

The effects of cystoscopy and hydrodistention on symptoms and bladder capacity in interstitial cystitis/bladder pain syndrome

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Aims: The use of cystoscopy and hydrodistention in the management of interstitial cystitis/bladder pain syndrome (IC/BPS) varies widely between providers. Current evidence regarding the risks and benefits of hydrodistention, as well as the long term effects of repeated hydrodistention are not well established. We sought to characterize the effects of hydrodistention on IC/BPS symptoms as well as bladder capacity.

Methods: We retrospectively queried our institutional records for patients with non-ulcerative IC/BPS who underwent hydrodistention over an 11-year period to obtain demographic and clinical factors at the time of diagnosis and treatment. Symptom relief and bladder capacity changes were assessed, and multivariable models were used to predict response to treatment.

Results: There were 328 patients who underwent hydrodistention during the study period, of whom 36% received the procedure multiple times, and overall median follow-up was 38.6 months. Patients with repeated hydrodistentions were more likely to be female, have more comorbid pain disorders, and have trialed anticholinergic medications and intravesical instillations. No decrease in mean bladder capacity was observed over time ($P = 0.40$). Significant decreases in symptom scores were observed following the procedure on multiple questionnaires.

Conclusions: Hydrodistention does not decrease bladder capacity even with multiple procedures, and measurably improves symptoms in some patients with IC/BPS. Continuing efforts to better identify those patients most likely to benefit from this procedure are justified.

KEYWORDS

cystitis, cystoscopy, interstitial, urinary bladder

1 | INTRODUCTION

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic, potentially devastating condition characterized chiefly by bladder pressure/discomfort/pain, and urinary

urgency.¹ While prevalence estimates vary, available data suggest that roughly 6% of women in the United States struggle with this disease, leading to significant suffering as well as economic burdens.²⁻⁴

Treatment selection may also be complex, proceeding from dietary modification to oral therapy to invasive procedures.⁵ Current guidance by the American Urological Association (AUA) includes cystoscopy with hydrodistention

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as a third-line treatment option in patients for whom conservative management and pharmacological options are insufficient.⁵ However, available data suggests that the use of this procedure varies widely across providers.^{6,7} These variations are likely driven not only by provider familiarity with the procedure, but also by a relatively small body of literature assessing its efficacy. Historical studies described high rates of complications such as bladder rupture, while a recent systematic review found a lack of high quality evidence and significant heterogeneity between reports.^{8,9}

In this context, we sought to characterize our institutional experience with hydrodistention in the management of IC/BPS. Specifically, we investigated the characteristics of patients undergoing the procedure, complications and readmissions, symptom relief as quantified by several common indices, the predictors of symptomatic response, and effects of repeated hydrodistention on bladder capacity. Increasing provider knowledge of this procedure and highlighting which patients are most likely to benefit may allow for more targeted use and improved symptom relief.

2 | MATERIALS AND METHODS

2.1 | Data source

We retrospectively queried our institutional records for all patients undergoing cystoscopy and hydrodistention over the 11-year period from January 2005 to December 2015 based on Common Procedural Terminology (CPT) code 52260. These records were then reviewed and only patients with a diagnosis of non-ulcerative IC/BPS were included. The follow-up interval was calculated as the time from hydrodistention to last contact with the Urology Department. Patients who only received a single hydrodistention and who had less than 1 year of follow-up were excluded ($n = 209$).

