

Cystoscopic Hydrodistension Under Local Anesthesia: Therapeutic Implications in Non-Hunner IC Subtypes

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Objective: This study aims to investigate the effect of hydrodistension under local anesthesia on clinical outcomes in subtypes of non-Hunner lesion interstitial cystitis (NHIC), categorized by hemorrhage severity.

Methods: Based on a simplified bladder hemorrhage grading system, we enrolled 12 female patients with multiple or diffuse punctate hemorrhage (Group IC1) and 12 female patients with focal punctate hemorrhage only (Group IC2). All participants underwent cystoscopy with hydrodistension (CWH). Maximum bladder capacity (MBC), Interstitial Cystitis Symptom Index (ICSI), Interstitial Cystitis Problem Index (ICPI), and visual analogue scale (VAS) were recorded at baseline, and participants were followed up for 6 months.

Results: Group IC1 exhibited significantly lower preoperative MBC ($p < 0.05$). All outcome measures improved significantly at one week post-procedure in both groups ($p < 0.05$), with no significant between-group difference in the magnitude of improvement ($p > 0.05$). During subsequent follow-up, ICSI scores in Group IC1 increased significantly at 3 months ($p < 0.05$), whereas ICPI scores in both groups increased significantly at 6 months ($p < 0.05$).

Conclusion: NHIC patients with more severe bladder mucosal hemorrhage exhibited smaller baseline MBC and earlier ICSI score elevation following CWH under local anesthesia. These findings may inform individualized intervention strategies, support the development of efficacy prediction models, and optimize follow-up protocols and treatment escalation timing, thereby contributing to improved quality of life in this patient population.

Keywords: bladder pain syndrome, cystoscopy with hydrodistension, interstitial cystitis, local anesthesia, non-Hunner's interstitial cystitis

Introduction

Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS) is a group of conditions primarily characterized by chronic pelvic pain, accompanied by at least one lower urinary tract symptom, excluding other diseases.^{1,2} The epidemiology of interstitial cystitis/bladder pain syndrome (IC/BPS) remains heterogeneous. Current evidence indicates that the male-to-female prevalence ratio ranges from 1:5 to 1:2.³ Although accumulating studies suggest a potential association between oxidative stress and the onset of IC/BPS,⁴ its underlying pathophysiological mechanisms remain incompletely understood. This lack of clarity contributes to the challenges encountered in both diagnosing and managing the condition. Submucosal hemorrhage observed during cystoscopy following hydrodistension was previously considered a typical manifestation of IC/BPS, though this view is now being challenged. Research by Alessandro Morlacco et al⁵ suggests that the results of cystoscopy with hydrodistension (CWH) and tissue biopsy must be interpreted within the clinical context. However, some studies continue to support the value of cystoscopy in the early diagnosis of IC/BPS.⁶ IC/BPS is recognized as a heterogeneous condition, divided into two subtypes: Hunner's interstitial cystitis (HIC) and Non-Hunner's interstitial cystitis (NHIC). HIC is characterized by distinct tissue-blood features, and increasing evidence suggests that it should be considered an independent phenotype of IC/BPS.⁷ Research on NHIC remains relatively limited. Zhu et al's study⁸ indicates that cystoscopy with hydrodistension under

anesthesia (epidural/general anesthesia) can significantly alleviate the clinical symptoms of HIC. This study also highlights the procedure's beneficial effects on symptom improvement in patients with NHIC.

Kinue Aihara et al conducted cystoscopy and hydrodistension following intravesical administration of 2% lidocaine. Approximately 77% of patients exhibited globular hemorrhage, nearly 7% developed Hunner ulcers, and 71% demonstrated therapeutic improvement within one month, with evidence of sustained long-term benefits.⁹ However, the study did not standardize the infusion pressure during hydrodistension, nor did it implement a stratified assessment and treatment approach for patients with globular hemorrhage. Yu et al proposed a hemorrhage grade classification for post-hydrodistension cystoscopy, where Grade 0 is defined as no spherical hemorrhage, Grade 1 as hemorrhage affecting up to half of the bladder quadrants, Grade 2 as diffuse hemorrhage in three to four quadrants, and Grade 3 as diffuse hemorrhage throughout the bladder. The study also highlighted the potential for recurrence in patients after hydrodistension, suggesting the need for repeated procedures.¹⁰

Although CWH under local anesthesia is clinically practiced, evidence stratifying NHIC by hemorrhage severity in this context remains limited. It is unclear whether therapeutic efficacy differs among NHIC subtypes classified by hemorrhage severity, or whether such classification holds prognostic value. Therefore, the present study was conducted to address these gaps.

