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Original Article

The sociodemographic and clinical predictors of symptom severity in patients with refractory interstitial cystitis/bladder pain syndrome

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ABSTRACT

Objectives: Interstitial cystitis/bladder pain syndrome (IC/BPS) has debilitating symptoms and results in a poor quality of life. This study investigated the associations between demographic and clinical factors and symptom severity in patients with IC/BPS in Taiwan.

Materials and Methods: Patients with documented IC/BPS refractory to conventional treatments from 2007 to 2009 were enrolled. Sociodemographic data and a medical history were obtained. Clinical assessments were performed using the O'Leary–Sant IC symptom index (ICSI) and problem index (ICPI), visual analog scale of bladder pain, and global response assessment to treatment. Patients kept a 3-day voiding diary of daytime and nighttime frequency, and functional bladder capacity (FBC) and uroflowmetry parameters (maximum flow rate, voided volume, and postvoid residual) were measured. Univariate and multivariate analyses were used to evaluate the associations between demographic/clinical factors and symptom severity.

Results: A total of 80 patients (75 women and 5 men) were enrolled. On univariate and multivariate analysis, the characteristics most associated with worse ICSI, ICPI, pain score, daytime frequency and nocturia episodes, and FBC were maximum bladder capacity (MBC) under anesthesia, duration of symptoms, body mass index (BMI), and employment status.

Conclusion: MBC and duration of symptoms were predictive factors of symptom severity in patients with refractory IC/BPS. BMI and employment status were also found to be associated with symptom severity in these patients.

1. Introduction

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic bladder condition, which includes chronic pelvic pain, pressure, or discomfort, and is perceived to be related to the urinary bladder in the absence of urinary infection or other pathology [1,2]. IC/BPS is seen mainly in women (90%), at a median age of onset of 40 years [3,4]. The prevalence varies between populations [3,5–8]. Without a pathognomonic picture, the diagnosis can only be based on a combination of a thorough patient history, sterile and cytologically negative urine, cystoscopic hydrodistention under anesthesia, and bladder biopsy [9].

IC/BPS is one of the most therapeutically frustrating problems of the urinary tract. Many different etiologies of IC/BPS have been proposed. However, none of these etiologies has been definitely proven. IC/BPS has been considered to result from long-standing inflammation of the bladder. Bladder histological analysis shows infiltrates of mast cells, eosinophilic leukocytes, and T-lymphocytes, which suggests the disease is mediated by the immune system [10–12]. Disruptions of the bladder mucosal barrier, the glycosaminoglycan layer, initiate a cascade of events in the bladder, leading to symptoms and IC/BPS [13,14]. A large range of treatments have been developed, but no single treatment has been reported to have long-term effects in eradicating symptoms [15–18].

Patients with IC/BPS have long-term bothersome symptoms characterized by suprapubic pain, urgency, frequency, and nocturia, and exacerbated by bladder filling. Their quality of life is markedly

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compromised. Researchers have documented the comorbidities, risk factors, and impact on quality of life including physical, mental, sexual, and social function [19–25]. Few studies have focused on demographic and clinical characteristics that increase symptom severity. Obesity, depression, a low education level, postmenopausal status, being unemployed, being unmarried, and never having been pregnant were associated with worse symptom severity [26,27]. Volumes at first sensation and at maximal cystometric capacity in urodynamic studies were inversely associated with symptom severity in IC [19,28]. Cystoscopic findings such as glomerulations, ulceration, and bladder capacity were significantly correlated with symptoms such as pain and nocturia [22,29]. Histological analysis showed the detrusor mast cell count and intrafascicular fibrosis had statistically significant prognostic value for treatment intensity [30]. We found no study that demonstrated the factors associated with IC/BPS in the Taiwanese population.

Symptom severity is strongly related to quality of life. The treatment of IC/BPS is meant to alleviate symptoms. Identifying factors associated with increased symptom severity may provide an insight into the etiology and add potential benefits in the management of difficult cases. To investigate the association between demographic/clinical characteristics and symptom severity in patients with IC/BPS and to determine the predictors of symptom severity, we carried out a retrospective study in patients with refractory IC/BPS in Taiwan.

