Published in final edited form as:
Urology. 2006 June ; 67(6): 1138–1143.

Using the International Continence Society's Definition of Painful Bladder Syndrome

John W. Warren[1], **Walter A. Meyer**[2], **Patty Greenberg**[1], **Linda Horne**[1], **Christina Diggs**[1], and **J. Kathleen Tracy**[2]

1*Departments of Medicine and*

2*Epidemiology and Preventive Medicine, University of Maryland School of Medicine*

Abstract

Objectives—The case definition of interstitial cystitis (IC) is in flux. The International Continence Society (ICS) suggested a definition for the painful bladder syndrome (PBS), a concept embraced by many IC investigators, some of whom have used the name IC/PBS. In a study of recent onset IC/PBS patients, we had two objectives: to determine 1) what proportion met the ICS definition and 2) how did those who met the definition differ from those who did not.

Methods—Having recruited women who had recent onset IC/PBS for an ongoing case control study to identify its risk factors, we studied our first 138 eligible cases to identify those who met the ICS definition. We then compared those who met the definition to those who did not by variables acquired through interviews and medical records.

Results—The 138 participants had intensities of pain, urgency, frequency, and nocturia as well as O'Leary-Sant Symptom Index scores similar to those of previously reported IC/PBS patients. Six percent of cystoscopies demonstrated Hunner's ulcers and 89% of hydrodistentions under anesthesia revealed glomerulations.

The most liberal interpretation of the ICS definition did not include 47/138 (34%) of our cases. Comparing these to the 91 (66%) who did meet the ICS criteria, we found that 96/97 clinical variables, including many generally thought characteristic of IC/PBS, were not significantly different between the 2 groups.

Conclusions—The ICS definition identified only 91/138 (66%) of those cases whom study investigators and caregivers diagnosed as IC/PBS. Furthermore, those who met the ICS definition did not differ in important ways from those who did not meet it. These observations taken together suggest that the ICS definition may not be sufficiently sensitive. Minor modifications of the definition appear to increase its sensitivity. Validation of a case definition, i.e. assessing its sensitivity and specificity, would require testing it in IC/PBS patients as well as patients with other diseases with similar symptoms.

Keywords

interstitial cystitis; painful bladder syndrome; case definition

The case definition of interstitial cystitis is in flux. In 1987 and 1988, the National Institute of Diabetes, Digestive and Kidney Diseases (NIDDK) convened a group of urologists who by consensus developed a case definition comprising symptoms, urodynamics, exclusionary diseases and two objective criteria: mucosal ulcers on cystoscopy or glomerulations, i.e.

Corresponding author: John W. Warren, MD, University of Maryland, School of Medicine, 10 South Pine Street, Room 9-00 MSTF, Baltimore, MD 21201, 1-877-788-3942 http://icresearch.umaryland.edu, Studyic@medicine.umaryland.edu.

petechial hemorrhages, elicited by bladder hydrodistention [1]. The mucosal ulcers, identified by Hunner almost 100 years ago, have persisted as a diagnostic finding in IC but only in a small minority of cases. However, glomerulations, the objective criterion found in most cases, may be non-specific [2] and may poorly distinguish patients from those without glomerulations in regard to outcomes from biopsies, urodynamics, urine markers, or hydrodistentions [3–5].

The International Continence Society (ICS) since 1976 has been standardizing terminology of lower urinary tract diseases. In 2002, for the first time, this body defined interstitial cystitis, calling it painful bladder syndrome (PBS) [6]:

> "*Painful bladder syndrome* is the complaint of suprapubic pain related to bladder filling, accompanied by other symptoms such as increased daytime and nighttime frequency, in the absence of proven urinary infection or other obvious pathology"

Since then, a number of international bodies have endorsed the concept of bladder pain as an integral part of interstitial cystitis [7–10]; several have suggested the term IC/PBS.

During this time of uncertainty about the case definition of IC/PBS, we have been charged by the NIDDK to perform a case-control study to determine risk factors for this disease. Anticipating that a patient-validated definition of IC/PBS would be forthcoming, we developed what we believe to be relaxed, or sensitive, recruitment criteria, reasoning that a subgroup of participants who met any future case definition of IC/PBS could be culled out and studied. Upon completion of approximately one third of our recruitment, in this report we had the following objectives: to determine 1) what proportion of our cases met the ICS definition and 2) how did those who met the definition differ from those who did not.

