

Prospective Study

Pelvic Floor Myofascial Pain Might Influence Treatment Outcome of Interstitial Cystitis/Bladder Pain Syndrome: A Prospective Study

Wan-Ru Yu, MS^{1,2}, Fei-Chi Chuang, MD³, Wei-Chuan Chang, MS⁴, and Hann-Chorng Kuo, MD^{2,5}

From: ¹Department of Nursing, Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Hualien, Taiwan; ²Department of Urology, School of Medicine, Tzu Chi University, Hualien, Taiwan; ³Department of Obstetrics and Gynecology, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan; ⁴Department of Medical Research, Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Hualien, Taiwan; ⁵Department of Urology, Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation

Address Correspondence:
Hann-Chorng Kuo, MD
Department of Urology, Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, 707, Section 3, Chung Yang Road Hualien, Taiwan
E-mail: wanzu666@gmail.com or hck@tzuchi.com.tw

Disclaimer: There was no external funding in the preparation of this manuscript.

Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.

Manuscript received: 04-30-2022
Revised manuscript received: 08-02-2022
Accepted for publication: 08-29-2022

Free full manuscript:
www.painphysicianjournal.com

Background: In patients with interstitial cystitis or bladder pain syndrome (IC/BPS), 85% were found to have pelvic floor myofascial pain (PFMP) and hypertonicity (PFH). However, they physicians are not typically trained to consider or assess PFMP as a contributing factor to patients' IC/BPS symptoms.

Objective: This study aimed to explore the relationship between PFMP and treatment outcomes in women with IC/BPS.

Study Design: A prospective study.

Setting: Department of Urology, Medical Center, Hualien, Taiwan.

Methods: Patients with IC/BPS who received any type of treatment were prospectively enrolled. They underwent vaginal digital examination at baseline. PFMP severity was quantified on the visual analog scale (VAS). Subject assessment items included O'Leary-Sant symptom score (OSS), Global Response Assessment (GRA), and Beck's anxiety inventory. Object assessment items included bladder computed tomography (CT), urodynamic parameters, maximum bladder capacity, and grade of glomerulation.

Results: A total of 65 women with IC/BPS (mean age, 57.1 ± 11.3 years) were enrolled in the study. Patients with more severe PFMP had significantly higher rate of dyspareunia ($P = 0.031$); more comorbidities ($P = 0.010$); higher number of PFMP sites ($P < 0.001$); and higher OSS ($P = 0.012$). PFMP severity was not significantly correlated with bladder conditions, whether subjective or objective. Moreover, PFMP severity (VAS) was significantly negatively associated with the GRA score.

Limitations: There was a small sample size and short follow-up duration, the patients in this study are all women, and the applicability to other populations is uncertain.

Conclusion: PFMP might affect the subjective results of IC/BPS treatment but not the bladder condition. Therefore, in the future treatment of patients with IC/BPS, digital vaginal examinations of pelvic floor muscles should be performed and focused more on the PFM-related conditions, and necessary PFM treatments, such as the vaginal pelvic floor muscle message, should be scheduled.

Key words: Interstitial cystitis/bladder pain syndrome, bladder pain, pelvic floor muscle, myofascial pain, trigger point, pelvic muscles hypertonicity, vaginal examination

Pain Physician 2022; 25:E1317-E1324

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a disease of unknown etiology. This multifactorial clinical condition is typically characterized by irritative voiding symptoms in the form of urinary frequency and urgency, with debilitating episodic, chronic pain (1). IC/BPS has been included in myofascial pain and neuropathic pain syndromes interrelated with the immune and inflammatory systems (2). The prevalence rate of IC/BPS is between 3% and 10% and more frequent among women (3). To date, classic Hunner's lesion interstitial cystitis (HIC) is a bladder disease, and bladder treatment improves symptoms. Non-Hunner's lesion interstitial cystitis (NHIC) likely has multiple etiologies and, in many cases, is difficult to treat. The bladder might be an innocent bystander in a larger pelvic process (4), and systemic and immune conditions are in need of further attention. Jiang et al even pointed out that suburothelial inflammation and apoptosis are highly prevalent in the bladders of patients with urolithiasis, which even had a smaller maximal bladder capacity (MBC) (5). Our previous study also demonstrated that stress is positively associated with pain in patients with IC/BPS, while stress reduction can lead to a simultaneous decrease in the severity of other symptoms (6).