2. Materials and methods

Patients who were diagnosed as IC/BPS refractory to conventional treatment at Hualien and Taipei Buddhist Tzu Chi General Hospitals from 2007 to 2009 were enrolled in this retrospective study. All patients were over 18 years old and had symptoms characteristic of IC/BPS. They had been previously treated conservatively with pentosan polysulfate and/or intravesical heparin instillation for at least 6 months without clinical improvement [31]. Urodynamic study with a 0.4 M potassium chloride (KCl) test was performed routinely at baseline. All descriptions and terminology in this report were in accordance with recommendations of the International Continence Society [1]. The patients received cystoscopic hydrodistention under general anesthesia at an intravesical pressure of 80 cm water and were proven to have characteristic glomerulations. The grade of glomerulations was classified as 0 to 4, indicating none, mild, moderate, or severe glomerulations and patients were also evaluated for the presence of Hunner's lesion [32,33]. The maximal bladder capacity (MBC) was recorded. Patients with a cystometric bladder capacity of more than 350 mL, without a positive KCl test, or with a glomerulation grade of less than 2 were not included in this study. Patients with a urinary tract infection, stress urinary incontinence, chronic urinary retention, pelvic organ prolapse, or neurogenic voiding dysfunction were also excluded.

Sociodemographic data including age, sex, body mass index (BMI), employment status, lifestyle factors such as smoking or consumption of alcohol, and a medical/reproductive history were obtained. The history considered comorbidities such as hypertension, myocardial infarction, irritable bowel syndrome, urinary incontinence, erectile dysfunction, arthritis, fibromyalgia, migraine headaches, diabetes, sinusitis, allergies, asthma, endometriosis, hysterectomy, and nonurogenital cancer.

Our patients were treated with intravesical hyaluronic acid (HA) instillations 40 mg in 50 mL solution (Cystistat) weekly for 4 weeks followed by monthly instillation for 5 months [34–37], or intravesical botulinum toxin A (Botox) 100 U injections as previously described [38–42]. Patients were informed of the possible complications associated with intravesical HA instillation, such as urinary tract infection. Written informed consent was obtained from every patient prior to participating in the present study.

Clinical assessments performed at baseline, 1 month, and 6 months after treatment start included IC/BPS symptoms, a 3-day voiding diary, and uroflowmetry. The IC/BPS symptoms were assessed using the O'Leary–Sant IC index, which is composed of two subscales that measure the frequency of IC/BPS symptoms (IC symptom index, ICSI; range 0–20) and the degree of bother associated with symptoms (IC problem index, ICPI; range 0–16) [43,44]. Bladder pain was assessed by a visual analog scale (VAS), ranging from 0 (no pain) to 10 (severe pain). The patients kept a 3-day voiding diary to record the functional bladder capacity (FBC), number of urinary daytime voidings, and nocturia episodes. Uroflowmetry and the postvoid residual volume measurement were also carried out at each time point. A self-assessed global response assessment (GRA) was used to rate bladder symptoms compared with baseline on a seven-point centered scale.

Continuous variables were expressed as mean ± standard deviation (SD), and categorical data were expressed as number and percentages. Statistical comparisons between the subgroups were tested using the Chi-square test for categorical variables, and the independent t test for continuous variables. The paired t test was used to evaluate significant differences in the variables at baseline and after treatment. All statistical assessments were two-sided and considered significant at $p < 0.05$.