Materials and Methods

Ethical Approval and Informed Consent

The Ethics Committee of the First Affiliated Hospital of Chongqing Medical University approved this study, and all data were managed in compliance with the *Declaration of Helsinki*. Informed consent was obtained from all participants.

Participants

From September 2023 to October 2024, we diagnosed 51 patients with IC/BPS in accordance with the definition of the International Continence Society. The patients were screened based on the following inclusion and exclusion criteria: Inclusion criteria: Female patients who only presented with mucosal bleeding under cystoscopy after CWH surgery under local anesthesia and had been followed up for at least six months. Exclusion criteria: Diagnosed with urinary system tumors, symptoms relieved after antibiotic treatment, concurrent uncontrolled urinary tract infections, urinary tract obstruction, chemical cystitis, tuberculous cystitis, radiation cystitis, pregnancy or childbirth, participation in other clinical trials within three months before the trial, mental disorders that prevent cooperation with doctors, and other conditions deemed unsuitable for participation in the study by the researchers. Among the 51 patients, 17 patients had no submucosal hemorrhage, 3 patients were lost to follow-up at 6 months postoperatively, 5 patients were excluded due to the absence of submucosal hemorrhage confirmed by rechecked imaging data during subsequent stratification, 1 patient had damaged imaging data that could not be confirmed, and 1 patient was male. Finally, 24 female patients with bladder mucosal hemorrhage were included in this study (see [Figure 1](#)). We simplified the grading method of Wan-Ru Yu et al, defining patients with grade 2 or above hemorrhage as having high-grade hemorrhage and those with grade 1 hemorrhage as having low-grade hemorrhage. Based on this, we collected 12 cases of high-grade hemorrhage in female patients (Group IC1) and 12 cases of low-grade hemorrhage in female patients (Group IC2).

Clinical Data

All patients in this study underwent CWH on an outpatient basis, received no concomitant treatments, and were regularly followed up at the outpatient clinic. Both patients and the operating surgeon, who also assessed the outcomes, were blinded to group allocation; furthermore, the statistical analysts were unaware of the actual significance of the group assignments. During the study period, general patient data, including age and body mass index (BMI), were recorded. Various variables, such as the number of irrigation cycles and the duration of hydrodistension retention, were also documented. Clinical symptoms were assessed using the following scores: interstitial cystitis problem index (ICPI), interstitial cystitis symptom index (ICSI), and the Visual Analogue Scale (VAS) was used to assess the degree of pain in