Pelvic floor muscle (PFM) is often associated with urological, gynecological, gastrointestinal, and sexual problems and chronic pelvic pain. Several researchers also noted that PFM hypertonicity (PFH), also called pelvic floor myofascial pain (PFMP), could affect treatment outcomes and quality of life (2,7-9). The prevalence of PFMP in patients with IC/BPS ranges from 50% to 90% (4). When muscle fiber trauma occurs, inflammatory mediators, such as bradykinin, serotonin, prostaglandins, adenosine triphosphate, and histamine, are released locally, which sensitize muscle nociceptors and reduce their mechanical threshold and result in muscle hyperalgesia and mechanical allodynia (10). Myofascial pain can also develop secondary to the presence of bladder pain syndrome (11). The location and severity of PFMP are significantly correlated with the degree of symptoms, even after controlling for postmenopausal status (9).

The PFMP may be quite severe and is usually accompanied by acute attacks that awaken patients and symptoms are usually vague and poorly localized (12). However, pelvic pain is not perceived at the site of the trigger point origin but at a remote site (referred pain) (11,13). Until very recently, these hypotheses were difficult to study because a standardized, reproducible

examination for PFMP did not exist (6). In patients with IC/BPS, 85% were found to have PFMP and PFH (14). However, PFMP has remained largely understudied and poorly recognized by women's health providers who are not typically trained to consider or assess for PFMP as a contributing factor to patients' IC/BPS symptoms (6). This study aimed to explore the relationship between PFMP and treatment outcomes in women with IC/BPS.

METHODS

This is a prospective study that enrolled 65 women who had been diagnosed with IC/BPS from September 2020 to June 2021. The Ethics Committee of Buddhist Tzu Chi General Hospital approved the study (IRB Number: IRB105-25-B). All methods were performed in accordance with the relevant guidelines and regulations. Patients were informed about the study rationale and procedures; written informed consent was obtained from all patients prior to enrolment and treatment. These women had been evaluated and treated by urologists, gynecologists, psychiatrists, and other medical specialists without resolution of their pain. The diagnosis of IC/BPS was established based on the characteristic symptoms and cystoscopy findings of glomerulations, petechiae, or mucosal fissures after hydrodistention (15). The glomerulation grade was classified according to the appearance of glomerulations as follows: 0, none; 1, less than half of the bladder wall; 2, more than half of the bladder wall; or 3, severe waterfall bleeding; 4, patients with Hunner's lesions with or without glomerulation were classified as having ulcer-type IC/BPS (16). They had received several treatments, including cystoscopic hydrodistention, intravesical botulinum toxin A injection, electrocauterization of Hunner's lesions, and platelet-rich plasma (PRP) intravesical injection. These treatments were performed following the recommendations of the American Urological Association (AUA) guidelines (17). All patients had received video urodynamic study (VUDS), bladder computed tomography (CT), and cystoscopic hydrodistention at baseline (15). All patients underwent a comprehensive VUDS with a Urolab Janus 6 device (LifeTech, Inc., Stafford, Texas) using a double lumen 6 Fr catheter by one examiner in an identically aseptic manner. The pressure flow study was performed using the standard procedure in a sitting position according to the International Continence Society standardization. After the VUDS, 40 mL of 0.4 M KCl solution was infused slowly into the bladder, and the test was regarded as positive when

painful (increased VAS score ≥ 2) or urgency sensation was elicited compared to normal saline infusion during the prior urodynamic study. A vaginal digital examination was performed at the first visit to evaluate their PFM condition before treatment. The patients were investigated thoroughly upon enrolment. Inclusion criteria included adults with the age of 20 years old or above, confirmed diagnosis of IC/BPS under the cystoscopic hydrodistention without bladder lesion, urinary tract infection, bladder outlet obstruction, or neurogenic bladder dysfunction. Exclusion criteria included patients with severe cardiopulmonary disease, post-void residual urine > 150 mL, bladder outlet dysfunction or acute urinary tract infection, chronic kidney disease, and pregnant or lactating patients, referring to the criteria of the National Institute of Diabetes and Digestive and Kidney Diseases (15).

Procedure

Our evaluation included a comprehensive history and pelvic examination: a certified nurse practitioner who executed internal palpation and pressed performing with the index finger of the dominant hand, following the pelvic floor anatomy and palpated each muscle group in the center of the muscle belly, then in a sweeping motion along the length of the muscle in the direction of the orientation of that muscle and proceeds clockwise to examine all women in a comfortable dorsal lithotomy position (18). The pelvic examination included assessment of pubovaginalis, puborectalis, iliococcygeus, coccygeus, anal sphincter, obturator internus, piriformis, and tendinous arch. Pain scores on palpation of the internal sites were reported on an 11-point (0-10) visual analog scale (VAS). A retrospective chart review was conducted to gather additional data. Descriptive statistics were used to describe the sample and distribution of variables, such as bladder condition and pain levels.