Materials and methods

In an ongoing study entitled Events Preceding Interstitial Cystitis (the EPIC study), we are performing a case control investigation to identify risk factors for IC/PBS. Uncertain that in men we could distinguish prostate disease from IC/PBS, we elected to study only women. Details of methodology have been reported elsewhere [11]. Briefly, in order to enhance recall of antecedent events, we recruited cases whose symptoms began within the prior 12 months. Because these recent onset IC/PBS cases comprise a small subgroup of those with this chronic disease, we recruited on a national basis assisted by urologists, urogynecologists, the Interstitial Cystitis Association, the Interstitial Cystitis Network, regional IC/PBS support groups and the internet. Eligibility criteria for EPIC included 1) women; 2) ≥18 years of age; and 3) a syndrome beginning within the prior 12 months and lasting ≥4 weeks comprising perceived bladder pain of ≥3 on a 0 – 10 Likert scale, and at least two of frequency (≥8/24 hours), urgency (≥3 on a Likert scale), or nocturia. Exclusionary criteria were essentially those of the NIDDK [1]; we also excluded those with a possible neurogenic bladder, i.e. history of spinal cord injury, stroke, Parkinson's disease, multiple sclerosis, or spina bifida. Although some had initial or interval UTIs, all had the above symptoms when they had negative urinalyses and/or cultures. Needing to recruit cases as early as possible after onset, we did not require urologic or gynecologic assessments, procedures, or diagnosis. Medical records from 12 months before onset through any diagnostic procedures were abstracted by JWW to confirm the diagnosis of IC/PBS. All eligible participants were interviewed by telephone at baseline and every 6 months.

At screening, female interviewers asked each participant to describe her symptoms when they were at their worst. We began by asking about "any bladder pain, pressure, or discomfort" and noted its intensity on a Likert scale. The interviewer then asked its location assisting as necessary with landmarks such as the pubic bone or pubic hair, checking any of the following as applicable: suprapubic, infrapubic, genital area, rectal, low back, other (specified), or cannot localize. The interviewer then asked: " Immediately after urination, on average, did your

bladder discomfort get better, get worse, or remain the same?" followed by "As your next urination approached, on average, did your bladder discomfort get better, get worse, or remain the same?". Likert scale assessment of urgency and estimates of frequency and nocturia were obtained as were answers to the 4 questions comprising the O'Leary-Sant Interstitial Cystitis Symptom Index [(12)].

Results

For this report we analyzed our first 138 participants who met the following criteria: 1) pelvic pain which the participant perceived to be coming from her bladder, 2) ≥2 of frequency, urgency, or nocturia with thresholds above, and 3) diagnosis of IC/PBS by a urologist or gynecologist and/or treatment with IC-specific medication (oral pentosanpolysulfate, amitriptyline, or hydroxyzine; or bladder instillations with dimethylsulfoxide, heparin, hyaluronic acid, or lidocaine). Characteristics of this group have been outlined [(11)]. Worst symptoms were described as a median pain of 9 and urgency of 8; 119 (86%) had urinary frequency of ≥11/24 hours; and 98 (71%) described ≥3/night nocturia. O'Leary-Sant scores [(12)] were very similar to those in a recent large clinical trial of IC/PBS [(13)]. Hunner's ulcers were found in 6/100 cystoscopies (6%). Seventy-two cystoscopies included hydrodistention under anesthesia and 64 (89%) revealed glomerulations; an additional 8 patients had glomerulations on cystoscopy without hydrodistention. Followups revealed that of the 122 followed ≥9 months since onset, 115 (94%) continued to have IC/PBS symptoms despite therapy.

Table 1 notes answers to questions about changes of discomfort with bladder filling and emptying. Using this to operationalize the IC/PBS definition proved deceptively complicated. A literal reading of "pain related to bladder filling" would dictate that we use only responses to the question about "as your next urination approached". If we assume that the ICS authors implied that pain would *worsen* with bladder filling, only 101 cases would meet this criterion. However, one might assume that the 6 whose pain *improved* with bladder filling would also meet this part of the definition. We reasoned that the ICS intended the phrase to connote that the bladder was involved in this pain syndrome. Consequently, we elected to interpret the ICS definition to mean any change in pain associated with any change in bladder volume, i.e. filling or emptying. In other words, in Table 1 only the 16 who answered, "remains the same" to both questions would not meet this part of the definition. This interpretation additionally had the salutary effect of increasing the sensitivity of the ICS definition.