CONSORT 2010 Flow Diagram

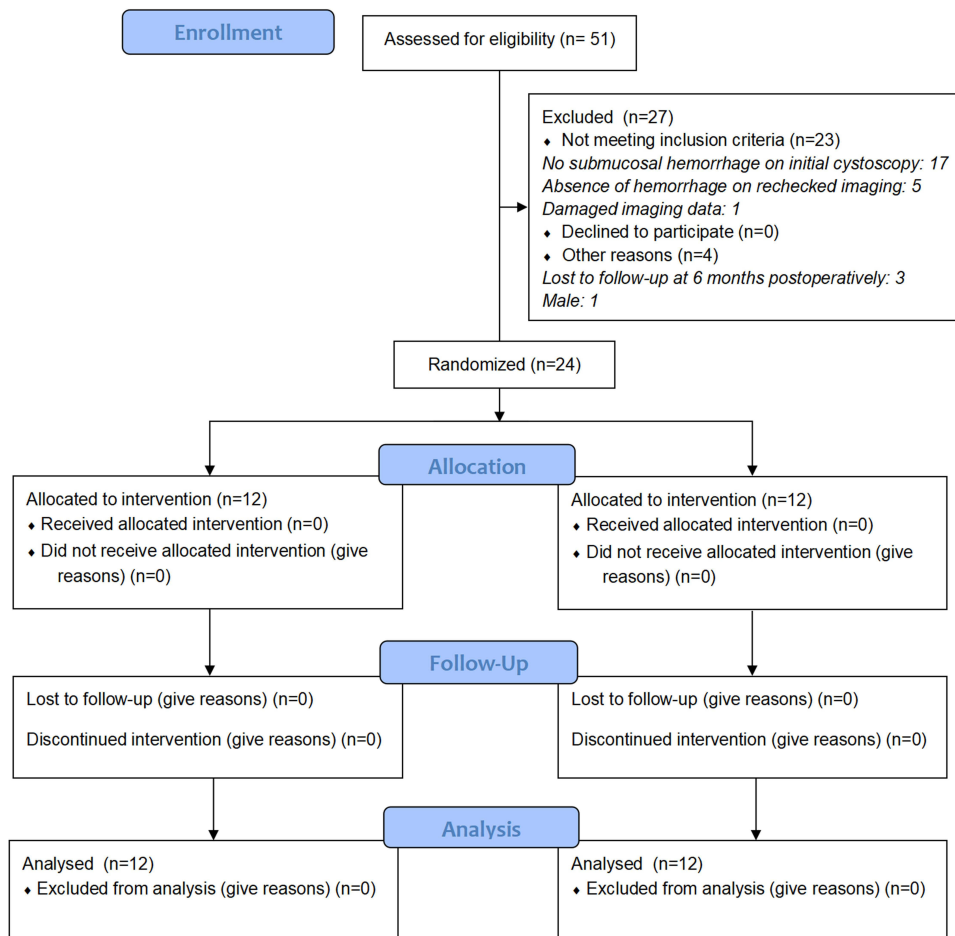


Figure 1 CONSORT flow diagram of patient recruitment and selection. Of the 51 patients screened, 17 exhibited no submucosal hemorrhage, 3 were lost to follow-up at 6 months postoperatively, 5 were excluded due to absence of submucosal hemorrhage on rechecked imaging data during subsequent stratification, 1 had damaged imaging data that precluded confirmation, and 1 was male. Ultimately, 24 female patients with bladder mucosal hemorrhage were included in the final analysis.

the bladder area of the patients. Each patient's maximum bladder capacity was recorded during the procedure to evaluate their overall condition.

Cystoscopy with Hydrodistension

All patients in this study underwent CWH surgery under local anesthesia in the outpatient department. Local urethral anesthesia was achieved using 2% lidocaine gel. Normal saline (0.9%) was employed as the irrigation fluid. Irrigation pressure was precisely controlled via a graduated water column, while procedural duration was recorded using a timer. Upon confirmation of adequate anesthesia, a rigid cystoscope (Fr 20–22) was advanced into the bladder. Each patient underwent cystoscopy first, including the trigone and all lateral walls of the bladder. Then, water dilation was performed according to the method described in the 11th edition of Campbell-Walsh Urology, Volume 2. The first dilation was maintained at a pressure of 80 cmH₂O for about 2 minutes. The bladder walls were examined to identify any bleeding

points and grade them. After the perfusion fluid was drained, water dilation was performed again and maintained at a pressure of 80 cmH₂O for 8 minutes for treatment.

Data Analysis

The experimental data were analyzed using SPSS 26.0 (IBM, Armonk, New York, USA). For quantitative data following a normal or approximate normal distribution, means and standard deviations were used for description. Inter-group differences were analyzed using the independent samples *t*-test, and intra-group differences were assessed with one-way repeated measures ANOVA, followed by paired sample *t*-tests. For data not following a normal distribution, the median (upper quartile, lower quartile) was used for description. Inter-group differences were analyzed using non-parametric tests, specifically the Mann–Whitney *U*-test, and intra-group differences were assessed using the Friedman test and Wilcoxon signed-rank test. A *p*-value < 0.05 was considered statistically significant, with all tests being two-tailed.

Results

As shown in Table 1, a total of 24 patients were included in the Group IC1 and Group IC2 (12 patients in each group). The mean maximum bladder capacity in the Group IC1 was 265.00 mL, while that in the Group IC2 was 422.50 mL. The mean maximum bladder capacity for all patients was 343.75 mL. It can be seen that the Group IC1 had a significantly lower maximum bladder capacity ($P < 0.05$). The ICSI, ICPI, and VAS scores of Group IC1 were 11.83 ± 2.95 , 11.00 ± 1.71 , and 3.50 ± 0.90 , respectively, while those of Group IC2 were 10.58 ± 2.07 , 9.92 ± 2.47 , and 3.17 ± 1.03 , respectively. There was no statistically significant difference in each score between the two groups ($P > 0.05$). (Figure 2).