Data Collection

The evaluation items included the patient's bladder characteristics, O'Leary-Sant score (OSS) with IC symptom index (ICSI) and IC problem index (ICPI), comorbidities, bladder CT, urodynamic parameters, MBC, and grade of glomerulation under cystoscopic hydrodistention. Comorbidities including depression or anxiety, myofascial pain, insomnia, diabetes, cardiovascular disease, reflux esophagitis, asthma, irritable bowel disease, constipation, lower back pain, and arrhythmia were recorded.

Global Response Assessment (GRA) was administered or determined one month after treatment, and anxiety severity was assessed by Beck's anxiety inventory (BAI). Patients were requested to rate their bladder symptoms compared with baseline on a 7-point centered scale, from markedly (-3), moderately (-2), and slightly worse (-1), no change (0), to slightly (+1), moderately (+2), and markedly improved (+3). Patients with moderately and markedly improved results after treatment were considered to have successful treatment outcomes. Otherwise, the treatment was considered to have failed (19). The BAI score was 0-18 points, indicating mild anxiety; 19-29 points indicating moderate anxiety; and 30-63 indicating severe anxiety (20). The ICSI and ICPI are 2 instruments questioning the overall level of severity of each symptom and the significance of the problem from the patient's perspective, respectively (21,22). Both indices included 4 questions, one for each of nocturia, frequency, urgency, and bladder-associated pain. The total ICSI score ranges from 0 to 20. Each of the questions in the ICPI has 5 response options ranging from 0 to 4, with a maximum total ICPI score of 16. The higher score indicates more severe IC/BPS symptoms and problem severity (21).

Statistical Analysis

Statistical comparisons between the groups were tested using the Pearson's chi-square test or Fisher's exact test for categorical variables and an independent t-test or analysis of variance for continuous variables to use multiple linear regression analyses on factors associated with PFMP and pain severity. All statistical analyses were performed using SPSS version 22.0 (SPSS Inc., Chicago, IL) with a *P* value < 0.05 being used as the criterion for statistical significance.

RESULT

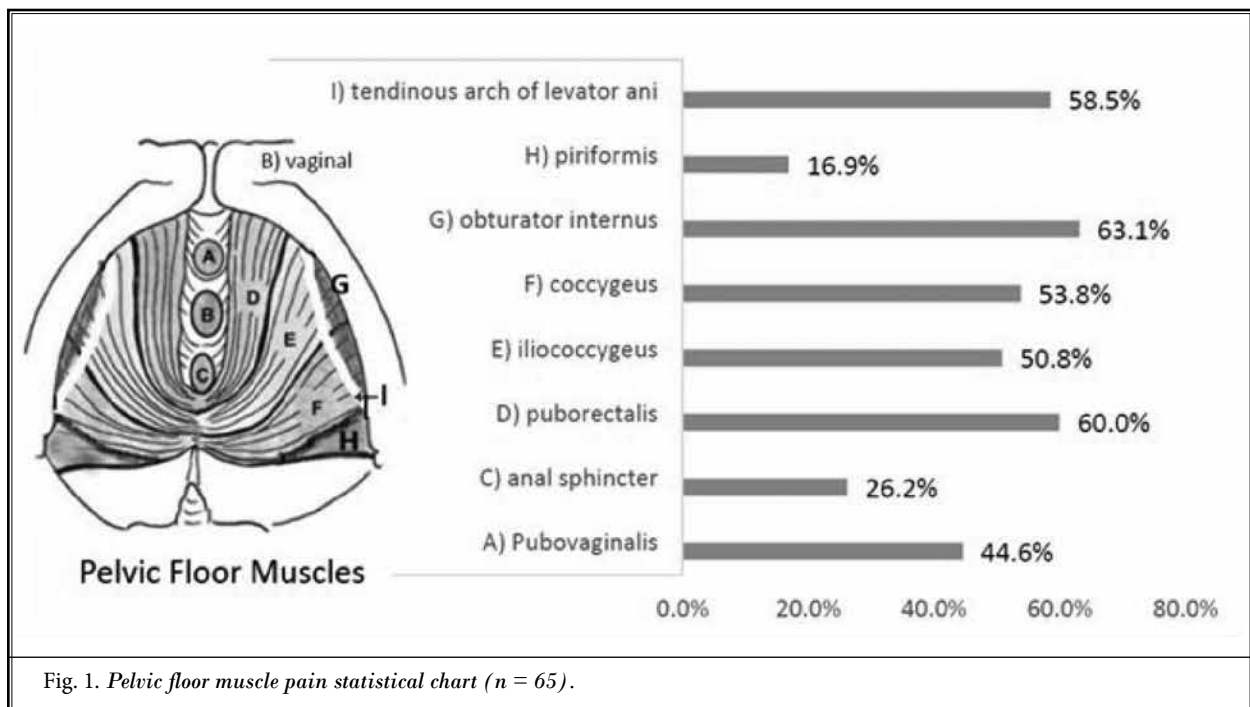
A total of 65 women with IC/BPS were included in this study. The mean age was 57.1 ± 11.3 years, and the mean duration of IC symptoms was 12.8 ± 10.5 years. They had received 3 types of treatment on average, 7 (11%) patients underwent cystoscopic hydrodistention, 3 (5%) received intravesical botulinum toxin A injection treatment, 53 (82%) patients received PRP intravesical injection, and 2 (3%) patients received the electrocoagulation of Hunner's lesions treatment. Moreover, 55 (73.8%) patients have had a vaginal delivery. Regarding sexual behavior, 30 (46.1%) patients had sex within the recent year, but 31 (47.7%) patients did not have sex for up to 5 years, and overall, up to 32 (49.2%) patients

