

# A survey on clinical practice of interstitial cystitis in Japan

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**Background:** To explore the real-life practice of clinical management of interstitial cystitis (IC) in Japan.

**Methods:** A questionnaire on the number of IC patients, cystoscopic findings, diagnostic methods, and the treatment modalities was sent via e-mail to 114 medical institutions belonging to the Society of Interstitial Cystitis of Japan (SICJ).

**Results:** Completed questionnaires were returned from 62 institutions (20 university hospitals, 26 general hospitals and 16 clinics), with a response rate of 54%. The median of patient number per institution was 20 and the national number of IC patients was counted as 4,531 in Japan. The number of new patients in 2013 was 7 (median) per institution and calculated as 1,214 in total. The case volume per institution distributed broadly and skewed to a lower volume. The patients were categorized according to cystoscopic findings as either Hunner type IC with Hunner lesions (n=2,066, 45%), non-Hunner type IC with glomerulations on hydrodistension (n=1,720, 38%) or hypersensitive bladder without endoscopic abnormalities (n=304, 7%), excluding unknown (n=441, 10%). The proportion of Hunner type IC was highly variable among the institutions, ranging from 0% to 100% with a median of 29%. As for evaluation, symptom and quality of life (QOL) assessment by questionnaires, frequency volume chart, urinalysis, urine cytology, urine culture, post-void residual measurement, uroflowmetry, ultrasound and cystoscopy were widely adapted. Administration of oral medicines and intravesical instillation therapy were undertaken at 98% and 63% of institutions, respectively. Hydrodistension was commonly performed, totaling in 812 procedures at 53 institutions, while only five cystectomies were reported from four institutions.

**Conclusions:** The survey estimated about 4,500 IC patients and 2,000 Hunner type IC patients in Japan. It also revealed a wide range of case volume, acceptable adherence to clinical guidelines, and high variability in the proportion of Hunner type IC. The variable proportions of Hunner type IC despite a high performing rate of endoscopy suggest inconsistency in diagnostic criteria for the Hunner lesion.

**Keywords:** Interstitial cystitis (IC); questionnaires; Hunner lesion

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## Introduction

Interstitial cystitis (IC) is a chronic inflammatory disease of the urinary bladder associated with lower urinary tract symptoms such as bladder hypersensitivity, urinary frequency and bladder pain, and resultant impairment of quality of life (QOL) (1). Clinical management of IC is expected to be enforced according to clinical guidelines for IC and hypersensitive bladder syndrome in Japan (1). However, the diagnostic and therapeutic practices may be heterogeneous due to its scarcity and unknown pathophysiology. Real feature of managing IC is obscure in Japan; a few reports appeared on the prevalence, diagnostic and therapeutic approaches (2-5). Therefore we conducted a questionnaire survey on the current clinical practice in managing IC among the members of the Society of Interstitial Cystitis of Japan (SICJ). The survey focused on the number of IC patients and diagnostic and therapeutic modalities.

## Methods

The study was approved by the Board of Trustees of SICJ. The survey was conducted in February, 2014. We sent a questionnaire via e-mail to all members of SICJ (n=169), who belonged to 114 medical institutions in total. SICJ is a medical society founded in 2001 to develop the clinical management and research of IC in Japan.

The first question was on the case volume of IC patients on follow-up at each institution, which was divided into four categories depending on cystoscopic findings; the Hunner lesion, glomerulations on hydrodistension, none of both, or unknown. The second question was also on the case volume of new patients seen in 2013 split in the same manner. The third was on the frequency of using diagnostic methods. The response was given as one of seven options; none (0%), rarely (<25%), occasionally (25-50%), about a half (50%), sometimes (50-75%), often ( $\geq 75\%$ ) or always (100%). The fourth was on the usage of behavioral therapy (diet manipulation or patient education) with the same response choices. Question 5 asked the number of intravesical instillation therapies, which were divided into dimethyl sulfoxide (DMSO), heparin, lidocaine, heparin plus lidocaine, or cocktail containing steroid. Question 6 asked the number of intra-detrusor injection with botulinum toxin A or steroid. Question 7 inquired the number of hydrodistensions or cystectomies carried out, and question 8, the number of pelvic floor physical therapies,

neuromodulation, or acupuncture. The last question was on use of oral medicine including opioids, non-steroidal anti-inflammatory drugs (NSAIDs), tricyclic antidepressants, pregabalin, selective serotonin reuptake inhibitors, gabapentin, anticholinergics, mirabegron, flavoxate, alpha-blockers, pentosan, citric acid/sodium bicarbonate, suplatast tosilate, hydroxyzine, steroids, cyclosporine, and herbal medicines. The response option was given either none, rarely, occasionally, about a half, sometimes, often or always, in the same way as question 3.

