	OR
Gender (F:M)	0.125	2.952	−1.2202 to 0.1547	0.999	-
Age	0.439	0.983	−0.0612 to 0.0318	0.999	-
Comorbidities					
Autoimmune diseases	0.641	1.736	−0.6471 to 1.7706	1.000	-
Irritable Bowel Syndrome	0.088	0.067	−3.0869 to 0.4141	0.999	-
Spinal disease	0.507	1.795	−1.0686 to 0.6383	0.998	-
Neurodegenerative diseases	0.999	-	−31 274 to 32 196	0.999	-
Depression	0.192	0.291	−1.4885 to 0.4310	1.000	-
Past surgical history of pelvic organs/spinal canal	0.999	-	−39 894 to 39 824	1.000	-
Maximum voided volume (mL)	0.006*	1.569	0.0038 to 0.0191	1.000	-
Bladder capacity under anesthesia (mL)	0.904	0.995	−0.0035 to 0.0037	1.000	-
Numbers of Hunner lesion	0.009*	1.859	0.0551 to 1.0234	N/A	

Abbreviations: BPS, bladder pain syndrome; IC, interstitial cystitis; NRS, Numerical Rating Scale for Pain. *Statistically significant ($p < 0.01$).

TABLE 7 Reported patient characteristics of IC/BPS.

Author	Year	Country	Race	Sample number	Cystoscopy performed	Gender male (%)	Hunner type (%)	Separate analysis
Holm-Bentzen M.	1987	Europe	-	115	115	-	3.5	No
Koziol	1994	USA	-	565	-	-	-	No
Simon L. J.	1997	USA	90% Caucasian	424	190	8.5	10.5	Yes
Hanno P. M. (NIDDK)	1999	USA	-	379	101	Female only	-	No
Peeker R.	2002	Sweden	-	231	231	-	55	Yes
Peters K. M.	2008	USA	97.7% Caucasian	87	87	Female only	-	No
Nickel, J. C.	2010	USA	-	205 IC/BPS 117 control	-	Female only	-	No
Richter B.	2010	Denmark	-	349	349	7.5	8.0	No
Berry S. H.	2011	USA	-	337	No	Female only	-	No
Konkle K. S.	2012	USA	83% Caucasian 6.5% Black 3.6% Hispanic	277	No	Female only	17.6	No
Logadottir Y.	2012	Sweden	-	379	379	16	57.2	Yes
Griffith J. W.	2016	USA	-	424	No	45.0	-	No
Yu W. R.	2020	Taiwan	100% Asian	486	486	13.4	3.91	No
Present study	2023	Japan	100% Asian	529	529	17.6	66.5	Yes

Note: Population based studies were excluded. Abbreviations: BPS, bladder pain syndrome; IC, interstitial cystitis.

peak was much flattened for BPS. Another difference was a higher proportion of women in IC (82. 7% vs. 69.9%). The unlike pattern of age/sex distribution may be related to different etiology of IC and BPS.

Among the comorbid conditions, the prevalence of autoimmune diseases is significantly higher in IC. This is consistent with previous studies, and recent reports on clonal expansion of B cells in IC or mice models mimicking IC induced by autoimmunity.[4,15] Important difference was more symptomatic severity in IC; OSSI total score was significantly higher in the IC group (mean value; 14.6) than in the BPS group (11.9). Among the symptoms assessed, the score of nighttime frequency was most remarkably different between IC (4.9 ± 2.9) and BPS (3.0 ± 2.8). This difference may be explained by older age and age-related increases in nocturnal urine output in IC patients, as Weiss et al. reported that age affects nocturnal bladder capacity.[16]

However, this increase in frequency of urination may also be attributed to a decrease in maximal voiding volume (160.9 mL in IC vs. 214.1 mL in BPS) and a decrease in anesthetic bladder capacity in IC (472.6 mL in IC vs. 669.1 mL in BPS). These reductions in bladder capacity may be due to reduction of bladder compliance caused by fibrosis and deformation of the bladder due to inflammation.[17] Scores for NRS and QOL were high in both groups, suggesting that patients' QOL is greatly impaired. It was significantly worse in IC group compared to BPS group (7.3 vs. 6.5, and 5.6 vs. 5.1, respectively). IC/BPS is known to significantly interfere with patients' QOL, with previous reports indicating that 55.8% of IC/BPS patients have depressive symptoms and that 50% of patients have difficulty finding full-time employment.[2] However, there have been no reports directly comparing the incidence of depression or unemployment between IC and BPS, therefore future studies are needed.

Symptomatic exacerbation by specific diets was reported by approximately 5% of respondents, with no significant difference between IC and BPS. Previous literature reported that approximately 90% of IC/BPS patients documented symptoms worsening after consuming certain foods and drinks.[18,19] Food items like coffee, tea, chocolate, alcohol, tomatoes, citrus fruits, spices, and vitamin C have been known as potential triggers.[20] Our study addressed no formulated questions on this subject, and this may result in a low incidence of association between diet and symptom exacerbation.