Because the outcomes of interest indicative of symptom severity of IC/BPS were in a repeated measurement manner, we used the generalized estimating equations (GEE) model to assess the association between them and demographics and clinical factors. The dependent variables including the ICSI, ICPI, pain score, frequency and nocturia episodes, and FBC measured at three time points were considered the repeated effect. The independent variables were demographics and clinical factors and were considered the fixed effect. The correlation structure was unstructured after fitness testing. Univariate and multivariate analyses were performed. Based on distribution of case volume, we stratified age, BMI, MBC, symptom duration, and number of children into tertiles. The estimate was exponentiated in the form of β. Covariates that retained $p < 0.15$ on univariate analysis or had a trend toward a worse outcome were entered into the multivariate regression models. There were similarities between our dependent variables (ICSI, ICPI, pain score, frequency, nocturia episodes, and FBC). There might have been collinearity between these variables. Therefore, an individual regression model was applied for each dependent variable. All statistical tests were two-sided and used a significance level of 5%. All statistical tests were performed using SAS for Windows, version 9.1 (SAS Institute Inc., Cary, NC, USA).

3. Results

A total of 80 patients including 75 women and 5 men were enrolled in this study. Their demographic characteristics and baseline data, such as symptom duration, daytime frequency and nocturia episodes, FBC, MBC, ICSI, ICPI, and VAS pain scores, are shown in Table 1. Fifty six patients received intravesical HA instillation and 24 patients received intravesical Botox injections. There were no significant differences in the demographic characteristics between the two treatment groups. All patients had moderate to severe glomerulations in cystoscopic hydrodistention, but none had a Hunner's ulcer.

3.1. Univariate analysis

On univariate analysis fitted by a GEE model, we found that the independent variables associated with outcome parameters indicative of symptom severity were MBC, duration of symptoms, BMI,

Table 1
Demographic and baseline characteristics of the study participants.

	Total	HA group	Botox group	*p*
Patient number	80	56	24	
Age (y)	49.5 ± 13.0	48.6 ± 13.8	51.6 ± 11.0	0.35
Female sex	75 (93.8)	52 (92.9)	23 (95.8)	0.61
BMI (kg/m^2)	23.4 ± 3.99	23.81 ± 4.31	22.38 ± 2.95	0.09
Comorbidity[a]	27 (33.8)	20 (35.7)	7 (29.2)	0.57
Marriage	49.5 ± 13.0	49 (87.5)	22 (91.7)	0.59
Children	69 (86.3)	47 (83.9)	22 (91.7.2)	0.36
Smoking	2 (2.5)	2 (3.6)	0	0.35
Alcohol	2 (2.5)	2 (3.6)	0	0.35
Employment	34 (42.5)	23 (41.1)	11 (45.8)	0.69
Symptom duration (y)	6.49 ± 5.03	6.22 ± 5.06	7.13 ± 5.02	0.46
MBC (mL)	664 ± 205	657.9 ± 210.3	679.6 ± 194.9	0.67
Frequency	10.8 ± 5.19	11.68 ± 5.82	8.63 ± 2.2	0.001
Nocturia	3.6 ± 1.67	3.11 ± 1.72	2.96 ± 1.57	0.72
FBC (mL)	162.8 ± 91.9	146.4 ± 82.4	200.8 ± 103.0	0.01
IC index (total)	20.7 ± 760	21.39 ± 6.83	19.0 ± 9.09	0.20
ICSI	10.8 ± 3.99	11.11 ± 3.71	10.13 ± 4.59	0.32
ICPI	9.86 ± 3.90	10.29 ± 3.47	8.88 ± 4.69	0.14
VAS score	4.41 ± 2.25	4.34 ± 2.0	4.58 ± 2.8	0.66

Data are shown as mean ± SD or *n* (%); *p* values indicate differences between groups based on Chi-square test or independent *t* test.
BMI = body mass index; Botox = botulinum toxin A; FBC = functional bladder capacity; HA = hyaluronic acid; IC = interstitial cystitis; ICPI = O'Leary–Sant IC problem index; ICSI = O'Leary–Sant IC symptom index; MBC = maximum bladder capacity; SD = standard deviation; VAS = visual analog scale.
[a] Comorbidity: as described in the text.

and employment status. A smaller MBC was significantly associated with a worse ICPI, more daytime frequency and nocturia episodes, and a smaller FBC. An MBC less than 500 mL was associated with a worse ICSI. A shorter symptom duration was significantly associated with a worse ICSI and ICPI, and more daytime frequency. A lower BMI was significantly associated with a worse ICSI and ICPI, higher pain score, and more daytime frequency and nocturia episodes. Unemployment was significantly associated with a worse ICSI, more frequency and nocturia, and a smaller FBC (Table 2). These four covariates were entered into multivariate analysis.