Based on the follow-up data of all patients, we compared the ICSI, ICPI, and VAS scores before the operation and one week after the operation. As shown in Figure 3, we found that the above scores after the operation were significantly improved compared with those before the operation ($P < 0.001$). Then we continued to follow up until 6 months. We compared the data between one week, three months, and six months after the operation. Overall, the ICSI score increased at three months after the operation (8.08 ± 2.36) compared with one week after the operation (7.58 ± 2.24) ($P < 0.05$), but there was no statistically significant change between six months (7.96 ± 2.33) and three months (8.08 ± 2.36) after the operation ($P > 0.05$); the ICPI score did not show a statistically significant change at three months after the operation (7.38 ± 2.04) compared with one week after the operation (7.04 ± 2.10) ($P > 0.05$), but it increased significantly at six months (7.88 ± 2.17) compared with three months after the operation ($P < 0.05$); while the VAS score did not show a statistically significant change at three months and six months compared with one week after the operation ($P > 0.05$).

We compared the ICSI, ICPI, and VAS scores of the Group IC1 and the Group IC2 at one week, three months, and six months after surgery to evaluate the clinical outcomes of different subtypes. As shown in Figure 4, for the ICSI score, the IC1 group had higher scores at three months (9.00 ± 2.70) and six months (9.00 ± 2.66) compared to one week (8.42 ± 2.68) ($P < 0.05$), while the Group IC2 did not show a statistically significant increase ($P > 0.05$). For the ICPI score, compared to one week (7.75 ± 2.26), the Group IC1 did not show a statistically significant increase at three months (8.08 ± 2.23), but did at six

Table 1 Basic Clinical Data of NHIC Patients

Clinical Data	IC1	IC2	P
Age	58.00±10.51	58.08±13.05	0.986
BMI (kg/m ²)	24.54±2.63	22.47±1.97	0.04*
Number of hydrodistension procedures	2	2	–
Duration of hydrodistension	10min	10min	–
Maximum bladder capacity (mL)	265.00±52.48	422.50±133.36	0.002*
ICSI	11.83±2.95	10.58±2.07	0.242
ICPI	11.00±1.71	9.92±2.47	0.224
VAS	3.50±0.90	3.17±1.03	0.409

Note: * $P < 0.05$.

Abbreviations: BMI, Body Mass Index; ICSI, Interstitial Cystitis Symptom Index; ICPI, Interstitial Cystitis Problem Index; vas, Visual Analogue Scale.