had pain during sexual intercourse. We also found that 29 (44.6%) patients had transvaginal surgery. The self-reported mean OSS was 25.9 ± 7.8 , the self-reported lower abdominal pain score under the Numeric Rating Scale (NRS) was 6.1 ± 2.6 , and the mean severity of anxiety using BAI was 21.4 ± 12.0 . All patients underwent cystoscopic hydrodistention, with a mean MBC of 801.6 ± 170.6 mL and a mean glomerulation grade of 1.4 ± 1.1 .

When these patients underwent vaginal examination to assess their PFM trigger points, 56 (86.2%) patients had PFMP. Among the 14 assessment sites, the mean number of painful sites was 5.2 ± 4.4 , and the mean PFMP severity by VAS score was 6.9 ± 3.0 points. One month after treatment, 17 (26.1%) patients reported no change in GRA or even poor change ($\Delta\text{GRA} = -1 \sim -3$), 9 (13.8%) patients had no change after treatment ($\Delta\text{GRA} = 0$), 20 (30%) patients reported slight improvement ($\Delta\text{GRA} = +1$), and 28 (43%) patients reported a significant improvement after treatment ($\Delta\text{GRA} = +2 \sim +3$). The most painful sites are the obturator internus (63.1%) and puborectalis (60%) (Fig. 1). In the bladder CT of each patient with IC/BPS, we also noted that the bladder wall phenotype of 42 (66.7%) patients is smooth bladder wall. Furthermore, the bladder wall of 21 (33.3%) patients has a focal thickness or diffuse thickening.

When we divided the vaginal examination PFM trigger point pain score into 3 groups, 12 patients had mild PFMP (VAS of 0 to 3), 11 patients had moderate PFMP (VAS of 4 to 6), and 42 patients had severe PFMP (VAS of 7-10). Patients with more severe PFMP had significantly higher rate of dyspareunia in the sexual life (16.7% in the mild pain group, 45.5% in the moderate pain group, and 59.5% in the severe pain group, $P = 0.031$); more comorbidities (mild pain group, $.7 \pm .7$; moderate pain group, 2.6 ± 1.7 ; severe pain group, 2.2 ± 1.8 ; $P = 0.010$); higher number of myofascial pain sites (mild pain group, $.8 \pm 1.4$; moderate pain group, 3.6 ± 1.5 ; severe pain group, 6.8 ± 4.4 ; $P < 0.001$); and significant correlation with OSS (mild pain group, 19.9 ± 8.4 ; moderate pain group, 27.1 ± 9.2 ; severe pain group, 27.3 ± 6.6 ; $P = 0.012$) (Table 1).

Meanwhile, the self-reported treatment outcome (GRA) also had a significant correlation with different PFMP severity groups ($P = 0.015$). The GRA score was 2.2 ± 0.9 in patients with mild PFMP, which was higher than that in patients with moderate PFMP (1.6 ± 0.7) and severe PFMP (0.9 ± 1.5) (Table 1). However, the PFMP severity was not significantly correlated with the bladder conditions, whether subjective or objective, such as the patient self-reported uncomfortable bladder condition severity (NRS), MBC, and glomerulation grade during cystoscopic hydrodistention, VUDS parameters, pelvic



Pelvic Floor Myofascial Pain Might Influence Treatment Outcome of Interstitial Cystitis

Table 1. Correlation between subjective measured parameters of IC/BPS among different PFM pain severities from vaginal digital examination (n = 65).

