

# Clinical Phenotyping Does Not Differentiate Hunner Lesion Subtype of Interstitial Cystitis/Bladder Pain Syndrome: A Relook at the Role of Cystoscopy



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## Abbreviations and Acronyms

BPS = bladder pain syndrome  
IBS = irritable bowel syndrome  
IC = interstitial cystitis  
ICPI = IC Problem Index

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**Purpose:** Identifying Hunner lesions in patients with interstitial cystitis/bladder pain syndrome presents an opportunity for objective classification into Hunner lesion interstitial cystitis/bladder pain syndrome (classic interstitial cystitis) and nonHunner lesion bladder pain syndrome. While currently the former diagnosis requires cystoscopy, limited data suggest that these subtypes can be distinguished without endoscopy based on the degree of bladder focused centricity and the infrequent association with generalized pain conditions.

**Materials and Methods:** Patients in a prospective, single center database of interstitial cystitis/bladder pain syndrome who had documented cystoscopic findings were categorized with Hunner lesion interstitial cystitis/bladder pain syndrome or nonHunner lesion bladder pain syndrome. Demographics, pain and symptom scores, voiding symptoms, irritable bowel syndrome and clinical UPOINT (urinary, psychosocial, organ specific, infection, neurological and tenderness) scoring were comparatively analyzed.

**Results:** We reviewed the records of 469 patients, including 359 with documented local anesthetic cystoscopic findings, 44 (12.3%) with Hunner lesion interstitial cystitis/bladder pain syndrome and 315 (87.7%) with nonHunner bladder pain syndrome. Patients with Hunner lesions were older ( $p = 0.004$ ) and had greater urinary frequency ( $p = 0.013$ ), more nocturia ( $p = 0.0004$ ) and higher ICSI (Interstitial Cystitis Symptom Index) scores ( $p = 0.017$ ). Hunner lesion prevalence was significantly lower in those younger than 50 years vs those 50 years old or older (7.8% vs 14.9%,  $p = 0.0095$ ). There was no difference in the number of UPOINT phenotype domains reported, overall UPOINT scores or the prevalence of irritable bowel syndrome between the groups.

**Conclusions:** A subtype of interstitial cystitis with Hunner lesions has worse bladder centric symptoms but did not show a distinct bladder centric phenotype. Given the management implications of distinguishing classic interstitial cystitis from nonHunner lesion bladder pain syndrome, we recommend cystoscopy with local anesthesia in patients diagnosed with interstitial cystitis/bladder pain syndrome.

**Key Words:** urinary bladder; cystitis, interstitial; pain; cystoscopy; diagnosis

HUNNER lesion IC/BPS, also described as ulcerative IC, comprises approximately 10% to 20% of North

American cases of IC/BPS.<sup>1-4</sup> The lesion was defined by ESSIC (International Society for the Study of

Bladder Pain Syndrome) as a “circumscribed, reddened mucosal area with small vessels radiating towards a central scar, with a fibrin deposit or coagulum attached” that “ruptures with increasing bladder distension, with petechial oozing of blood from the lesion and the mucosal margins in a waterfall manner.”<sup>5</sup> Patients with the classic subtype have been described as older<sup>4,6</sup> with smaller bladder capacity,<sup>1,6</sup> and worse storage and voiding symptoms.<sup>1,4,6</sup> Peters et al reported significant differences in some comorbid diagnoses but not in others between the 2 groups.<sup>4</sup>