2.2 | Baseline and procedural characteristics

Baseline demographic and clinical information as well as prior trials of therapeutic agents were obtained from records of clinic visits prior to initial hydrodistention. This included age at diagnosis, gender, race, and ethnicity, body mass index (BMI), comorbid pain disorders (fibromyalgia, irritable bowel syndrome, back pain, joint pain, vulvodynia, migraine, temporomandibular joint syndrome), menstrual status, prior oral or intravesical therapies, prior pregnancy, history of pelvic surgery, prior implantable neurostimulator device, and previous hydrodistention at an outside hospital. Procedural characteristics were collected from operative notes and included bladder capacity and intraoperative complications. Cystoscopy and hydrodistention is performed by all surgeons at our institution in a standardized fashion with deep IV sedation or general anesthetic: cystourethroscopy is performed with close examination of the bladder

mucosa for stigmata of IC/BPS. We retrograde fill the bladder until reaching an intravesical pressure of 80 cm of water, which is held for 2 min. The bladder is then drained into a graduated cylinder for measurement of the volume of the fluid instilled. The mucosa undergoes a repeat inspection, and an additional 2 min distention is performed at the same pressure. This is followed by routine instillation of 40 mL of 2% lidocaine into the bladder and a belladonna and opium suppository for pain control. In patients who underwent multiple hydrodistention procedures, bladder capacity was tracked serially across procedures, and the presence of any incident ulceration was recorded. Information regarding unplanned readmissions within 30 days of hydrodistention, as well as post-operative complications as described in subsequent clinic notes was recorded.

2.3 | Outcome

Our primary outcome was symptomatic improvement as measured by three common urological symptom questionnaires: the AUA symptom index, the Michigan Incontinence Severity Index (ISI), and the Genitourinary Pain Index (GUPI). The AUA symptom index, developed to measure symptoms of benign prostatic hyperplasia, includes measures of lower urinary tract symptoms as well as quality of life.¹⁰ The ISI specifically assesses severity and bother associated with incontinence.¹¹ The GUPI was developed and validated to measure urological pain symptoms in both genders, and includes subscales for pain symptoms, urinary symptoms, and quality of life.¹² Notably, the GUPI was more recently developed than the other symptom assessments and so had fewer completed responses to analyze. Responses were characterized as preoperative if they were recorded in the 3 months preceding hydrodistention, and post-operative if they were recorded in the 3 months following hydrodistention, which are typically four to 8 weeks post procedure at our routine follow up. Hydrodistention observations were only included in the symptomatic improvement portion of analysis if both a preoperative and post-operative measurement were available.

2.4 | Statistical analysis

To understand differences in patients who elected to undergo multiple procedures, we first compared demographic and baseline clinical characteristics between patients undergoing multiple and single hydrodistentions. Continuous variables were assessed with Student's *t*-tests and the Wilcoxon rank sum, while categorical variables were compared with Chi-square-tests and Fisher's exact test. Among patients with multiple hydrodistentions, initial and final bladder capacity were compared with paired *t*-tests. Paired *t*-tests were also used for raw comparisons of preoperative and post-operative symptom scores.

We then created three multivariable, mixed-effects linear models, one for each of our symptom questionnaires. The

dependent variable for each model was the change from preoperative to post-operative symptom score. To account for patients with multiple observations, a random intercept effect was included at the patient level. We also included independent fixed effects guided by comparisons of patients with multiple versus single hydrodistentions as well as a priori knowledge of which variables were reflective of increased IC/BPS severity: comorbid pain conditions, intravesical treatments, gender, anticholinergic use.

All analyses were performed in SAS version 9.4 (SAS Institute, Cary, NC) at the 5% significance level. This study was approved by the University of Michigan Institutional Review Board.

3 | RESULTS

There were 328 patients identified who underwent hydrodistention at our institution during the 11-year study period, of whom 119 (36%) received the procedure multiple times based on patient request (Table 1). Overall median follow-up was 38.6 months (range 7.9-128.4). Patients who received multiple procedures were more likely to be female, have a higher number of comorbid pain conditions, had prior intravesical instillations, and previously undergone hydrodistention at an outside hospital, while they were less likely to have previously taken anticholinergic medications. Complication and 30-day readmission rates were both extremely low. Among those patients who underwent multiple hydrodistentions, median number of procedures was three (range 2-18) and median time between hydrodistentions was 253 days. The patterns of bladder capacity change in individual patients over the course of multiple procedures are illustrated in Figure 1. There was no significant difference observed between initial and final mean bladder capacities (730 cc vs 750 cc, $P = 0.40$ range 250-1400 cc).