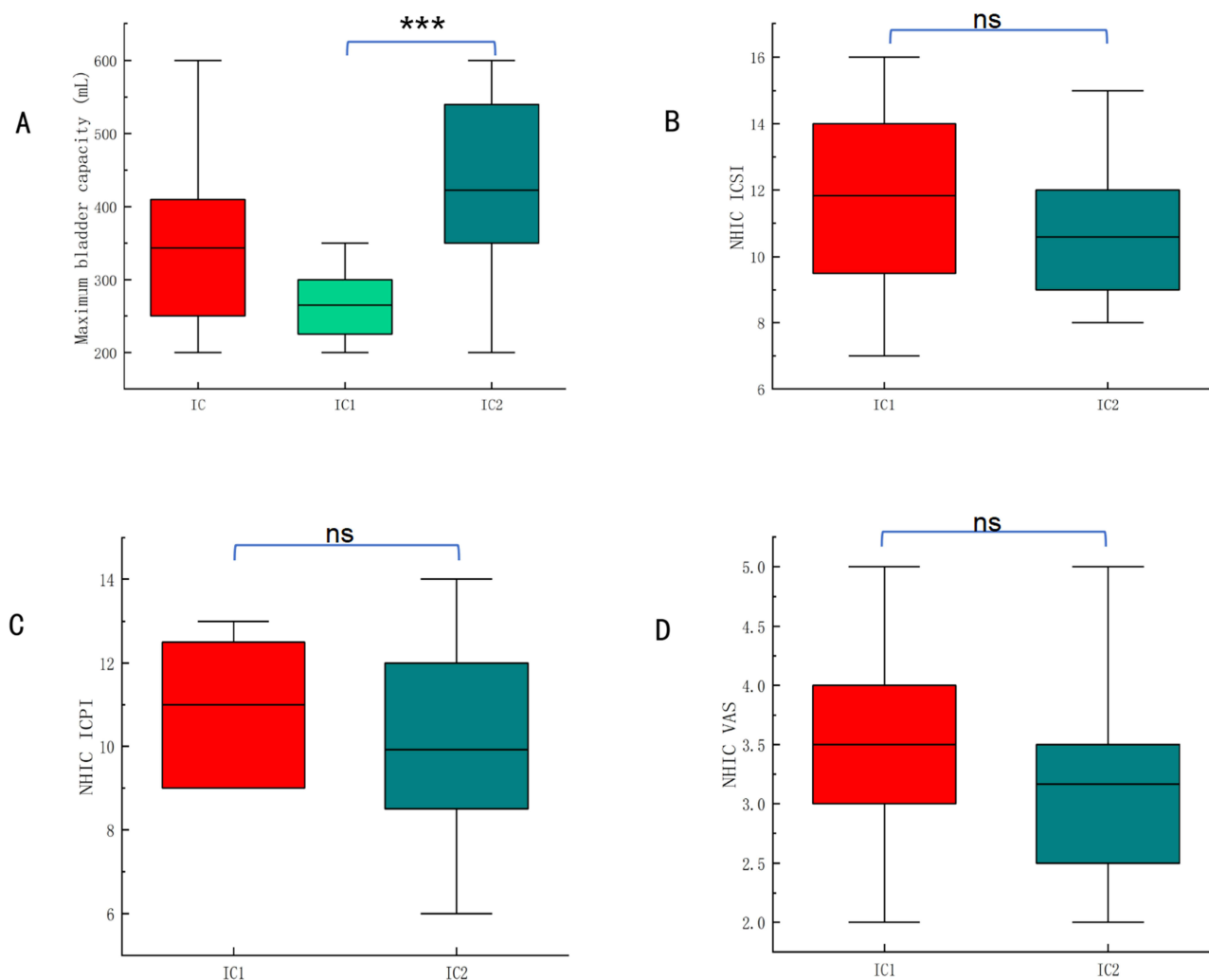


Figure 2 Comparative analysis of clinical parameters between the Group IC1 and the Group IC2. **(A)** Comparison of maximum bladder capacity between Group IC1 and Group IC2. **(B)** Comparison of ICSI between Group IC1 and Group IC2. **(C)** Comparison of ICPI between Group IC1 and Group IC2. **(D)** Comparison of vas between Group IC1 and Group IC2. *** $P < 0.001$.

Abbreviations: ICPI, Interstitial Cystitis Problem Index; ICSI, Interstitial Cystitis Symptom Index; VAS, Visual Analogue Scale; NS, not significant.

months (8.67 ± 2.23) ($P < 0.05$); for the Group IC2, compared to one week (6.33 ± 1.72), there was no statistically significant increase at three months (6.67 ± 1.61), but there was at six months (7.08 ± 1.88) ($P < 0.05$). The VAS score did not show a statistically significant increase in either group during the follow-up period ($P > 0.05$). To better compare the early treatment effects of the two groups, we compared the decline rates of each score at one week after surgery between the two groups. The results showed that there was no statistically significant difference in the decline rates of ICSI, ICPI, and VAS between the two groups ($P > 0.05$), as shown in Table 2.

Overall, all groups demonstrated significant reductions in all outcome measures one week postoperatively, indicating that this treatment modality achieved favorable short-term efficacy across different NHIC subtypes. During the 6-month follow-up period, ICSI scores increased significantly in Group IC1 at 3 months, whereas ICPI scores increased significantly in both groups at 6 months. VAS scores remained stable without statistically significant increases in either group. No serious complications were observed in this study.

Discussion

Among the female IC/BPS patients selected this time, the BMI of the IC1 group was higher than that of the Group IC2 ($P < 0.05$); while a previous study showed that the BMI and waist circumference of IC/BPS patients were higher than those of non-IC/BPS