3.2. Multivariate analysis

We anticipated that MBC and symptom duration would reflect the severity of disease, whereas BMI and employment status might show the impact of disease severity. Thus, we considered MBC and symptom duration as the main covariates, and BMI and employment status as confounders on multivariate analysis. Three regression models were applied by GEE (Table 3).

Model 1 included MBC and symptom duration. A smaller MBC was significantly associated with a worse ICPI, more daytime frequency and nocturia, and a smaller FBC. A shorter duration of symptoms was associated with a worse ICSI and ICPI, and more daytime frequency.

Model 2 was adjusted for age, sex, and treatment group, which were considered *a priori* factors. A smaller MBC was significantly associated with a worse ICPI, more daytime frequency and nocturia, and a smaller FBC. A shorter symptom duration was associated with a worse ICSI and ICPI, and more daytime frequency.

Model 3 was adjusted for age, sex, treatment group, BMI, and employment status. A smaller MBC was significantly associated with a worse ICPI, more daytime frequency and nocturia, and a smaller FBC. A shorter duration of symptoms was significantly associated with a worse ICSI and ICPI and more daytime frequency.

In addition, a lower BMI was found to be significantly associated with a worse ICSI and more nocturia episodes, and was associated with a worse ICPI, higher pain score, and more daytime frequency. Unemployment was significantly associated with more daytime frequency.

Multivariate analyses were also performed for ICSI, ICPI, and GRA in three regression models fitted by GEE when these outcome parameters were considered binary variables. ICSI and ICPI scores of $\geq$12 indicated severe IC symptoms, and a GRA $\geq$ 2 indicated a successful treatment result. A smaller MBC was significantly associated with a worse ICPI. A shorter duration of symptoms was associated with a worse ICSI. There were no significant associations between covariates and treatment results based on GRA (Table 4).

4. Discussion

This current study revealed that MBC on cystoscopic hydrodistention and symptom duration had significant associations with symptom severity in IC/BPS. In addition, BMI and employment status were observed to have significant associations with symptom severity in these patients. There were no definite interactions between MBC, symptom duration, and treatment arms in symptom severity and therapeutic effect.

The main finding of our study was that the MBC was inversely correlated with symptom severity in our patients. A smaller MBC, especially in patients with an MBC less than 500 mL, was significantly associated with a worse ICPI, more daytime frequency and nocturia, and a smaller FBC, suggesting that a small MBC is indicative of severe symptoms. This result was consistent with an Interstitial Cystitis Data Base study by Kirkemo et al [28] who reported that daytime and nighttime frequency were correlated with a decreased volume at first sensation to void and a lower maximal cystometric capacity. We believe that bladder capacity under anesthesia reflects the severity of the disease itself, and thus, a smaller MBC indicates a more severe IC/BPS. Lamale et al [29] demonstrated that pain and nocturia were significantly correlated with the cystoscopic findings and bladder capacity in patients with newly diagnosed IC. All of our patients had moderate to severe glomerulations and none had a Hunner's ulcer. However, we did not assess the association between cystoscopic findings and symptom severity.

Another result of our study is that a shorter symptom duration was significantly associated with a worse ICSI, and correlated with a worse ICPI and more daytime frequency, suggesting that a short symptom duration is indicative of severe symptoms. This finding is in contrast to that of Koziol et al [22] who found an apparent plateau in frequency and urgency among patients after approximately 5 years of symptoms. IC/BPS is a chronic disease, and most patients have bothersome symptoms occurring in a pattern of flare and remission [3]. No current treatments have a significant impact on symptoms with time [45]. Patients with a long disease duration may adjust themselves psychologically or socially across time. In addition, patients might experience milder symptoms with the effects of previous treatments. Those with shorter disease duration may perceive that their symptoms are severe. We did not assess psychological factors among our patients, and it was not possible to draw a conclusion.