Comparisons of preoperative and post-operative symptom questionnaires are illustrated in Figure 2. AUA symptom and quality of life scores as well as GUPI urinary and quality of life scores were all significantly lower following hydrodistention, while GUPI pain scores, and ISI scores did not differ. Multivariable, mixed-effects linear models including gender, comorbid pain disorders, anticholinergic use, and intravesical instillations were not predictive of change in any of the three symptoms questionnaires.

4 | DISCUSSION

We found that hydrodistention is a safe, well-tolerated procedure with very low complication, and readmission rates. Undergoing the procedure multiple times did not reduce bladder capacity or promote the development of ulcerative disease. Lastly, we found significant symptomatic relief

following the treatment as measured by several validated instruments, but were not able to identify clear predictors of this symptomatic improvement. Taken together, these results help to confirm that hydrodistention is a worthwhile procedure with significant therapeutic benefits for some patients with severe IC/BPS. Additionally, in our clinical experience knowledge of anesthetic capacity can be helpful to guide management. When patients have a normal anesthetic bladder capacity and consequently an anatomically intact bladder our treatment focuses on pain management and bladder retraining, conversely in patients who have a very small bladder capacities we focus exclusively on pain.

Our findings of symptomatic improvement following hydrodistention are consistent with previously published results, though differences in technique and reporting make it difficult to compare results directly.¹³⁻¹⁸ Indeed, a recent analysis of the literature on hydrodistention found the evidence base overall to be severely lacking, in large part due to these differences in reported techniques, and outcome measures.⁹ However, published studies have reported that 40-70% of patients exhibited at least some degree of symptomatic response with varying degrees of durability.^{13,18} In this context our study helps expand the evidence for hydrodistention by adding to the body of reports showing a measure of symptomatic benefit following the procedure as well as acceptable rates of complications and readmissions. Further, our longitudinal assessment of bladder capacity across repeated procedures addresses the historical concern that post-procedural scarring and fibrosis could lead to reduction in bladder capacity beyond that which might be inherent to the disease process. These results are consistent with other recent data suggesting that, similar to stratification of IC/BPS into ulcerative and non-ulcerative subtypes, bladder capacity may be a unique marker of disease severity, prognosis, and comorbidity burden.¹⁹⁻²¹ The absence of development of new Hunner lesions in this cohort combined with anesthetic bladder capacities higher than what has been typically reported in the literature regarding ulcerative IC/BPS may also lend support to the idea that ulcerative and non-ulcerative IC/BPS could be two distinct disease processes. In combination with prior work these results suggest that important therapeutic benefits can be achieved through the use of hydrodistention in patients suffering from interstitial cystitis. The mechanism for these responses, however, has not yet been clearly described. It has long been believed to be related to mechanical or ischemic damage to the submucosal nerve endings within the bladder, and more recent studies have found measurable changes in urinary biomarkers following hydrodistention.^{14,22} Better characterization of the molecular mechanism of hydrodistention could also enable improved identification of patients more likely to benefit.

There are some limitations to this work. Most importantly, as a retrospective study these findings are limited in that not all

TABLE 1 Clinical and demographic comparisons between patients who underwent single and multiple hydrodistention procedures