PFM pain severity (VAS)		Mild pain VAS 0-3 (n = 12)	Moderate pain VAS 4-6 (n = 11)	Severe pain VAS 7-10 (n = 42)	P value
Age		55.2 ± 13.9	52.4 ± 8.7	58.8 ± 10.9	0.199
Sexual activity	Continue to have sex	7(58.4%)	5(45.5%)	15(35.7%)	0.734
	No sexual intercourse within a year	1(8.3%)	0(.0%)	2(4.8%)	
	No sexual intercourse within 3 years	1(8.3%)	1(9.0%)	2(4.8%)	
	No sexual intercourse for more than 5 years	3(25.0%)	5(45.5%)	23(54.7%)	
Dyspareunia		2(16.7%)	5(45.5%)	25(59.5%)	0.031*
Duration of IC/BPS		10.4 ± 10.1	9.9 ± 6.5	14.2 ± 11.3	0.340
Transvaginal surgery experience		5(41.7%)	3(27.3%)	21(50.0%)	0.392
Comorbidities		.7 ± .7	2.6 ± 1.7	2.2 ± 1.8	0.010*
Type of treatment\$		3.7 ± 1.3	3.2 ± .9	3.2 ± 1.4	0.513
Number of PFMP sites		.8 ± 1.4	3.6 ± 1.5	6.8 ± 4.4	< 0.001*
BAI		15.3 ± 8.3	19.5 ± 11.5	23.7 ± 12.6	0.082
ICSI		10.1 ± 4.9	14.1 ± 5.0	13.8 ± 4.0	0.029*
ICPI		9.8 ± 3.8	13.0 ± 4.4	13.5 ± 3.0	0.007*
OSS		19.9 ± 8.4	27.1 ± 9.2	27.3 ± 6.6	0.012*
NRS (self-reported lower abdomen pain severity)		4.7 ± 3.2	6.7 ± 2.6	6.4 ± 2.3	0.093
GRA		2.2 ± .9	1.6 ± .7	.9 ± 1.5	0.015*

IC/BPS, interstitial cystitis/bladder pain syndrome; PFM, pelvic floor muscle; VAS, visual analog scale; BAI, Beck's anxiety inventory; ICSI, interstitial cystitis symptom index; ICPI, interstitial cystitis problem index; OSS, O'Leary-Sant score; NRS, numerical rating scale; GRA, global response assessment; *P < 0.05

\$: type of treatment included cystoscopic hydrodistension, intravesical hyaluronic acid (HA) instillations, electrocoagulation of Hunner's lesions, and intravesical botulinum toxin A (BoNT-A) injections, or novel treatment with plasma-rich platelet (PRP) injection.

CT image, and even uroflowmetry parameters such as Qmax (ΔP value = 0.176), voiding volume (ΔP value = 0.31), and post-void residual urine (PVR) (ΔP value = 0.770) (Table 2).

The final regression model revealed that the PFMP severity (VAS) as a dependent variable, including 6 independent variables of which only GRA ($P < 0.001$) was statistically significant, and there was no significant difference with age, OSS, anxiety severity (BAI), glomerulation grade, and MBC. The results showed that an improvement of 0.10 on the PFMP severity (VAS) of relatives' GRA was associated with a decreased burden of 1.65 scale steps (Table 3).

DISCUSSION

Pelvic floor myofascial pain might influence the treatment outcome of IC/BPS patients of women.

To date, there is no gold standard treatment strategy for patients with IC/BPS, only a suitable treatment (23). Many efforts have been attempted to find a better treatment outcome for patients with IC/BPS, including antiviral treatment for Epstein-Barr virus infection

(24,25). PRP injection for an increase in regenerative deficits in IC/BPS, and psychiatric consultation for psychosomatic dysfunction associated with IC/BPS (24,25). In this study, we also found that patients with IC/BPS have 2.0 ± 1.7 comorbid psychosomatic disorders, such as depression, insomnia, reflux esophagitis, asthma, irritable colon, and arrhythmia (26).

Simultaneously, Gisela also reported the high frequency of comorbid disorders well beyond geographic contiguity with the bladder region affecting our pathophysiologic construct of IC/BPS, suggesting either some type of systemic disorder, a process under the central nervous system (CNS) control, or both (27). An abnormal CNS drive seems likely to cause a secondary psycho-neuro-endocrine-immune dysfunction in patients with IC/BPS (25). Significantly more psychosomatic comorbidities are noted in the moderate PFMP severity group than that in the mild PFMP group ($P = 0.010$). Similarly, dyspareunia is also a significantly more common complaint in the severe PFMP group than in other groups ($P = 0.031$). These results are consistent with the results of a previous study (7).

Table 2. Correlation between objective measured parameters of IC/BPS among different PFM pain severity from vaginal digital examination (n = 65).

