



## Original article

## Increased bladder wall thickness is associated with severe symptoms and reduced bladder capacity in patients with bladder pain syndrome



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## ABSTRACT

**Objective:** Patients with interstitial cystitis (IC) and ketamine cystitis (KC) usually have similar symptoms, such as frequency, urgency, and bladder pain. In patients with IC, ulcer type and nonulcer type may have different cystoscopic features. This study investigated the clinical characteristics and bladder wall thickness (BWT) measured using computed tomography (CT) in patients with nonulcer IC, ulcer IC, and KC.

**Materials and methods:** The detailed history and bladder condition of patients with a clinical diagnosis of IC and KC were retrospectively analyzed. An abdominal to pelvis CT scan with/without contrast was performed in every patient. Ulcer type IC was noted in nine patients, nonulcer IC in seven patients, and KC in 13 patients. The bladder mass volume and BWT were measured. Bladder CT images of 10 patients with nonmetastatic renal cancer served as controls.

**Results:** The bladder wall was significantly thicker in all patients with ulcer type IC ( $8.91 \pm 2.67$  mm) and KC ( $10.7 \pm 3.44$  mm) than in those with nonulcer IC ( $2.89 \pm 0.73$  mm) or controls ( $2.65 \pm 0.97$  mm). Among KC patients, eight patients received augmentation enterocystoplasty. Moreover, the bladder wall was significantly thicker in patients who underwent augmentation enterocystoplasty ( $11.50 \pm 3.21$  mm) than those who did not ( $9.50 \pm 3.81$  mm). The bladder mass volume was increased in patients with KC who received augmentation enterocystoplasty ( $35.67 \pm 11.19$  mL) compared with those who did not ( $21.24 \pm 7.25$  mL). BWT significantly correlated with visual analogue scores for pain ( $R^2 = 0.484$ ,  $p < 0.001$ ), functional bladder capacity ( $R^2 = 0.31$ ,  $p = 0.002$ ), and maximum bladder capacity ( $R^2 = 0.469$ ,  $p < 0.001$ ) in overall patients.

**Conclusion:** There are obvious differences in bladder CT scans of patients with symptoms of bladder pain due to different etiology. Increased BWT was associated with increased pain scores and decreased bladder capacity in patients with KC and IC. BWT on a CT scan might be considered a marker for the severity of bladder inflammation.

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## 1. Introduction

Bladder pain syndrome (BPS) is a poorly defined clinical condition characterized by pelvic pain and urinary storage symptoms such as urinary urgency and frequency. In a European Society for the Study of Interstitial Cystitis proposal, BPS/interstitial cystitis (IC) is defined as “chronic pelvic pain, pressure, or discomfort perceived to be related to the urinary bladder, with at least one other urinary symptom such as persistent urge to void or urinary

frequency.”<sup>1</sup> The American Urological Association recently modified the definition of IC/BPS to “an unpleasant sensation (pain, pressure, discomfort) perceived to be related to the urinary bladder, associated with lower urinary tract symptom(s) of more than 6 weeks' duration, in the absence of infection or other identifiable causes.”<sup>2</sup> Clinically, several bladder diseases may present with bladder pain, including ulcer type IC, nonulcer type IC, and ketamine cystitis (KC).

There is no definite agreement about the pathophysiology of and treatment algorithm for these diseases, mostly because of the lack of objective markers and development of a clinical diagnostic protocol.<sup>3</sup> The clinical presentation of severe lower urinary tract symptoms and a history of ketamine abuse usually can establish a diagnosis of KC. A urine examination and urodynamic studies can

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exclude other diseases such as urinary tract infection, urinary tract stone, and bladder outlet obstruction. Cystoscopy to evaluate the severity of cystitis using visual inspection and biopsy has played a pivotal role in the diagnosis of KC.<sup>4</sup> In a previous study, the most useful imaging technique was computed tomographic (CT) urography, which allowed assessment of both upper and lower urinary tract dysfunction. CT findings associated with ketamine-induced cystitis include a small bladder, diffuse bladder wall thickening, mucosal enhancement, and inflammatory changes in the perivesical tissue.<sup>5</sup> In contrast to KC, few studies of CT findings in patients with IC have been reported.

Patients with a long duration of ketamine abuse might suffer from severe bladder pain that does not respond to empirical oral or intravesical treatment. Most of these patients have a remarkably impaired quality of life and are at risk of developing upper urinary tract damage including bilateral hydronephrosis and kidney injury.<sup>6</sup> Shahani et al<sup>7</sup> reported CT findings in KC bladders and found marked thickening of the bladder wall, a small capacity bladder, and perivesical stranding consistent with severe inflammation. In KC patients with severely contracted bladders and intractable pain, augmentation enterocystoplasty (AE) might be necessary to relieve refractory bladder pain and lower urinary tract symptoms.<sup>8</sup>

Although patients with symptoms of bladder pain due to different diseases have similar symptoms, there is no good objective diagnostic tool to evaluate the inflammatory status or serve as a guide for intervention. It is mandatory to search for biomarkers in patients with bladder pain. The aim of this study was to evaluate the radiological features of the bladder wall on CT scans in KC and IC patients presenting with bladder pain and to investigate the relationship between clinical characteristics and bladder wall thickness (BWT). The results of this study may help in decision making in the treatment of these patients.