Characteristic	Single hydrodistention (N = 209)	Multiple hydrodistentions (N = 119)	P-value
Mean age, years (SD)	39.0 (14.2)	35.5 (15.1)	0.058
Mean BMI, Kg/m ² (SD)	27.6 (6.5)	27.3 (6.2)	0.60
Gender, % female	89.5	98.3	<0.01
Smoker (current or former), %	40.8	39.8	0.44
History of pregnancy, %	64.9	67.0	0.74
History of pelvic surgery, %	50.2	58.8	0.13
Postmenopausal, %	30.8	41.4	0.071
Comorbid pain disorder, %	53.6	61.3	0.17
Mean number comorbid pain disorders (SD)	0.9	1.3	0.012
Oral therapy, %	86.5	83.9	0.53
Anticholinergic, %	56.3	38.1	<0.01
Tricyclic antidepressant, %	36.4	36.4	0.99
Neuropathic pain medication, %	16.0	22.0	0.18
Pentosan, %	33.5	36.4	0.59
Pyridium, %	33.0	40.7	0.17
Hydroxyzine, %	8.7	9.3	0.86
Intravesical instillation, %	19.1	35.3	<0.01
Interstim device, %	4.8	6.8	0.45
History of prior hydrodistention, %	20.1	48.7	<0.001
Median follow-up time, months (range)	32.3 (12-128.4)	50.5 (7.9-127.2)	<0.01
Complications, %	0.5	0.7	0.78
30-day readmissions, %	0.5	1.8	0.18
Median number of hydrodistentions (range)	-	3 (2-18)	-
Median time between hydrodistentions, days	-	253	-

Bold values signify statistically significant values.

patients had complete symptom questionnaire data available from both pre-and post-operative clinic visits. As such, we may have been unable to detect smaller differences or accurately identify predictors of symptomatic response. This missing data

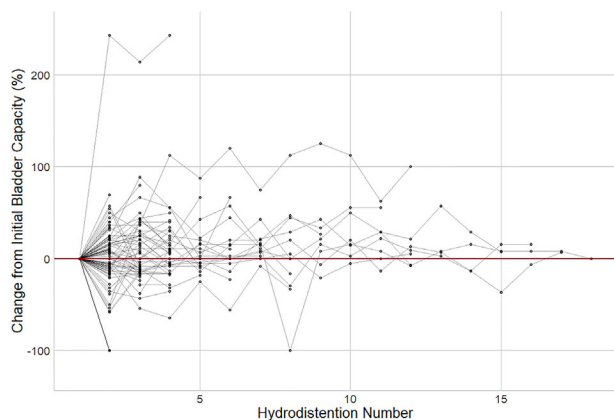


FIGURE 1 Change in bladder capacity over multiple hydrodistention procedures. Dots represent an individual capacity measurement in an individual patient, and each patient's measurements are linked by a line

also precluded a meaningful analysis of what proportion of patients were responders to therapy. Second, while we conducted a thorough chart review of the initial clinic visit, these data provide only a snapshot, and do not fully reflect the dynamic nature of therapeutic choices in IC/BPS. Also, due to the previously discussed variability in techniques and use of this procedure across providers and institutions these results may not be generalizable to all settings. Among the administered symptom questionnaires, the GUPI was only recently incorporated into regular clinical visits, which lead to comparatively few patients in this cohort having available GUPI results to analyze. This is of particular importance because of the three symptom questionnaires included in this analysis the GUPI is the only one designed to directly assess the pain symptoms suffered by IC/BPS patients. Due to the inclusion of patients who received the procedure multiple times, our findings are likely reflective of a self-selected group of patients more likely to feel hydrodistention is of symptomatic benefit (ie, selection bias), thus the effect sizes observed here may be larger than in some patient populations. However, the presence of a significant number of such patients can itself be interpreted as evidence that the procedure is effective at least for some sufferers of IC/BPS.