We observed that BMI was independently associated with IC/BPS symptom severity. A lower BMI was significantly associated with a worse ICSI and more nocturia episodes, and correlated with a worse ICPI, more pain, and more daytime frequency. The relationship between symptoms and body weight in IC/BPS is not well defined in the literature. El Khoudary et al [27] reported that obesity was associated with one quality of life domain. The reason may be due to the chronic nature of IC/BPS and the impaired quality of life and psychological function in these patients. Our patients were generalized as thin, with BMIs of about 22–23 kg/m^2. We did not assess the BMI of patients prior to the onset of IC, and it was

Table 2
Univariate analysis for IC/BPS symptoms severity by study covariates.[a]

Variable (number of patients)	ICSI		ICPI		Pain		Frequency		Nocturia		FBC	
	β	*p*	β	*p*	β	*p*	β	*P*	β	*p*	β	*p*
Treatment												
HA (56)	0.18	0.80	0.55	0.50	−0.44	0.31	1.65	0.002	−0.34	0.22	−37.0	0.07
Botox + HA (24)	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
Age (y)												
<41 (22)	0.08	0.92	0.64	0.42	0.89	0.07	0.63	0.50	−0.49	0.16	23.5	0.33
41–55 (32)	−0.83	0.26	−0.62	0.44	0.26	0.54	−0.52	0.47	−0.80	0.005	12.3	0.55
>55 (26)	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
p for trend	0.98		0.47		0.08		0.54		0.13		0.33	
Sex												
Female (75)	0.26	0.87	0.57	0.67	−0.68	0.31	1.09	0.26	0.82	0.19	−22.9	0.49
Male (5)	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
BMI (kg/m^2)												
<20 (13)	1.76	0.05	1.54	0.17	1.08	0.08	1.33	0.24	0.52	0.15	−19.5	0.41
20–25 (45)	0.81	0.24	0.48	0.53	0.22	0.61	0.09	0.91	0.37	0.17	17.1	0.36
>25 (22)	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
p for trend	0.05		0.18		0.10		0.29		0.11		0.61	
Comorbidity												
No (53)	−1.20	0.09	−1.41	0.05	−0.60	0.14	−0.56	0.41	−0.26	0.41	35.5	0.04
Yes (27)	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
MBC (mL)												
<500 (12)	1.10	0.14	2.02	0.02	−0.66	0.29	3.09	0.002	1.26	0.005	−124.1	<0.001
500–800 (39)	−0.16	0.83	0.10	0.89	−0.90	0.03	0.63	0.30	0.51	0.06	−61.5	<0.001
>800 (29)	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
p for trend	0.33		0.08		0.13		0.003		0.004		<0.001	
Duration (y)												
<3 (20)	1.46	0.09	1.53	0.09	0.28	0.58	1.42	0.11	0.44	0.27	−10.2	0.66
3–7 (32)	1.06	0.145	0.85	0.29	0.19	0.66	0.10	0.88	0.59	0.02	19.3	0.35
>7 (28)	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
p for trend	0.08		0.09		0.57		0.12		0.21		0.77	
Marriage												
No (9)	1.20	0.29	1.57	0.20	1.08	0.18	0.05	0.95	0.18	0.66	−1.37	0.96
Yes (71)	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
Number of children												
0 (11)	0.25	0.80	0.68	0.53	0.48	0.51	0.06	0.94	−0.24	0.54	6.7	0.83
1–2 (43)	−1.0	0.11	−1.07	0.12	−0.53	0.17	−0.09	0.91	−0.53	0.07	−2.1	0.92
>2 (26)	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
p for trend	0.77		0.99		0.86		1.00		0.28		0.89	
Work												
No (46)	0.92	0.14	0.38	0.58	0.01	0.98	1.48	0.01	0.40	0.12	−28.2	0.10
Yes (34)	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
Smoking												
No (78)	−3.61	0.009	−3.08	0.13	−0.32	0.90	−0.81	0.53	−1.42	<0.001	33.4	0.002
Yes (2)	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	

BMI = body mass index; Botox = botulinum toxin A; FBC = functional bladder capacity; GEE = generalized estimating equation; HA = hyaluronic acid; IC/BPS = interstitial cystitis/bladder pain syndrome; ICPI = O'Leary–Sant IC problem index; ICSI = O'Leary–Sant IC symptom index; MBC = maximal bladder capacity; Ref. = reference.
[a] Models were fitted by GEE.

impossible to know whether patients with a low BMI experienced more severe symptoms or if it was a preexisting condition.