PFM pain severity (VAS)		Mild pain VAS 0-3 (n = 12)	Moderate pain VAS 4-6 (n = 11)	Severe pain VAS 7-10 (n = 42)	P value		
MBC		750.0 ± 179.6	804.6 ± 179.5	816.3 ± 166.9	0.505		
Glomerulation grade		1.5 ± 1.2	1.3 ± .9	1.3 ± 1.2	0.875		
Bladder CT finding		Smooth	10(83.4%)	5(50.0%)	27(65.9%)	0.474	
		Focal	1(8.3%)	4(40.0%)	9(22.0%)		
		diffuse	1(8.3%)	1(10.0%)	5(12.1%)		
VUDS parameter	FSF	125.9 ± 38.0	122.5 ± 46.2	116.8 ± 46.4	0.800		
	FS	217.1 ± 81.7	194.6 ± 62.9	197.3 ± 74.5	0.688		
	CBC	254.8 ± 91.5	243.6 ± 66.2	259.8 ± 126.9	0.914		
	Pdet	15.5 ± 7.3	19.3 ± 6.4	19.3 ± 12.6	0.569		
KCL test		Negative	2(16.7%)	0(.0%)	2(4.8%)	0.065	
		Positive with pain	7(58.3%)	7(63.6%)	36(85.6%)		
		Positive with urge	3(25.0%)	2(18.2%)	2(4.8%)		
		Positive with pain and urgency	0(.0%)	2(18.2%)	2(4.8%)		
Uroflowmetry		Qmax	Baseline	12.3 ± 5.5	10.9 ± 5.9	11.1 ± 5.5	0.771
			After-treatment 1M	13.8 ± 8.3	16.7 ± 6.4	19.0 ± 11.8	0.318
			Δ	1.5 ± 8.7	5.6 ± 6.4	7.9 ± 11.5	0.176
		Voiding volume	Baseline	233.4 ± 111.0	214.2 ± 85.0	221.4 ± 118.2	0.915
			After-treatment 1M	172.8 ± 72.9	237.4 ± 171.7	197.3 ± 104.6	0.392
			Δ	-60.7 ± 110.4	23.2 ± 161.6	-24.1 ± 126.9	0.311
		PVR	Baseline	42.1 ± 86.6	45.5 ± 71.0	54.5 ± 108.3	0.913
			After-treatment 1M	17.3 ± 18.4	37.4 ± 48.5	23.4 ± 28.7	0.290
			Δ	-24.8 ± 77.3	-8.1 ± 88.5	-31.1 ± 99.3	0.770
Voiding condition		PRES	2(16.7%)	0(.0%)	8(19.0%)	0.640	
		DV	1(8.3%)	1(9.1%)	4(9.6%)		
Storage condition		HSB	9(75.0%)	8(72.7%)	32(76.2%)	0.267	
		DO	1(8.3%)	3(27.3%)	3(7.1%)		

IC/BPS, interstitial cystitis/bladder pain syndrome; PFM, pelvic floor muscle; VAS, visual analog score; MBC, maximal bladder capacity; CT, computed tomography; VUDS, video urodynamic study; FSF, first sensation of filling; FS, full sensation; CBC, cytometric bladder capacity; Pdet, detrusor pressure; Qmax, maximum flow rate; PVR, post-void residual urine; PRES, poor relaxation of external urethral sphincter; DV, dysfunctional voiding; HSB, hypersensitivity bladder; DO, detrusor overactivity; *P < 0.05

Table 3. Multiple linear regression analyses on factors associated with PFM pain severity (VAS) (n = 65).

Constant	Coefficient (β)	95% CI		P value
Age	-0.059	-0.015	0.133	0.116
OSS	0.096	-0.018	0.210	0.098
BAI	-0.001	-0.082	0.080	0.975
Glomerulation grade	-0.099	-1.054	0.856	0.836
GRA	-1.645	-2.293	-0.996	< 0.001*
MBC	-0.001	-0.007	0.004	0.597

OSS, O’Leary-Sant score; BAI, Beck’s anxiety inventory; GRA, global response assessment; MBC, maximal bladder capacity; *P < 0.05

One previous study has revealed the high prevalence (78% to 87%) of concomitant myofascial pain, frequently extending beyond the anatomical boundaries of the pelvis in women with IC/BPS. Almost a quarter of women with chronic pelvic pain (CPP) have musculoskeletal abnormalities (27-30). Interestingly, the mean PFM trigger point pain scores in healthy control women were lower than that in CPP and IC/BPS subjects (29). It is likely that patients with CPP and IC/BPS might have more discomfort in the PFMs. Although the self-report IC/BPS symptom scores (ICSI, ICPI) are indeed relatively higher in the moderate to severe PFMP group (P = 0.012), there is no difference in the MBC (P = 0.505)

and glomerulation grade ($P = 0.875$) and changes of uroflowmetry parameters (changes of P-value, Qmax: 0.176; voiding volume: 0.311; PVR: 0.770) among different PFMP groups. The self-report IC/BPS symptom and problem index (OSS) might be more related to the psychological condition rather than the bladder conditions, causing an increase in the patient's anxiety status score (BAI) with PFMP (6).