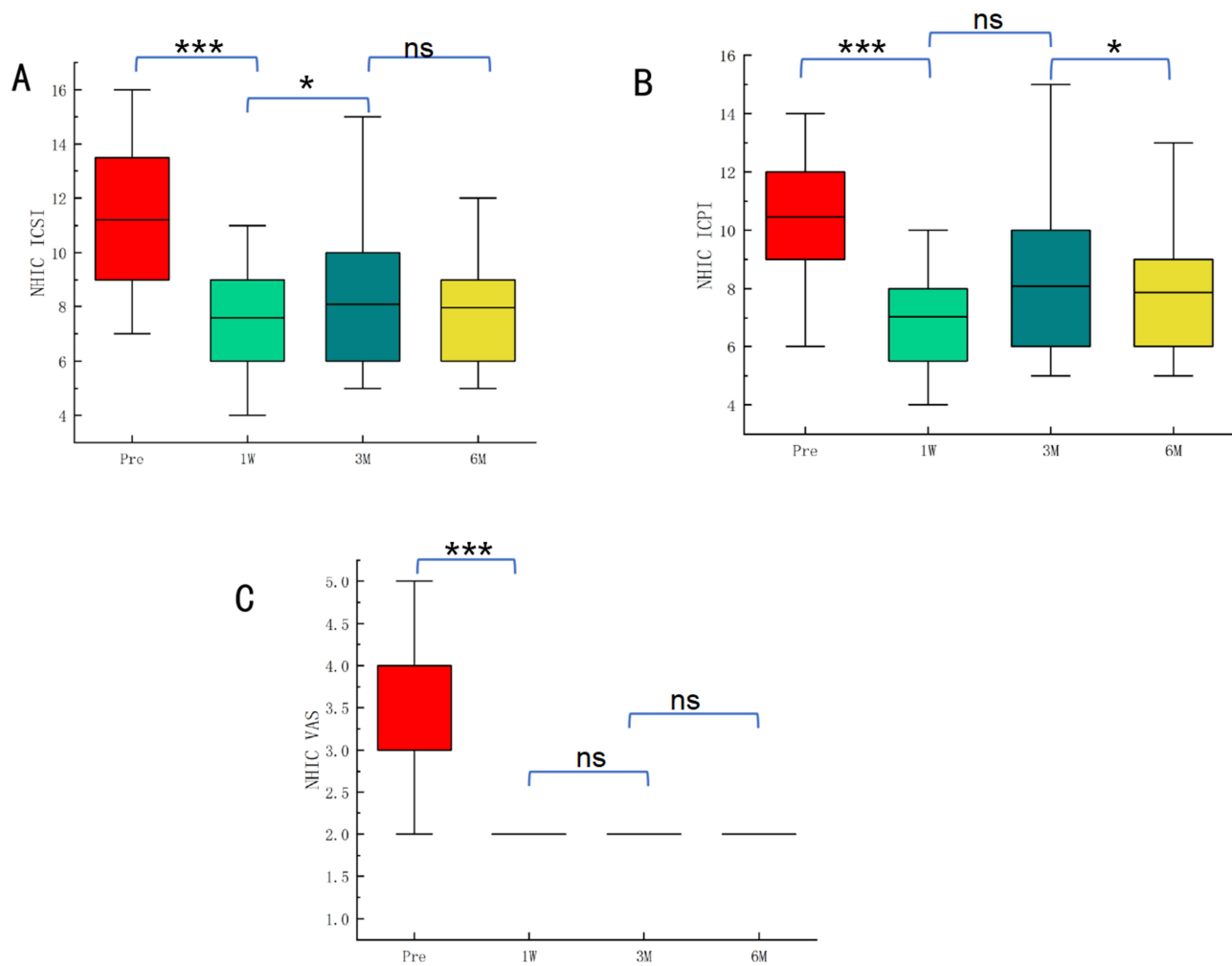


Figure 3 AComparative Analysis of the Outcomes of NHIC Patients at Six Months Postoperatively .(A) Comparison of ICSI scores of NHIC patients at 6 months. (B) Comparison of ICPI scores of NHIC patients at 6 months. (C) Comparison of VAS scores of NHIC patients at 6 months. *P<0.05,**P<0.001. ***P<0.001. **Abbreviations:** ICPI, Interstitial Cystitis Problem Index; ICSI, Interstitial Cystitis Symptom Index; VAS, Visual Analogue Scale; NS, not significant.

patients¹¹. The degree of bladder mucosal hemorrhage in NHIC patients may be positively correlated with body mass index, although further investigation with larger sample sizes is warranted. Patients in Group IC1 exhibited lower maximum bladder capacity compared with those in Group IC2, consistent with previous findings demonstrating a negative correlation between maximum bladder capacity and severity of bladder mucosal changes in IC/BPS.¹² Previous studies have shown that bladder capacity under anesthesia is negatively correlated with ICSI¹³. This might be because a smaller maximum bladder capacity could lead to a reduced effective bladder capacity, ultimately exacerbating symptoms such as frequent urination and resulting in a higher ICSI score. However, in this study, patients in the Group IC1 did not show a higher ICSI score. This could be due to the strong subjectivity of the ICSI score and the fact that the bladder capacity of the patients in this study did not fall below a certain limit. It is also possible that the small number of cases contributed to this result.