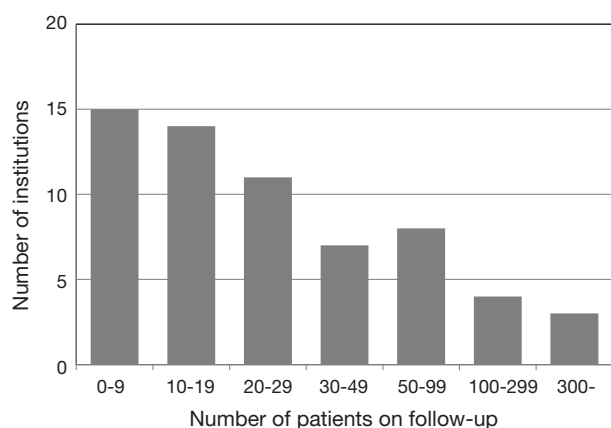
## Results

Completed questionnaires were returned from 62 institutions (20 university hospitals, 26 general hospitals and 16 clinics), with a response rate of 54% (62/114).

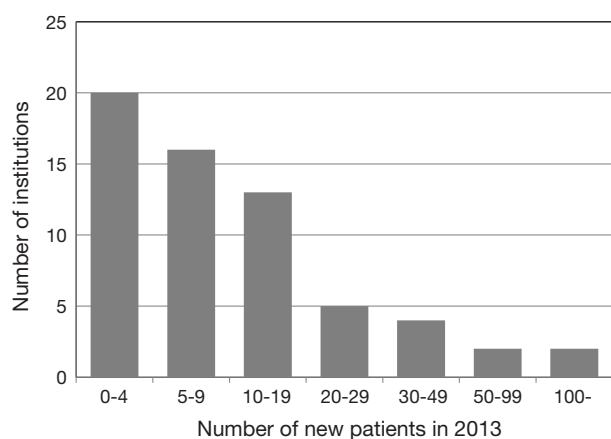
The total number of patients on follow-up was 4,531. The distribution of case volume was broad; it was more than 100 patients at seven institutions, while less than 10 at 15 institutions (*Figure 1*). The average and the median of the number of patients per institution was 73 and 20, respectively. As for new patients in 2013, the total number was 1,214, with more than 50 at four institutions and less than five patients at 20 institutions (*Figure 2*). Again the distribution of case volume was broad and skewed to a lower value; the average was 20 and the median was 7. Cystoscopic findings of the 4,531 patients on follow-up were Hunner lesion in 2,066 (45%), glomerulations after hydrodistension but no Hunner lesions in 1,720 (38%), no endoscopic abnormalities in 304 (7%), or undetermined in 451 (10%) (*Figure 3*). The proportion of Hunner type IC was highly variable among the institutions (*Figure 4*). It was rarely observed at 23 institutions, roughly a half at most institutions, but often or always at four institutions. The proportion of Hunner type IC was not related with the case volume of institution ( $R^2=0.037$ ,  $P=0.138$ ).

Among evaluation methods, urinalysis, post-void residual measurement, urine cytology and cystoscopy were indicated for most of cases at more than 75% of institutions. Questionnaire assessment of symptoms and QOL impairment, frequency volume chart, bladder ultrasonography were conducted in most of cases at more than a half of institutions. Urine culture and uroflowmetry were applied at less than a half, and urodynamics, X-ray, and potassium test, at less than 25% of institutions (*Figure 5*).

Common treatment measures were oral medicine, dietary manipulation, education, hydrodistension with or without fulguration and intravesical instillations (*Figure 6*).



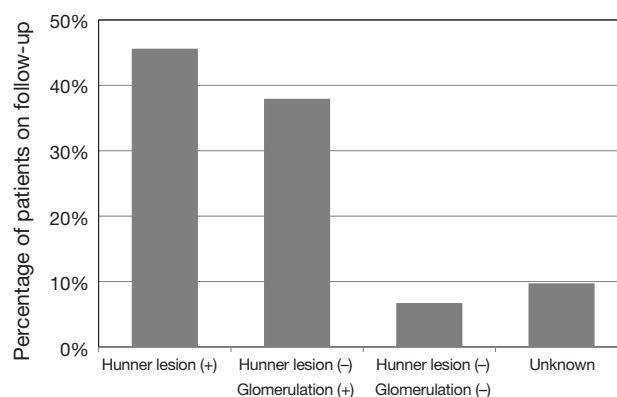
**Figure 1** The number of institutions by the number of IC patients on follow-up: seven institutions had more than 100 patients, while 15 institutions had less than 10. IC, interstitial cystitis.