Parsing the rest of the ICS definition, we assumed "other symptoms…" to mean only urinary symptoms: each of our cases had at least 2 other urinary symptoms. None of our cases had "other obvious pathology", as denoted by the use of NIDDK exclusion criteria. Although some participants had initial or intercurrent UTIs, all had IC/PBS symptoms when their urinalyses or urine cultures were negative.

Of our 138 participants, 105 reported suprapubic pain of whom 14 reported that their pain "remains the same" to both questions. Thus, 91 (66%) met the ICS criteria.

We speculated that if the ICS criteria distinguished those who had IC/PBS from those who did not, then the two groups would differ in important ways. Consequently, we compared them by 97 variables clustered in the following sets: demographics (N=9); symptoms at onset, worst, and at present (17), sufficient medical records (3), findings at first medical encounter after symptom onset (14), findings at subsequent evaluations of their bladder disease (29), IC-specific therapy initially and ever (14), and medical history (11). Because of the large number of comparisons, we used a p-value of .01 to identify those with possibly significant differences. Of these variables, 96/97 were found not to be significantly different between those who met

or did not meet the ICS definition. Of particular note are the findings pertinent to the diagnosis of IC/PBS noted in Table 2.

For only one of the variables did the groups differ significantly at the .01 level. This was urinary urgency starting on the date of onset: of those who met the ICS definition, 72/91 (75%) reported this symptom versus 24/47 (51%) of those who did not meet the definition. It is interesting to note that for other symptoms on the date of onset (pelvic pain, vaginal pain, dysuria, and frequency) the groups were not significantly different. Furthermore, urgency at other times (measured on a 0 – 10 Likert scale) was not significantly different between the groups: when symptoms were at their worst (means of 7.7 of those who met versus 7.0 of those who did not meet the ICS criteria, p=0.09) or in the week prior to interview (means of 3.8 versus 4.2, p=0.37).

Only one other variable almost met our significance threshold. This was self-report of laparoscopically- diagnosed endometriosis: 24/91 (26%) of those who met versus 4/47 (9%) of those who did not meet the ICS criteria (P=0.013).

Variations of the ICS definition

We were interested to note in another section of the 2002 ICS report [(6)] the definition of "bladder pain":

> *Bladder pain* is felt suprapubically or retropubically, usually increases with bladder filling, and may persist after voiding.

Some of our patients did not report suprapubic pain but did report infrapubic pain. Of the 138 patients, 124 had suprapubic and/or infrapubic pain (which we recognize may be different from retropubic pain). Of these, 16 reported that their pain "remains the same" to both questions; thus 108 (78%) of our cases meet this "revised" definition. Finally, "may persist after voiding" above seems to imply that cases whose pain "remains the same" with filling or emptying could meet this definition. Therefore, this interpretation indicates that 124/138 (90%) of our participants would meet this revised definition.

Because a number of investigators have described the pain of IC/PBS in pelvic locations other than suprapubic or infrapubic [(14–16)], one can make a case that any pelvic pain should be incorporated into the definition of IC/PBS. Consequently, if one were to insert "pelvic pain", which in our study would include suprapubic, infrapubic, genital, rectal or urethral, then all 138 (100%) of our participants would meet this case definition.

Discussion

Use of the phrase "painful bladder" goes back at least to 1951 (17). Indeed, in the 1987 meeting which led to the NIDDK criteria, pain was a prominent part of the discussion [(18)]. More recently, a number of international meetings have endorsed this concept and in two recent epidemiologic studies pain was a necessary component of the case definition [(19–20)]. So the concept of the painful bladder syndrome put forth by the ICS appears attractive. However, the actual phrasing of the ICS definition is susceptible to a variety of interpretations. And even the most liberal interpretation appears to be insufficiently sensitive. Based on our interviews and medical record reviews, treating physicians' diagnoses, and the findings in Table 2, we feel confident that the cases in the study indeed have IC/PBS yet the ICS definition excluded one third of them. The primary reason for this apparent misclassification was the ICS restriction to suprapubic pain. Others have noted lower abdominal or suprapubic pain to be present in the majority of IC/PBS patients; however, one quarter to one half do not report such pain but do report pain in other parts of the pelvis [(14–16)]. Indeed, in the ICS document itself, there is reason to believe that the authors intended at least retropubic pain to be additionally included as a symptom of IC/PBS.