In this study, all NHIC patients exhibited significant reductions in ICSI, ICPI, and VAS scores one week following CWH, further substantiating the efficacy of this procedure under local anesthesia. In terms of safety, no serious complications occurred in all patients after CWH surgery in this study, while there have been reports of bladder necrosis after water expansion in the past.¹⁴ This may be due to the fact that patients under local anesthesia can better reflect their subjective feelings, and the degree of tissue expansion under local anesthesia is slightly lower. However, this needs further exploration. There have also been studies that chose lower pressure water expansion for diagnosis in the past, but no comparison of therapeutic effects was made.¹⁵ Six months after water expansion, both ICSI and ICPI increased to

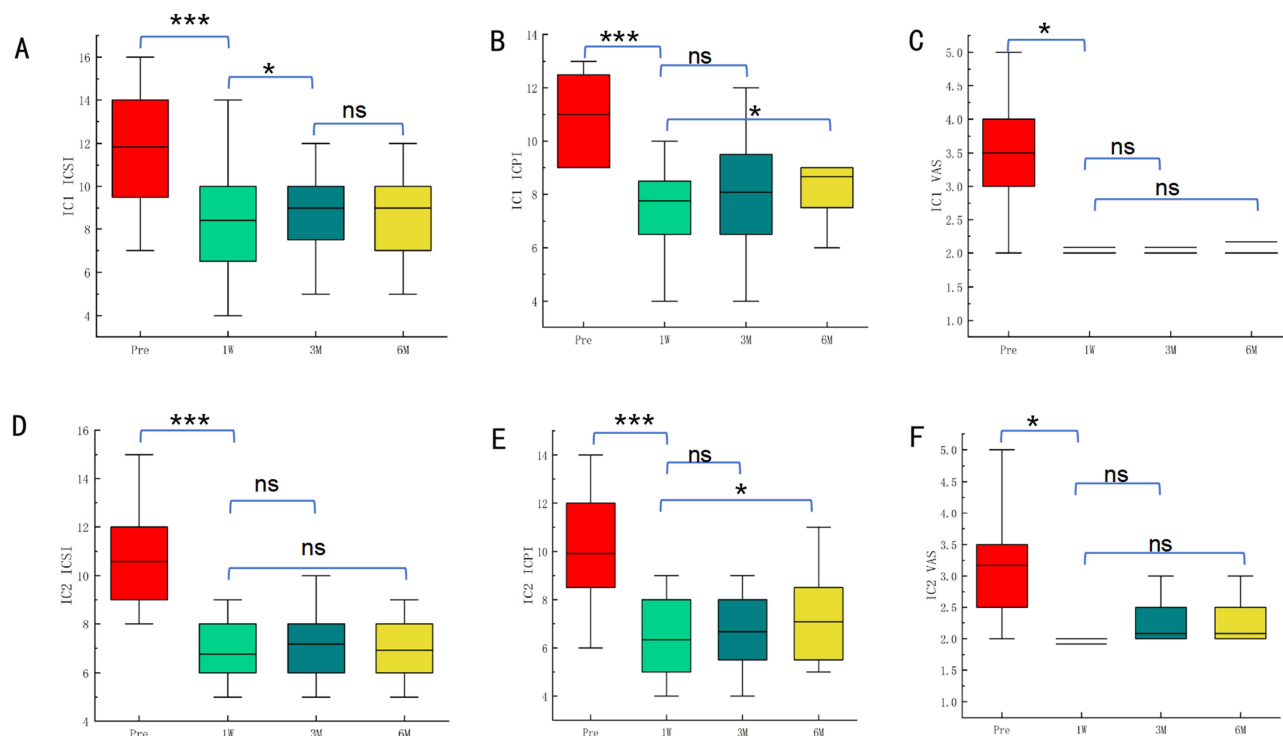


Figure 4 Comparison of ICSI, ICPI and VAS scores at different time points between Group IC1 and Group IC2. (A) Comparison of ICSI scores at different time points in the Group IC1. (B) Comparison of ICPI scores at different time points in the Group IC1. (C) Comparison of VAS scores at different time points in the group IC1. (D) Comparison of ICSI scores at different time points in the Group IC2. (E) Comparison of ICPI scores at different scores at different time points in the Group IC2. (F) Comparison of VAS scores at different time points in the Group IC2. * $P < 0.05$; *** $P < 0.001$.

varying degrees, but they were still significantly lower than the levels before the surgery. Meanwhile, VAS did not show a statistically significant increase, which is not entirely consistent with previous studies.⁸ Previous animal experiments have demonstrated that hydrodistension can induce structural damage to the bladder wall and peripheral nerves;¹⁶ consequently, tissue repair processes may contribute to the subsequent increase in the aforementioned scores.