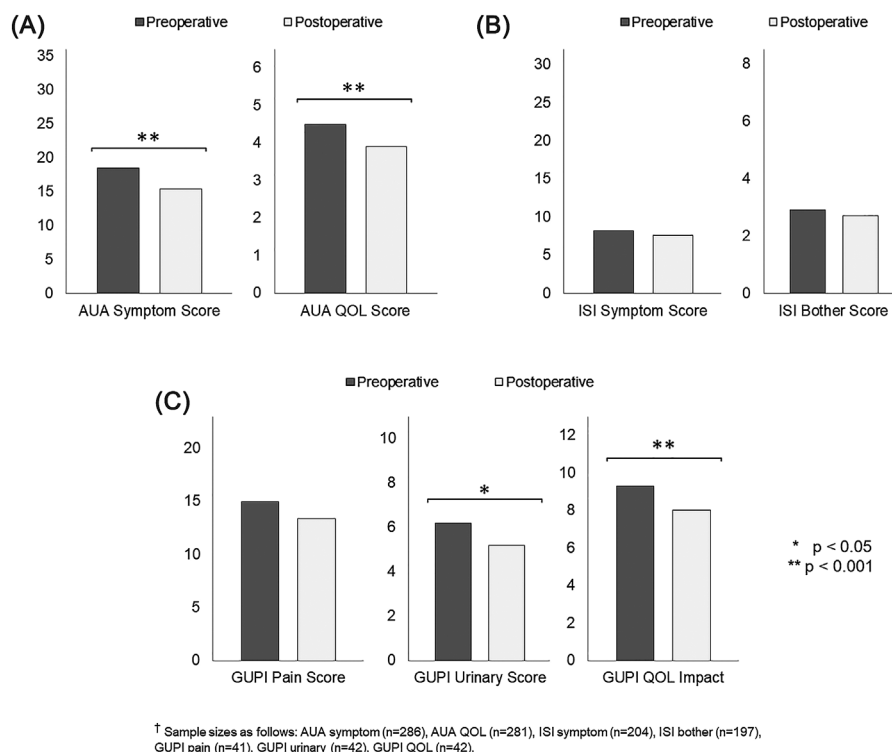


FIGURE 2 Pre- and post-operative results of AUA (A), ISI (B), and GUPI (C) questionnaires[†]

Additionally, an important clinical factor not reflected in this analysis is the phenomenon of flares following hydrodistention, in which patients may find their IC/BPS symptoms become worse immediately after hydrodistention before they subsequently improve from baseline. These flares may make some providers hesitate to offer hydrodistention, and it is important that patients be counseled regarding this outcome prior to undergoing the procedure.

Despite these limitations this study adds significantly to the existing literature on the use of hydrodistention in IC/BPS. The symptomatic benefits and favorable safety profile observed here may help to improve perception of the procedure among some clinicians while confirming what others may have already observed in practice. Further, our bladder capacity results can ease concerns about the repeated use of this procedure in those patients who experience significant therapeutic results. IC/BPS remains a difficult condition for both patients and providers; as such it is imperative to continue to improve our understanding of the disease pathophysiology and offer patients access to the full range of options in the urologist's armamentarium.

5 | CONCLUSIONS

We observed symptomatic benefits, excellent safety profile, and no significant impact on bladder capacity in this retrospective study of our institutional experience using hydrodistention to treat interstitial cystitis/bladder pain syndrome, though we were

not able to identify clear predictors of symptom response. Ongoing research must work to improve the uniformity of outcome measurement and hydrodistention technique, while helping to better identify those patients most likely to benefit from the procedure. Efforts to further our understanding of the benefits of hydrodistention should help to improve the experiences of patients with interstitial cystitis/bladder pain syndrome as well as their providers.


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CONFLICTS OF INTEREST

None.

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REFERENCES

- Teichman JM, Parsons CL. Contemporary clinical presentation of interstitial cystitis. *Urology*. 2007;69:41–47.