We also found that unemployment was significantly associated with more daytime frequency, consistent with the study of El Khoudary et al [27] who reported a significant association between employment status and physical functioning in IC patients. This result may be due to the "healthy worker effect" reported in research on other diseases. That is, healthier and better functioning individuals are employed. However, whether IC patients who are employed experience fewer symptoms or whether increased symptoms are related to not being currently employed is a difficult relationship to determine in a short-term study. A long-term prospective study is necessary to confirm this observation.

It is notable that MBC, symptom duration, BMI, and employment status were not correlated with the severity of bladder/pelvic pain, characteristics of IC/BPS, in our patients. One explanation is that all of our participants had previously been treated for IC/BPS. Patients may experience less pain if they have had analgesics or anti-inflammatory therapy, regardless of the organic or nonorganic origin of the disease. Treatments may affect pain more than the cystoscopic findings. Another reason could be confusion about the definition of pain. A study of Sirinian et al [46] showed that tandem pain questions on the ICSI and ICPI did not correlate as highly as might be expected.

This study is the first to comprehensively assess the socio-demographic and clinical factors that affect the symptom severity of patients with IC/BPS in Taiwan. After adjusting for important covariates and using validated instruments, we demonstrated significant associations between the MBC and disease duration and IC/BPS symptom severity. In previous research, IC/BPS symptoms were studied in a cross-sectional manner. The symptoms of IC/BPS are not constant with time. Variation in symptoms may not reflect the typical symptoms experienced by patients and could result in changes in predictors of symptom severity. Given the repeated measurements of outcome parameters, we believe that the associations found in this study are likely to be representative of symptoms experienced by patients with IC/BPS, rather than statistical anomalies.

The main limitation of our study was the relatively small sample size. Our study participants were restricted to patients with IC/BPS

Table 3
Multivariate analysis for IC/BPS symptoms severity by MBC and symptom duration.[a]

	ICSI			ICPI			Pain		
	β	95% CI	*p*	β	95% CI	*p*	β	95% CI	*p*
Model 1									
MBC (mL)									
<500	1.10	−0.45–2.64	0.16	2.01	0.34–3.68	0.02	−0.67	−1.92–0.58	0.29
500–800	−0.25	−1.74–1.24	0.74	−0.01	−1.47–1.45	0.99	−0.95	−1.75–0.15	0.02
> 800	Ref.			Ref.			Ref.		
p for trend	0.37			0.08			0.13		
Duration (y)									
<3	1.51	−0.15–3.17	0.07	1.59	−0.05–3.22	0.06	0.41	−0.50–1.32	0.38
3–7	1.12	−0.32–2.56	0.13	0.96	−0.60–2.53	0.23	0.14	−0.72–1.00	0.75
>7	Ref.			Ref.			Ref.		
p for trend	0.07			0.06			0.40		
Model 2									
MBC (mL)									
<500	1.14	−0.54–2.82	0.18	2.45	0.76–4.15	0.005	−0.19	−1.48–1.11	0.78
500–800	−0.20	−1.66–1.26	0.79	0.08	−1.36–1.52	0.91	−0.83	−1.53–0.12	0.02
>800	Ref.			Ref.			Ref.		
p for trend	0.42			0.05			0.33		
Duration (y)									
<3	1.41	−0.30–3.11	0.11	1.25	−0.48–2.99	0.16	0.21	−0.79–1.22	0.67
3–7	0.94	−0.61–2.48	0.24	0.74	−0.91–2.39	0.38	0.23	−0.59–1.06	0.58
>7	Ref.			Ref.			Ref.		
p for trend	0.10			0.16			0.64		
Model 3									
MBC (mL)									
<500	0.86	−0.75–2.46	0.29	2.29	0.52–4.06	0.01	−0.31	−1.62–1.00	0.64
500–800	−0.12	−1.54–1.30	0.87	0.06	−1.34–1.46	0.93	−0.85	−1.55–0.15	0.02
>800	Ref.			Ref.			Ref.		
p for trend	0.50			0.07			0.26		
Duration (y)									
<3	1.53	0.07–2.99	0.04	1.38	−0.25–3.01	0.10	0.31	−0.61–1.23	0.51
3–7	1.00	−0.50–2.50	0.19	0.69	−0.94–2.31	0.41	0.23	−0.58–1.04	0.58
>7	Ref.			Ref.			Ref.		
p for trend	0.04			0.10			0.49		