We compared postoperative remission rates at one week with baseline values separately for Group IC1 and Group IC2; however, no statistically significant between-group differences were identified. Nevertheless, the differential clinical responses of NHIC subtypes to CWH under local anesthesia warrant continued investigation, and further case accumulation is required for definitive inference and validation.

The follow-up outcomes diverged between the two groups. Within the 6-month observation period, ICSI scores in Group IC1 demonstrated a statistically significant increase commencing at 3 months postoperatively, whereas Group IC2 remained stable; conversely, ICPI scores exhibited an upward trend in both groups. VAS scores showed no statistically significant changes in either cohort. These findings suggest that NHIC subtypes characterized by reduced maximum bladder capacity and more severe bladder mucosal hemorrhage may experience earlier symptomatic recurrence, although this hypothesis requires further empirical investigation. The results of a study involving 141 cases also demonstrated that the lower the maximum bladder capacity under anesthesia, the higher the recurrence rate of the patients.¹⁷ This might be

Table 2 Comparison of Improvement Rates of ICSI, ICPI, and VAS at 1 week After Surgery Between the IC1 Group and the IC2 Group

Variable	Group IC1 (n=12)	Group IC2 (n=12)	t/Z	P
ICSI Improvement Rate	0.30±0.10	0.36±0.09	-1.658	0.112
ICPI Improvement Rate	0.30±0.15	0.35±0.14	-0.891	0.383
VAS Improvement Rate	0.37(0.33,0.50)	0.33(0.33,0.50)	-0.368	0.713

due to the fact that patients with a lower maximum bladder capacity experience a faster decline in bladder capacity, and their subjective feelings are more pronounced, leading to earlier changes in the ICSI score. However, this still requires further research data for verification.

Although this study yielded significant results, several limitations remain. Firstly, the small sample size limits statistical power and may introduce selection bias, necessitating larger, multi-center studies. Secondly, the follow-up period was relatively short, demonstrating the short-term efficacy of CWH for varying degrees of NHIC. However, longer-term follow-up is essential to assess the sustainability of these outcomes. Additionally, although previous studies have indicated that repeated CWH does not significantly affect bladder capacity, changes in maximum bladder capacity after CWH in patients with varying degrees of NHIC remain a critical factor to monitor.^{18,19} Finally, this study did not conduct more detailed subgroup analysis based on the degree of bladder mucosal hemorrhage. Currently, there are no large-scale, multi-center studies to reference. Therefore, further subtype classification of NHIC according to the severity of bladder mucosal hemorrhage, along with an evaluation of the long-term efficacy of CWH, is warranted in studies with larger sample sizes. The differential clinical responses of distinct NHIC subtypes to CWH under local anesthesia warrant further investigation. Given that IC/BPS is a heterogeneous condition, non-surgical treatment is generally recommended for NHIC.²⁰ Thus, further research into the efficacy of CWH and other treatment options for NHIC is needed.

Overall, this study preliminarily evaluated the safety, efficacy, and durability of CWH under local anesthesia in NHIC patients, a procedure feasible for outpatient implementation. Additionally, we investigated the feasibility of stratifying NHIC patients using this technique and characterized the differential clinical responses across subtypes. The severity of bladder mucosal hemorrhage following CWH under local anesthesia varied among patients; those with more severe hemorrhage exhibited smaller maximum bladder capacity and earlier elevation of ICSI scores, suggesting heightened vigilance for accelerated postoperative disease progression in this subgroup. These findings may inform individualized intervention strategies, facilitate the development of efficacy prediction models, and optimize follow-up protocols and treatment escalation timing, thereby contributing to sustained quality-of-life improvements in NHIC patients.

Abbreviations

BPS, bladder pain syndrome; CWH, cystoscopy with hydrodistensio; IC, interstitial cystitis; ICPI, Interstitial Cystitis Problem Index; ICSI, Interstitial Cystitis Symptom Index; NHIC, interstitial cystitis without Hunner lesions; HIC, cystitis with Hunner lesions; VAS, Visual Analogue Scale; BMI, Body Mass Index; MBC, The maximum bladder capacity.

Data Sharing Statement

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

This study was conducted with approval from the Ethics Committee of the First Affiliated Hospital of Chongqing Medical University (No.CY2023-068-01). This study was conducted in accordance with the declaration of Helsinki. Written informed consent was obtained from all participants.

Acknowledgments

We would like to acknowledge the hard and dedicated work of all the staff that implemented the intervention and evaluation components of the study.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

There is no funding to report.

Disclosure

The authors declare that they have no competing interests for this work.

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