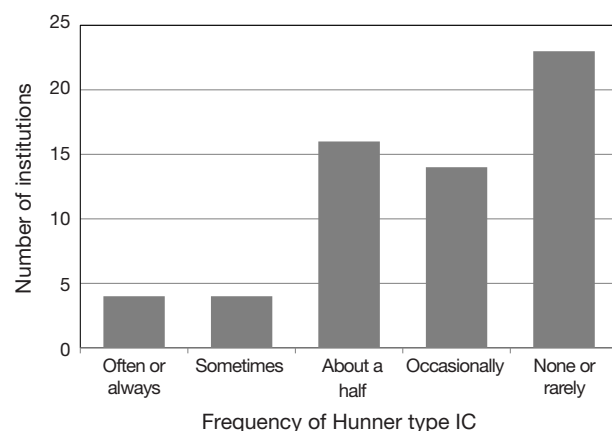
**Figure 2** The number of institutions by the number of new patients in 2013: four institutions had more than 50 new patients, while 20 institutions had less than five.

Among oral medicines, suplatast tosilate, NSAIDs and tricyclic antidepressants were most commonly prescribed.

It was estimated that 812 hydrodistensions were performed at 53 institutions (85% of responded institutions) in 2013. DMSO was most often used for bladder instillation (20 institutions), followed by heparin plus lidocaine [11], lidocaine [9], heparin [7], and steroid cocktail [4]. Intra-detrusor injection of botulinum toxin A, neuromodulation, pelvic floor physical therapy, acupuncture were scarcely performed. Only five cases underwent cystectomies at four institutions.



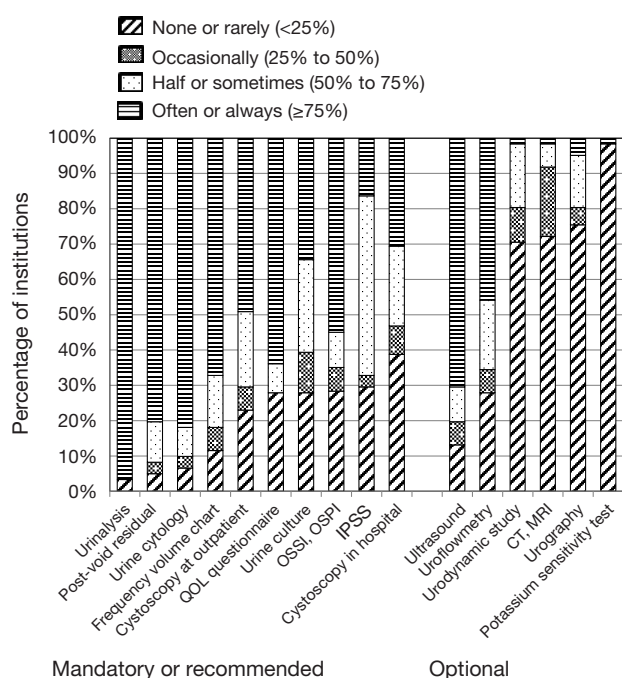
**Figure 3** Cystoscopic findings of the patients on follow-up: the number of Hunner type IC with Hunner lesions, non-Hunner type IC with glomerulations on hydrodistension, hypersensitive bladder without endoscopic abnormalities, and undetermined was 2,066 (45%), 1,720 (38%), 304 (7%), and 451 (10%) respectively. IC, interstitial cystitis.



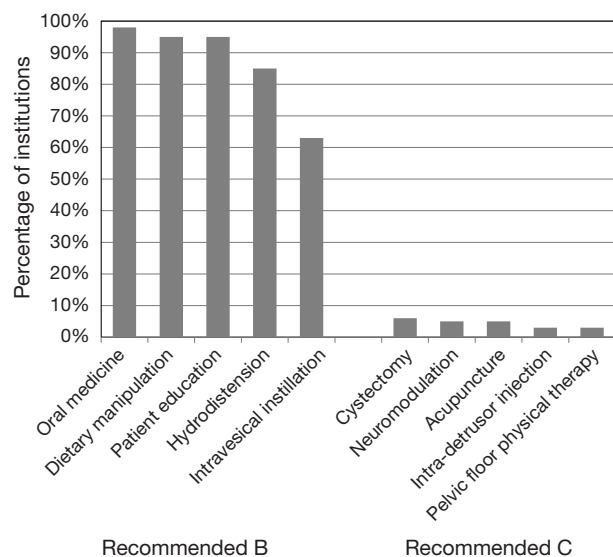
**Figure 4** The number of institutions by the frequency of Hunner type IC on follow-up: the frequency of Hunner type IC was none or rarely (<20%) at 23 institutions (38%), occasionally (20% to 39%) at 14 institutions (23%), about a half (40% to 59%) at 16 institutions (26%), sometimes (60% to 79%) at four institutions (7%), often or always (≥80%) at four institutions (7%). IC, interstitial cystitis.