	Frequency			Nocturia			FBC		
	β	95% CI	*p*	β	95% CI	*p*	β	95% CI	*p*
Model 1									
MBC (mL)									
<500	3.00	0.87–5.13	0.006	1.35	0.49–2.21	0.002	−121.9	−161.2–82.5	<0.001
500–800	0.45	−0.63–1.54	0.41	0.52	−0.04–1.08	0.07	−59.5	−93.8–25.1	<0.001
>800	Ref.			Ref.			Ref.		
p for trend	0.008			0.002			<0.001		
Duration (y)									
<3	1.43	−0.24–3.10	0.09	0.41	−0.30–1.11	0.26	−5.3	−42.0–31.5	0.78
3–7	0.28	−0.93–1.49	0.65	0.69	0.18–1.20	0.008	11.8	−23.9–47.5	0.52
>7	Ref.			Ref.			Ref.		
p for trend	0.10			0.19			0.87		
Model 2									
MBC (mL)									
<500	3.38	1.26–5.49	0.002	1.38	0.54–2.21	0.001	−120.5	−163.7–77.3	<0.001
500–800	0.50	−0.66–1.66	0.40	0.54	−0.04–1.11	0.07	−56.4	−88.9–23.9	<0.001
>800	Ref.			Ref.			Ref.		
p for trend	0.005			0.001			<0.001		
Duration (y)									
<3	1.03	−0.41–2.47	0.16	0.40	−0.29–1.09	0.26	−3.1	−37.7–31.5	0.86
3–7	−0.02	−1.24–1.19	0.97	0.46	−0.04–0.95	0.07	16.0	−23.7–55.7	0.43
>7	Ref.			Ref.			Ref.		
p for trend	0.18			0.20			0.98		
Model 3									
MBC (mL)									
<500	3.08	1.27–4.90	0.001	1.33	0.54–2.12	0.001	−114.7	−157.6–71.7	<0.001
500–800	0.67	−0.56–1.90	0.28	0.58	−0.02–1.17	0.057	−55.0	−88.3–21.8	0.001
>800	Ref.			Ref.			Ref.		
p for trend	0.002			0.001			<0.001		
Duration (y)									
<3	1.18	−0.10–2.45	0.07	0.43	−0.22–1.08	0.20	−7.3	−41.9–27.4	0.68
3–7	0.12	−0.94–1.18	0.83	0.47	−0.02–0.96	0.06	16.7	−21.1–54.4	0.39
>7	Ref.			Ref.			Ref.		
p for trend	0.08			0.15			0.84		

BMI = body mass index; CI = confidence interval; FBC = functional bladder capacity; GEE = generalized estimating equation; IC/BPS = interstitial cystitis/bladder pain syndrome; ICPI = O'Leary–Sant IC problem index; ICSI = O'Leary–Sant IC symptom index; MBC = maximal bladder capacity; Ref. = reference.

[a] Models were fitted by GEE. Model 1: included MBC and duration; Model 2: adjusted for age, sex, and treatment; Model 3: adjusted for age, sex, treatment, BMI, and work.