Likewise, the GRA score also has a significant association with different PFMP severities. This result has repeatedly demonstrated that self-report treatment outcomes are closely related to PFM conditions, such as in the ICSI ($P = 0.029$), ICPI ($P = 0.007$), and even GRA ($P = 0.015$). Compared with another study reporting on CPP in women, PFMP was significantly higher than that in healthy women (58.3% vs 4.2%, $P < 0.001$), and women with CPP had higher BAI score (22 vs 13, $P = 0.02$), higher dyspareunia rate (63.5% vs 28.9%, $P < 0.004$), and higher constipation rate (46.0% vs 26.7%, $P = 0.05$) than those without PFMP (10).

As mentioned above, the HIC subtype is a distinct inflammatory disease with proven bladder etiology and is characterized by epithelial denudation and enhanced immune responses (30). Meanwhile, the NHIC subtype is potentially associated with urothelial malfunction and neurophysiological dysfunction and frequently presents with somatic and/or psychological symptoms, which might result from psychosomatic disorders due to CNS sensitization. Furthermore, if CNS inflammation is the cause of bladder disorders in IC/BPS, the inflammatory responses in the CNS involve the participation of different cellular immune systems and resident cells of the CNS, adhesion molecules, cytokines, and chemokines, among other protein components. If this process is not well controlled or is prolonged, the bladder will ultimately lose its regenerative and repair function and can be the cause of urothelial damage and bladder dysfunction (31).

In this study, 86.2% of patients with IC/BPS have PFMP, and patients with a higher pelvic pain severity also have more CNS sensitization comorbidities. However, the severity of pelvic pain is not significantly related to bladder conditions, such as MBC, glomerulation grade, and even urodynamic parameters, but is significantly related to self-reported bladder symptom index.

Moreover, the multiple linear regression analyses also show that PFMP severity is significantly correlated with patient's self-reported treatment outcomes. The results of this study reveal that the PFMP could influence the treatment outcome of women with IC/BPS.

CONCLUSION

PFMP might affect the subjective results of IC/BPS treatment but not bladder conditions. Therefore, in the future treatment of patients with IC/BPS, digital vaginal examinations of PFMs should be performed in every patient with IC/BPS and focused more on PFM-related conditions, and necessary PFM treatments, such as the vaginal PFM message, should be scheduled.

Author Contributions

HCK conceived the study and provided supervision. HCK and FCC made critical comments. WRY designed the study workflow, and acquired and analyzed it in addition to drafting the article and making critical revisions; WCC interoperated the data. All the authors reviewed the manuscript.

Author Contributions

Drs. Yu and Chang had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Drs. Kuo and Yu designed the study protocol. Dr. Yu managed the literature searches and summaries of previous related work and wrote the first draft of the manuscript. Drs. Chuang and Kuo provided revision for intellectual content and final approval of the manuscript.

Acknowledgments

This study was supported by TCGH IRB: 105-25-B from the Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation.

We also would like to thank the editorial board of Pain Physician for review and criticism in improving the manuscript.

Institutional Review

This study was supported by TCGH IRB: 105-25-B from the Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation.