## Discussion

This survey covered the majority of high volume centers of IC in Japan thus presumably reflects the real clinical picture of IC in Japan. The number of IC patients, 4,531 or 3.56 per 100,000, is a reasonable estimate of patients requiring intensive medical care in the whole nation.



**Figure 5** Percentage of institutions by the frequency of performing diagnostic tests. The recommendation levels in the East Asian guidelines at the bottom. QOL, quality of life; OSSI, O'Leary-Sant's symptom index; OSPI, O'Leary-Sant's problem index; IPSS, International prostate symptom score; CT, computed tomography; MRI, magnetic resonance imaging.



**Figure 6** Percentage of institutions where each therapy is conducted: the grade of recommendation in the East Asian guidelines at the bottom.

A previous study indicated that the prevalence of IC in Japan was 4.5 per 100,000 female patients, or 1.2 per 100,000 patients (2). A survey of IC patients in Kyushu area estimated the prevalence in general population as 3.1 per 100,000 (3). Analysis of the Japanese Diagnosis Procedure Combination database indicated 996 admissions due to IC in 2007-2009 (4), and extrapolated 1,117 new patients a year, which is a comparable value with the result of our survey [1,214]. Much higher prevalence was reported in another study in Japan (265 per 100,000) (5) and studies abroad (10.1-500 per 100,000) (6-11), although some of these studies utilized a symptom assessment alone for diagnosis (5,7,9). The real prevalence or the real clinical demand of IC should be critically evaluated in the future.

The number of patients per institution varied widely. Top seven institutions had a total of 3,245 patients, 72% of the whole patients. A majority of IC patients were treated at high volume centers in Japan.

Management of IC in Japan is expected to follow the clinical guidelines for IC and hypersensitive bladder syndrome (1). The guidelines define IC as a disease of the urinary bladder diagnosed by three requirements; (I) a characteristic complex of lower urinary tract symptoms; (II) bladder pathology such as the Hunner lesion and bladder bleeding after overdistension; and (III) exclusions of confusable diseases. The characteristic symptom complex is usually associated with urinary frequency, bladder discomfort or bladder pain. Thus cystoscopy or hydrodistension is required for the diagnosis of IC. Hypersensitive bladder is the diagnosis when IC is suspected but the confirmatory cystoscopic findings are lacking. The survey indicated that 90% of patients had undergone cystoscopy for diagnosis. These practices are so different from the American Urological Association's guidelines for IC/bladder pain syndrome, which considered cystoscopy as a diagnostic test only for complex presentations (12).

Evaluation methods were relatively homogenous among institutions and most of tests recommended by guidelines were adapted to a majority of cases. This was exemplified by a high performing rate of cystoscopy and hydrodistension, which are highly recommended for diagnosis and/or treatment by the guidelines. Despite common use of cystoscopy, however, the proportion of Hunner type IC was highly variable among the institutions. The proportion of Hunner type IC reportedly varies from 5% to 55% in various populations, centers and series (13-15). This suggests that the diagnostic criteria for the Hunner lesion may be inconsistent among the physicians.

Regarding therapeutic management, oral medicine, dietary manipulation, and hydrodistension with or without fulguration are most commonly used. Intravesical instillation is also a common remedy. On the other hand, intra-detrusor injection therapy, pelvic floor massage or pentosan polysulfate are rarely employed in Japan, most probably because these treatments are not approved by national health-care insurance system. Oral medicines were also variable among institutions; suplatast tosilate, NSAIDs and tricyclic antidepressants were used occasionally or more often at a half of institutions. These treatment modalities were compatible with the recommendation Grade B or C of the clinical guidelines (1).

## Conclusions

The survey estimated about 4,500 IC patients and 2,000 Hunner type IC patients in Japan. It also revealed a wide range of case volume, acceptable adherence to clinical guidelines, and a high variability in the proportion of Hunner type IC. The variable proportions of Hunner type IC despite a high performing rate of endoscopy suggest inconsistency in diagnostic criteria for the Hunner lesion.

## Acknowledgements

None.

## Footnote

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

*Ethical Statement:* The study was approved by the board of trustees of the Society of Interstitial Cystitis of Japan. The study was a survey directed to institutions thus not related to patient consent, so informed consent is waived for this publication.

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