2. Berry SH, Elliott MN, Suttorp M, et al. Prevalence of symptoms of bladder pain syndrome/interstitial cystitis among adult females in the United States. *J Urol*. 2011;186:540–544.
3. Tung A, Hepp Z, Bansal A, Devine EB. Characterizing health care utilization, direct costs, and comorbidities associated with interstitial cystitis: a retrospective claims analysis. *J Manag Care Spec Pharm*. 2017;23:474–482.
4. Konkle KS, Berry SH, Elliott MN, et al. Comparison of an interstitial cystitis/bladder pain syndrome clinical cohort with symptomatic community women from the RAND Interstitial Cystitis Epidemiology study. *J Urol*. 2012;187:508–512.
5. 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.
6. Mahendru AA, Al-TaHER H. Cystodistension: certainly no standards and possibly no benefits—survey of UK practice. *Int Urogynecol J*. 2010;21:135–139.
7. Turner KJ, Stewart LH. How do you stretch a bladder? A survey of UK practice, a literature review, and a recommendation of a standard approach. *Neurourol Urodyn*. 2005;24:74–76.
8. Higson RH, Smith JC, Whelan P. Bladder rupture: an acceptable complication of distension therapy? *Br J Urol*. 1978;50:529–534.
9. Olson LE, Dyer JE, Haq A, Ockrim J, Greenwell TJ. A systematic review of the literature on cystodistension in bladder pain syndrome. *Int Urogynecol J*. 2018;29:251–257.
10. Barry MJ, Fowler FJ Jr., O'Leary MP, et al. The american urological association symptom index for benign prostatic hyperplasia. the measurement committee of the american urological association. *J Urol*. 1992;148:1549–1557 discussion 1564.
11. Suskind AM, Dunn RL, Morgan DM, DeLancey JO, McGuire EJ, Wei JT. The Michigan Incontinence Symptom Index (M-ISI): a clinical measure for type, severity, and bother related to urinary incontinence. *Neurourol Urodyn*. 2014;33:1128–1134.
12. Clemens JQ, Calhoun EA, Litwin MS, et al. Validation of a modified National Institutes of Health chronic prostatitis symptom index to assess genitourinary pain in both men and women. *Urology*. 2009;74:983–987 quiz 987 e981–983.
13. Yamada T, Murayama T, Andoh M. Adjuvant hydrodistension under epidural anesthesia for interstitial cystitis. *Int J Urol*. 2003;10:463–469 discussion 469.
14. Erickson DR, Kunselman AR, Bentley CM, et al. Changes in urine markers and symptoms after bladder distention for interstitial cystitis. *J Urol*. 2007;177:556–560.
15. Aihara K, Hirayama A, Tanaka N, Fujimoto K, Yoshida K, Hirao Y. Hydrodistension under local anesthesia for patients with suspected painful bladder syndrome/interstitial cystitis: safety, diagnostic potential and therapeutic efficacy. *Int J Urol*. 2009;16:947–952.
16. Ottem DP, Teichman JM. What is the value of cystoscopy with hydrodistension for interstitial cystitis? *Urology*. 2005;66:494–499.
17. Hsieh CH, Chang ST, Hsieh CJ, et al. Treatment of interstitial cystitis with hydrodistention and bladder training. *Int Urogynecol J Pelvic Floor Dysfunct*. 2008;19:1379–1384.
18. Glemain P, Riviere C, Lenormand L, Karam G, Bouchot O, Buzelin JM. Prolonged hydrodistention of the bladder for symptomatic treatment of interstitial cystitis: efficacy at 6 months and 1 year. *Eur Urol*. 2002;41:79–84.
19. Peters KM, Killinger KA, Mounayer MH, Boura JA. Are ulcerative and nonulcerative interstitial cystitis/painful bladder syndrome 2 distinct diseases? A study of coexisting conditions. *Urology*. 2011;78:301–308.
20. Walker SJ, Zambon J, Andersson KE, et al. Bladder capacity is a biomarker for a bladder centric versus systemic manifestation in interstitial Cystitis/Bladder pain syndrome. *J Urol*. 2017;198:369–375.
21. Chiu CD, Lee MH, Chen WC, Ho HL, Wu HC. Alexithymia and anesthetic bladder capacity in interstitial cystitis/bladder pain syndrome. *J Psychosom Res*. 2017;100:15–21.
22. Dunn M, Ramsden PD, Roberts JB, Smith JC, Smith PJ. Interstitial cystitis, treated by prolonged bladder distension. *Br J Urol*. 1977;49:641–645.

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