## 2. Materials and methods

### 2.1. Patient enrollment

Patients who had symptoms of frequency, urgency, and bladder pain and had been diagnosed as ulcer type IC, nonulcer type IC, or KC by clinical history, physical examination, and cystoscopic hydrodistention were enrolled in this study. Abdominal CT scan was performed after the diagnosis of bladder diseases. All patients with these enrolled criteria were retrospectively included in this study. All patients had been treated for >6 months and had failed previous medical treatments. Most of the patients were referred from other hospitals for a definite treatment of their bladder pain syndrome. In addition to the patients with KC and IC, we selected 10 patients with nonmetastatic renal cell carcinoma ready for radical nephrectomy to serve as controls.

### 2.2. Clinical assessment

The patients were assessed by complete history, clinical symptoms, urinalysis, physical examination, uroflowmetry, and a voiding diary. Patients were requested to complete a 3-day voiding diary prior to the treatment. The functional bladder capacity (FBC) was determined by the maximal voided volume recorded in the voiding diary or voided volume on uroflowmetry. The pain score was reported by patient self-assessment using a 10-point visual analogue scale (VAS) system.

Cystoscopic hydrodistention was routinely performed under general anesthesia to search for glomerulations or bladder ulcers (Hunner's lesion), and the maximal bladder capacity (MBC) was determined by the bladder capacity under the intravesical pressure

of 80 cm H<sub>2</sub>O during cystoscopic hydrodistention. Hunner's lesion was defined by the presence of a distinct inflammatory lesion with a circumscribed, reddened mucosal area with small vessels radiating toward a central scar that ruptures with increasing bladder distention. The ulcer might also be seen at cystoscopy without hydrodistention.<sup>1</sup> A bladder biopsy was performed after cystoscopic hydrodistention in all patients to investigate the histopathology of bladder inflammation and determine if malignancy was present.

### 2.3. Bladder CT scan and measurements

An abdominal to pelvic CT scan with or without contrast medium was performed by a radiologist prior to cystoscopic hydrodistention. During the CT scan, patients were asked to hold urine until they felt a strong desire to void. If the patient had more than one CT scan, only the first CT scan prior to cystoscopic hydrodistention was analyzed in this study.

The CT images were retrospectively reviewed by two investigators. The intravesical bladder width, height, and length were measured from the inner border of the bladder wall at the section with the maximal bladder size. The intravesical bladder volume was calculated according to the following formula: intravesical bladder height × bladder depth × bladder width × 0.52. The total bladder volume was also measured by the bladder height × bladder depth × bladder width × 0.52, which were measured from the outer border of the bladder wall. If the BWT was equal in all parts of the bladder wall, the maximal BWT was measured at the middle portion of the bladder wall at the section with the maximal bladder size. If the BWT was not equally distributed (such as in ulcer type IC), the thickest part of the bladder wall was measured as the maximal BWT. The bladder mass volume (BMV) was measured by subtracting the intravesical bladder volume from the total bladder volume.

### 2.4. Statistical analysis

Statistical analysis was performed using one-way analysis of variance with *post hoc* analysis and Pearson's regression. The VAS, MBC, FBC, and BWT were compared among disease subgroups, with  $p < 0.05$  considered statistically significant. Pearson correlation coefficients were calculated to determine the correlations of VAS, FBC, and MBC with BWT. All analyses were performed using IBM SPSS for Windows, version 12.

## 3. Results

The patients in the study included seven with nonulcer IC (6 women and 1 man, mean age  $48.4 \pm 14.4$  years), nine with ulcer type IC (all women, mean age  $62.2 \pm 9.71$  years), and 13 KC patients. Among the 10 control patients, eight were men and two were women, with a mean age of  $52.1 \pm 17.1$  years. No bladder outlet obstruction or neurogenic bladder dysfunction was noted in these control patients.

Among the patients with KC, eight underwent AE owing to intractable bladder pain (4 women and 4 men, mean age  $28.5 \pm 5.88$  years), and five did not undergo AE (1 woman and 4 men, mean age  $30.0 \pm 3.32$  years) because their symptoms improved after hydrodistention and they requested for conservative treatment. Table 1 lists the clinical characteristics, BWT, and perivesical infiltration in these patients. Increased perivesical infiltrations were found in five of nine patients (56%) with ulcer type IC, in six of eight KC patients with AE (75%), and in four of five KC patients without AE (80%), but none in patients with nonulcer IC. Bilateral hydronephrosis was noted in three KC patients with AE.

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