Another restrictive aspect of the ICS definition is the concept of changes in pain associated with changes in bladder volume. Previous investigators reported 57 – 73% of IC/PBS patients gained relief of pain with urination [15, 21]. Of our patients, 67 (49%) reported this symptom. We could find no publications of the proportion of IC/PBS patients reporting pain increasing with bladder filling, but our experience suggests that this is common. Our experience also suggests that a proportion of patients who appear to have IC/PBS have pain which does not change with bladder filling or emptying. Indeed, Clemens, et al. recently reported a prevalence study in which they used two definitions of IC/PBS: 1) ≥3 months of pelvic pain plus urgency or frequency and 2) the same criteria plus these items: increasing pain as the bladder fills and/or pain relieved by urination [20]. Of 316 women meeting the first definition, only 178 (56%) met the second definition.

Among our patients, those who were excluded by the ICS definition appeared to be identical to those who met it as judged by demographics, medical history, symptoms, findings on initial and subsequent evaluations, as well as numerous diagnostic and management features thought to be indicative of IC/PBS. This type of reasoning, i.e. identity of group characteristics, has been used in other arenas to consolidate diseases which previously were thought to be distinct. This includes primary and secondary fibromyalgia [22] as well as vulvodynia subtypes [23,24].

This was not a validation study [25]. While manipulating the definition as we did above might allow inclusion of most or all of our participants, and thus might increase the sensitivity of the definition, we have no idea how specific such a definition would be, i.e. how effective it would be in excluding patients with diseases of similar symptoms such as overactive bladder, endometriosis, etc. To our knowledge, such a patient-based study of the ICS definition, or for that matter of any IC/PBS definition, has not been performed. Such a study would properly determine whether a proposed case definition were sufficiently sensitive, identifying >90%, say, of IC/PBS cases and specific, excluding >90%, say, of those with similar diseases.

We must offer a caveat. Because of our need to enhance recall of antecedent events in this case control study, all patients had recent onset of IC/PBS, i.e. with symptoms ≤12 months. The ICS definition may be more sensitive for established IC/PBS patients. However, it is not unreasonable to expect that a case definition be quite sensitive and specific for patients at a time in their disease when it would be most useful, i.e. soon after onset.

Conclusions

The ICS definition identified only 91/138 (66%) of those cases whom study investigators and caregivers diagnosed as IC/PBS. Furthermore, those who met the ICS definition did not differ in important ways from those who did not meet it. These observations taken together suggest that the ICS definition may not be sufficiently sensitive. Minor modifications of the definition appear to increase its sensitivity. Validation of a case definition, i.e. assessing its sensitivity and specificity, would require testing it in IC/PBS patients as well as patients with other diseases with similar symptoms.

Acknowledgements

The study was funded by the NIDDK (DK 064880) and approved by the University of Maryland Institutional Review Board.

Our thanks to the women with IC/PBS who are participating in this study, to their physicians, to the Interstitial Cystitis Association and the Interstitial Cystitis Network and to Patricia W. Langenberg, PhD, Vivian Brown, Suzanne Markowitz, MS and Theresa Yates.