Table 4
Multivariate analysis for ICSI, ICPI, and GRA by MBC and symptom duration.[a]

	ICSI			ICPI			GRA		
	OR	95% CI	*p*	OR	95% CI	*p*	OR	95% CI	*p*
Model 1									
MBC (mL)									
<500	0.72	−1.33–0.67	0.52	3.55	0.18–2.36	0.02	0.74	−1.68–1.08	0.67
500–800	0.72	−1.22–0.57	0.48	1.15	−0.79–1.07	0.76	1.06	−0.82–0.94	0.89
>800	Ref.			Ref.			Ref.		
p for trend	0.47			0.06				0.74	
Duration (y)									
<3	2.17	−0.29–1.84	0.15	1.50	−0.63–1.45	0.44	0.78	−1.35–0.86	0.67
3–7	1.34	−0.66–1.25	0.55	1.17	−0.76–1.09	0.73	2.57	0.01–1.88	0.05
>7	Ref.			Ref.			Ref.		
p for trend	0.16			0.45				0.90	
Model 2									
MBC (mL)									
<500	0.55	−1.65–0.45	0.26	4.30	0.31–2.60	0.01	0.59	−1.98–0.94	0.49
500–800	0.76	−1.18–0.63	0.56	1.18	−0.78–1.10	0.73	1.12	−0.82–1.05	0.81
>800	Ref.			Ref.			Ref.		
p for trend	0.30			0.06				0.66	
Duration (y)									
<3	2.14	−0.38–1.90	0.19	1.38	−0.83–1.47	0.58	0.79	−1.41–0.93	0.69
3–7	1.08	−0.99–1.14	0.89	0.96	−1.00–0.92	0.93	2.37	−0.09–1.82	0.08
>7	Ref.			Ref.			Ref.		
p for trend	0.23			0.62				0.89	
Model 3									
MBC (mL)									
<500	0.46	−1.86–0.32	0.17	4.12	0.21–2.62	0.02	0.65	−1.90–1.05	0.57
500–800	0.77	−1.17–0.64	0.56	1.11	−0.85–1.07	0.83	1.11	−0.84–1.05	0.83
>800	Ref.			Ref.			Ref.		
p for trend	0.21			0.08				0.72	
Duration (y)									
<3	2.30	−0.20–1.86	0.11	1.41	−0.79–1.47	0.55	0.74	−1.50–0.90	0.62
3–7	1.09	−0.99–1.16	0.87	0.90	−0.10–0.89	0.84	2.41	−0.07–1.83	0.07
>7	Ref.			Ref.			Ref.		
p for trend	0.16			0.60			0.84		

BMI = body mass index; CI = confidence interval; FBC = functional bladder capacity; GEE = generalized estimating equation; GRA = global response assessment; IC/BPS = interstitial cystitis/bladder pain syndrome; ICPI = O'Leary–Sant IC problem index; ICSI = O'Leary–Sant IC symptom index; OR = odds ratio; MBC = maximal bladder capacity; Ref. = reference.

[a] Models were fitted by GEE, outcome parameters as binary variables, severe symptom defined as ICSI ≥ 12, ICPI ≥ 12, successful result defined as GRA ≥ 2; Model 1: included MBC and duration; Model 2: adjusted for age, sex, and treatment; Model 3: adjusted for age, sex, treatment, BMI, and work.

refractory to conventional treatments. The results may not be generalized to mild cases, although one can argue that mild cases would not be bad enough to prompt patients to seek care or to show improvement results. The study follow-up was short. Our outcome measures may not necessarily correlate with long-term results after treatment. Also, the lack of an objective assessment for urgency and an evaluation of the impact on quality of life may have subjected our data to omitted variable bias. Further large-scale and long-time follow-up studies are needed to minimize bias.

In conclusion, our current study showed that MBC and symptom duration significantly correlated with symptom severity in patients with refractory IC/BPS in Taiwan, indicative of possible predictive factors. BMI and employment status were independently associated with symptom severity in these patients.

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