The presence of a Hunner lesion remains an unchallenged finding in the NIDDK (National Institute for Diabetes and Digestive and Kidney Diseases) diagnostic criteria for IC/BPS.<sup>7</sup> However, clinically there is consensus that a Hunner lesion is not required for the diagnosis of IC/BPS.<sup>8,9</sup> Recommendations for routine cystoscopy in the evaluation of IC/BPS vary greatly among professional urological organizations.<sup>10</sup> Current EAU (European Association of Urology)<sup>11</sup> and Asian guidelines<sup>12</sup> call for cystoscopy with hydrodistension in the routine workup of those evaluated for IC/BPS while AUA (American Urological Association) guidelines state that cystoscopy is not a necessary part of the routine evaluation of these patients.<sup>13</sup> There is no doubt that hydrodistension increases the sensitivity of detecting bladder mucosal glomerulations while many urologists, including the current investigators, believe that Hunner lesions can be documented by cystoscopy using local anesthesia. Glomerulations, which should be regarded as distinct from Hunner lesions and are also traditionally believed to be part of the diagnostic criteria,<sup>7</sup> have been shown to be neither a sensitive nor a specific diagnostic criterion of IC/BPS.<sup>14</sup>

Patients diagnosed with IC/BPS comprise a diverse group with varied clinical phenotypes.<sup>15,16</sup> The presence of various other comorbid chronic pain and symptom based syndromes has been widely reported.<sup>17–19</sup> The heterogeneity of this patient population suggests that IC/BPS, instead of existing as 1 entity to be diagnosed, is more likely a combination of etiologies with a varied pathogenesis and symptom patterns. The cystoscopic finding of a Hunner lesion, referred to as classic IC,<sup>20</sup> provides an opportunity to objectively classify subtypes of patients with IC/BPS. Furthermore, there is evidence to suggest that those with Hunner lesion IC/BPS may respond to direct treatment of these identified lesions.<sup>21</sup>

There are only limited data on these 2 subtypes. Questions remain regarding whether they represent 2 distinct patient groups and whether this subclassification is clinically relevant. Although some

minor differences were noted, Peters et al were unable to reliably distinguish clinically between Hunner lesion IC/BPS and nonHunner lesion BPS.<sup>4</sup> Braunstein et al concluded that despite thorough clinical examination cystoscopy was still required to identify patients with Hunner lesions.<sup>6</sup> Previous studies have not evaluated clinical phenotyping (eg UPOINT) to differentiate the 2 patient groups.

We hypothesized that patients with Hunner lesions who have IC/BPS pain would have more of a bladder or pelvis focus with more reported bladder symptoms and fewer systemic symptom patterns. Therefore, they could be distinguished by clinical phenotyping. We report the characteristics of patients with Hunner lesion IC/BPS and nonHunner lesion BPS through an analysis of a prospectively collected database of those with IC/BPS who were evaluated at a single center outpatient clinic. We improved previously published studies of differences between these groups due to use of the UPOINT phenotyping tool and the large size of our single center database.

## METHODS

### Participants and Study Design

The current study is a retrospective evaluation of a large, prospective, clinical quality assurance database of patients with IC/BPS treated at our outpatient clinic by a single urologist (JCN). Our patient sample has been described in a previous publication.<sup>17</sup> Only patients with documented cystoscopic findings were included in analysis. The Hunner lesion IC/BPS group included all patients who had a documented Hunner lesion on cystoscopy while the nonHunner BPS group included those without a documented Hunner lesion on cystoscopy. This retrospective study was done under ongoing institutional review board approval for continued quality assurance with all patient data de-identified before analysis.

### Measures

Data on patient demographics, symptom duration, ICSI and ICPI scores, average pain (rated 0 to 10 on an 11-point numerical rating scale), frequency and urgency scores, UPOINT scoring and the presence or absence of IBS as diagnosed and/or according to Rome III criteria were collected through initial evaluations at the IC/BPS outpatient clinic. The data have been previously reported.<sup>16,17</sup>

### Data Analysis

Statistical analysis was completed using the Microsoft® Excel® 2010 Data Analysis package and the Social Science Statistics (<http://www.socscistatistics.com/>). In all cases statistical analysis was done between the 2 groups, including those with vs without Hunner lesions. Categorical data, including UPOINT domains and the presence or absence of IBS, were analyzed using the 2-tailed z-test for population proportions. Other quantitative data, age, symptom duration and all questionnaire scores were

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