The multivariate analysis predicting pain (NRS >4) identified the maximum voided volume and number of Hunner lesions as the significant factors in IC patients. This finding is compatible with a previous study showing the correlation of the extent of Hunner lesions to pain intensity.[21] The correlation suggests that urine infiltrating at Hunner lesions may be responsible for painful symptoms in IC. In turn, pain in BPS patients may be of different etiology. It is presumed that bladder hypersensitivity indicated by elevated expression of nerve growth factor and/or associated systemic somatoform disorders may cause the symptoms.[22,23]

Limitations of this study derive from the study's nature involving multiple centers. There would be inconsistency in clinical practice, especially at performing cystoscopy to detect Hunner lesions. However, to overcome this problem, the diagnostic procedures of the atlas described in the guidelines were followed at each institution. Another limitation of this study is the lack of formulated questions in patient demography due to its retrospective nature of patient registry. The questions regarding comorbidity or dietary habits were not standardized. However, this large-scale study highlighted different characteristics of IC and BPS, providing useful information to understand the etiology and management of IC/BPS.

In conclusion, this study revealed clinical manifestations of IC/BPS using the largest cohort in Japan, highlighting the differences between IC and BPS. IC patients showed higher age, higher female proportion, and worse symptomatic and functional severity compared to BPS.

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AUTHOR CONTRIBUTIONS

Aya Niimi: Writing – original draft; software; investigation; formal analysis; data curation; project administration. **Yoshiyuki Akiyama:** Methodology; investigation; writing – review and editing; formal analysis; validation. **Yamanishi Tomonori:** Project administration; writing – review and editing; methodology. **Akira Furuta:** Writing – review and editing; project administration. **Tomohiro Matsuo:** Project administration; writing – review and editing. **Hikaru Tomoe:** Project administration; writing – review and editing; methodology. **Hidehiro Kakizaki:** Writing – review and editing; project administration; methodology. **Yoshihisa Matsukawa:** Project administration; writing – review and editing. **Teruyuki Ogawa:** Project administration; writing – review and editing. **Takahiko Mitsui:** Project administration; writing – review and editing. **Naoya Masumori:** Project administration; writing – review and editing; methodology. **Soh Inamura:** Writing – review and editing. **Yutaka Enomoto:** Project administration; writing – review and editing. **Akira Nomiya:** Writing – review and editing; project administration. **Daichi Maeda:** Writing – review and editing; investigation. **Yasuhiko Igawa:** Writing – review and editing; supervision. **Haruki Kume:** Writing – review and editing; resources; supervision. **Yukio Homma:** Funding acquisition; writing – review and editing; supervision; conceptualization; methodology; data curation; formal analysis; validation; resources.

CONFLICT OF INTEREST STATEMENT

The authors have no relevant financial interests to disclose regarding the materials discussed in the manuscript. Takahiko Mitsui, Naoya Masumori, and Haruki Kume are Editorial Board members of International Journal of Urology and co-authors of this article. To minimize bias, they were excluded from all editorial decision-making related to the acceptance of this article for publication.

APPROVAL OF THE RESEARCH PROTOCOL BY AN INSTITUTIONAL REVIEWER BOARD

The study protocol was approved by the institutional review board of the University of Tokyo (approval no. 11523) and it conforms to the provisions of the Declaration of Helsinki.

INFORMED CONSENT

Participants were informed about this study using generally accessible contact information. Written informed consent was obtained from all patients who chose to participate in this study. All procedures followed appropriate guidelines.

REGISTRY AND THE REGISTRATION NO. OF THE STUDY/TRIAL

Not applicable.

ANIMAL STUDIES

Not applicable.

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Editorial Comment

Editorial Comment for "Clinical manifestations of patients with interstitial cystitis and bladder pain syndrome using a patient registry in Japan"

The study conducted by Niimi et al. makes a valuable contribution to understanding interstitial cystitis (IC) and bladder pain syndrome (BPS) through an extensive patient registry analysis.[1] With data from 529 patients across 14 university hospitals, this study represents one of Japan's most comprehensive assessments of IC/BPS. The research confirms established trends by identifying critical clinical differences between IC and BPS while providing new insights into pain predictors for IC patients, such as maximum voided volume and the number of Hunner lesions.

One of the significant strengths of this study is its precise classification of IC and BPS based on cystoscopic findings, which allows for a clear clinical differentiation between these often misdiagnosed conditions.[2] The observation that IC patients tend to be older, predominantly female, and suffer from more severe symptoms and bladder dysfunction is consistent with prior research.[3,4] However, this study's detailed assessment of bladder capacity under anesthesia and during normal voiding adds valuable detail to these established findings.

Additionally, the discovery of a higher prevalence of comorbid autoimmune diseases among IC patients suggests new directions for understanding the pathophysiological mechanisms that may link these conditions. This is an essential step toward improving the multidisciplinary management of IC, particularly in aging female populations who may experience a complex range of symptoms.

Another significant contribution of this study is its multivariate analysis, which identifies maximum voided volume and the presence of Hunner lesions as important predictors of pain in IC patients. This finding underscores the importance of Hunner lesion identification in clinical practice, further solidifying its role as a critical diagnostic marker distinguishing IC from BPS. The results suggest that a more focused assessment of these variables could lead to better pain management strategies for IC patients.

While the study offers substantial insights, it also highlights areas requiring further investigation, particularly concerning the underlying mechanisms behind the more severe clinical manifestations of IC compared to BPS. Future