References

1. Wein A J, Hanno PM and Gillenwater JY: Interstitial cystitis: an introduction to the problem, In Interstitial Cystitis, P.M. Hanno, et al., Editors. Springer-Verlag, 1990, 3–15.
2. Waxman JA, Sulak PJ, Kuehl TJ. Cystoscopic findings consistent with interstitial cystitis in normal women undergoing tubal ligation. J Urol 1998;160(5):1663–1667. [PubMed: 9783927]
3. Awad SA, et al. Idiopathic reduced bladder storage versus interstitial cystitis. J Urol 1992;148(5): 1409–1412. [PubMed: 1433539]
4. Erickson DR, et al. Do the National Institute of Diabetes and Digestive and Kidney Diseases cystoscopic criteria associate with other clinical and objective features of interstitial cystitis? J Urol 2005;173(1):93–97. [PubMed: 15592040]
5. Al-Hadithi H, et al. Leucocyte populations interstitial cystitis and idiopathic reduced bladder storage. Urology 2002;59:851–855. [PubMed: 12031367]
6. Abrams P, et al. Report from the Standardisation Sub-committee of the International Continence Society. Am J Obstet Gynecol 2002;187(1):116–126. [PubMed: 12114899]
7. Proceedings of the International Consultations on Interstitial Cystitis, Kyoto Japan, March 29–30. Int J Urol 2003;(10 Suppl):i–iv. [PubMed: 14641403]S1–70, 2003.
8. Nordling J, et al. Primary evaluations of patients suspected of having interstitial cystitis (IC). Eur Urol 2004;45(5):662–669. [PubMed: 15082211]
9. International Consultation on Interstitial Cystitis - Rome (ICICR) and Proceedings of the Multinational Interstitial Cystitis Association (MICA) September 21–22, 2004: International Urogynecology Journal including pelvic floor dysfunction. p. S1–S34, 2005
10. Hanno P. Painful Bladder Syndrome (including interstitial cystitis). Committee 2005;21:1–66.
11. Warren JW, et al: Presentation and evaluation of early interstitial cystitis/painful bladder syndrome in women. J Urol. Submitted for publication.
12. O'Leary MP, et al. The interstitial cystitis symptom index and problem index. Urology 1997;49(5A Suppl):58–63. [PubMed: 9146003]
13. Lubeck DP, et al. Psychometric validation of the O'Leary-Sant interstitial cystitis symptom index in a clinical trial of pentosanpolysulfate sodium. Urology 2001;57(6 Suppl 1):62–66. [PubMed: 11378052]
14. Simon LJ, et al. The Interstitial Cystitis Data Base Study: concepts and preliminary baseline descriptive statistics. Urology 1997;49(5A Suppl):64–75. [PubMed: 9146004]
15. Koziol JA. Epidemiology of interstitial cystitis. Urol Clin North Am 1994;21(1):7–20. [PubMed: 8284848]
16. Tincello DG, Walker AC. Interstitial cystitis in the UK: results of a questionnaire survey of member of the Interstitial Cystitis Support Group. Eur J Obstet Gynecol Reprod Biol 2005;118(1):91–95. [PubMed: 15596280]
17. Bourque J. Surgical management of the painful bladder. J Urol 1951;65:25–35. [PubMed: 14804764]
18. Gillenwater JY, Wein AJ. Summary of the National Institute of Arthritis, Diabetes, Digestive and Kidney Diseases Workshop on Interstitial Cystitis, National Institutes of Health, Bethesda, Maryland, August 28–29,1987. J Urol 1988;140(1):203–6. [PubMed: 3379688]
19. Leppilahti M, et al. Prevalence of symptoms related to interstitial cystitis in women: a population based study in Finland. J Urol 2002;168(1):139–143. [PubMed: 12050508]
20. Clemens JQ, Meenan RT, Rosetti MC, Brown SO, Gao SY, Calhoun EA. Prevalence of interstitial cystitis symptoms in a managed care population. J Urol 2005;174:576–80. [PubMed: 16006901]
21. Held P J: Epidemiology of interstitial cystitis, in Interstitial Cystitis, P.M. Hanno, et al., Editors. Springer-Verlag, 1990, 29–48.
22. Wolfe F, Smythe HA, Yunus MB. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. Arthritis and Rheumatism 1990;33(2):160–72. [PubMed: 2306288]
23. Reed BD, Gorenflo W, Haefner JK. Generalized vulvar dysesthesia vs. vestibulodynia. Are they distinct diagnoses? J Reprod Med 2003;48(11):858–64. [PubMed: 14686018]
24. Masheb RM, et al. On the reliability and validity of physician ratings for vulvodynia and the discriminant validity of its subtypes. Pain Med 2004;5(4):349–58. [PubMed: 15563320]

25. Tan EM, Cohen AS, Fries JF. The 1982 Revised Criteria for the classification of systemic lupus erythematosus. Arthritis and Rheumatism 1982;25(11):1271–77. [PubMed: 7138600]

Table 1

Changes in bladder discomfort with changes in bladder volume

After urination, discomfort…	As next urination approached, discomfort…			
	Gets better	Gets worse	Remains the same	Total
Gets better	0	62	5	67
Gets worse	4	18	10	32
Remains the same	2	21	16	39
Total	6	101	31	138

Table 2

Selected characteristics of IC/PBS of those who met or did not meet the ICS definition

	Number (%)	
	Met	**Did not meet**
Number	91	47
Cystoscopy	60	40
Hunner's ulcers	3 (5%)	3 (8%)
Hydrodistention	46	26
Glomerulations	40 (87%)	24 (92%)
Urol/gyn Dx IC/PBS*	78 (86%)	41 (87%)
IC-specific medications	80 (88%)	44 (94%)
O'Leary-Sant Symptom Index (means)		
Total score	14.6	14.7
Urgency	2.8	2.9
Frequency	4.3	4.3
Nocturia	3.6	3.2
Pain	4.0	4.4

* Urologist or gynecologist has diagnosed IC/PBS