REFERENCES

- Lukban JC, Parkin JV, Holzberg AS, Caraballo R, Kellogg-Spadt S, Whitmore KE. Interstitial cystitis and pelvic floor dysfunction: A comprehensive review. *Pain Med* 2001; 2:60-71.
- Borrego-Jimenez PS, Flores-Fraile J, Padilla-Fernández BY, et al. Improvement in quality of life with pelvic floor muscle training and biofeedback in patients with painful bladder syndrome/interstitial cystitis. *J Clin Med* 2021; 10:862.
- Grinberg K, Sela Y, Nissanholtz-Gannot R. New Insights about Chronic Pelvic Pain Syndrome (CPPS). *Int J Environ Res Public Health* 2020; 17:3005.
- Han E, Nguyen L, Sirls L, Peters K. Current best practice management of interstitial cystitis/bladder pain syndrome. *Ther Adv Urol* 2018; 10:197-211.
- Jiang YH, Kuo HC. Urothelial dysfunction and increased suburothelial inflammation of urinary bladder are involved in patients with upper urinary tract urolithiasis—clinical and immunohistochemistry study. *PLoS One* 2014; 9:e110754.
- Yu WR, Peng TC, Yeh HL, Kuo HC. Anxiety severity does not influence treatment outcomes in patients with interstitial cystitis/bladder pain syndrome. *NeuroUrol Urodyn* 2019; 38:1602-1610.
- van Reijn-Baggen DA, Han-Geurts IJM, Voorham-van der Zalm PJ, Pelger RCM, Hagenaaars-van Miert CHAC, Laan ETM. Pelvic floor physical therapy for pelvic floor hypertonicity: A systematic review of treatment efficacy. *Sex Med Rev* 2022; 10:209-230.
- Bartley J, Han E, Gupta P, et al. Transvaginal trigger point injections improve pain scores in women with pelvic floor hypertonicity and pelvic pain conditions. *Female Pelvic Med Reconstr Surg* 2019; 25:392-396.
- Meister MR, Sutcliffe S, Badu A, Ghetti C, Lowder JL. Pelvic floor myofascial pain severity and pelvic floor disorder symptom bother: Is there a correlation? *Am J Obstet Gynecol* 2019; 221:235.e1-235.e15.
- Montenegro ML, Mateus-Vasconcelos EC, Rosa e Silva JC, Nogueira AA, Dos Reis FJ, Poli Neto OB. Importance of pelvic muscle tenderness evaluation in women with chronic pelvic pain. *Pain Med* 2010; 11:224-228.
- Gyang A, Hartman M, Lamvu G. Musculoskeletal causes of chronic pelvic pain: What a gynecologist should know. *Obstet Gynecol* 2013; 121:645-650.
- Howard FM, ed. Pelvic pain: Diagnosis and management. *Lippincott Williams & Wilkins Publishing*; 2000.
- Gerwin RD. Myofascial pain syndromes from trigger points. *Curr Rev Pain* 1999; 3:153-159.
- Butrick CW. Interstitial cystitis and chronic pelvic pain: New insights in neuropathology, diagnosis, and treatment. *Clin Obstet Gynecol* 2003; 46:811-823.
- Hanno PM, Sant GR. Clinical highlights of the National Institute of Diabetes and Digestive and Kidney Diseases/Interstitial Cystitis Association scientific conference on interstitial cystitis. *Urology* 2001; 57:2-6.
- Yu WR, Jhang JF, Ho HC, et al. Cystoscopic hydrodistention characteristics provide clinical and long-term prognostic features of interstitial cystitis after treatment. *Sci Rep* 2021; 11(11):455.
- Hanno PM, Burks DA, Clemens JQ, et al. AUA guideline for the diagnosis and treatment of interstitial cystitis/bladder pain syndrome. *J Urol* 2011; 185:2162-2170.
- Meister MR, Sutcliffe S, Ghetti C, et al. Development of a standardized, reproducible screening examination for assessment of pelvic floor myofascial pain. *Am J Obstet Gynecol* 2019; 220:255.e1-255.e9.
- Kuo HC. Repeated onabotulinumtoxin-a injections provide better results than single injection in treatment of painful bladder syndrome. *Pain Physician* 2013; 16:E15-E23.
- Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: Psychometric properties. *J Consult Clin Psychol* 1988; 56:893-897.
- Esen B, Obaid K, Süer E, et al. Reliability and validity of Turkish versions of the interstitial cystitis symptom index and interstitial cystitis problem index. *NeuroUrol Urodyn* 2020; 39:2338-2343.
- O'Leary MP, Sant GR, Fowler FJ Jr, Whitmore KE, Spolarich-Kroll J. The interstitial cystitis symptom index and problem index. *Urology* 1997; 49:58-63.
- Hanno PM, Nordling J, Staskin DR, Wein AJ, Wyndaele JJ. Bladder Pain Syndrome—An Evolution (e-book). *Springer Cham Publishing*; 2018.
- Jhang JF, Hsu YH, Peng CW, Jiang YH, Ho HC, Kuo HC. Epstein-Barr virus as a potential etiology of persistent bladder inflammation in human interstitial cystitis/bladder pain syndrome. *J Urol* 2018; 200:590-596.
- Akiyama Y. Update on the pathophysiology of interstitial cystitis/bladder pain syndrome. *Curr Bladder Dysfunct Rep* 2020; 15:1-8.
- Irwin MR, Cole SW. Reciprocal regulation of the neural and innate immune systems. *Nat Rev Immunol* 2011; 11:625-632.
- Chelimsky G, Heller E, Buffington CA, Rackley R, Zhang D, Chelimsky T. Comorbidities of interstitial cystitis. *Front Neurosci* 2012; 6:114.
- Wang Y, Kasper LH. The role of microbiome in central nervous system disorders. *Brain Behav Immun* 2014; 38:1-12.
- Sanses TV, Chelimsky G, McCabe NP, et al. The pelvis and beyond: Musculoskeletal tender points in women with chronic pelvic pain. *Clin J Pain* 2016; 32:659-665.
- Akiyama Y, Luo Y, Hanno PM, Maeda D, Homma Y. Interstitial cystitis/bladder pain syndrome: The evolving landscape, animal models and future perspectives. *Int J Urol* 2020; 27:491-503.
- Chavarria A, Alcocer-Varela J. Is damage in central nervous system due to inflammation? *Autoimmun Rev* 2004; 3:251-260.