

## Voiding Dysfunction/Female Urology

# Effect of Transurethral Resection With Hydrodistention for the Treatment of Ulcerative Interstitial Cystitis

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**Purpose:** Many treatment options to help relieve the symptoms of interstitial cystitis (IC) are available, but none are effective. Because no reports of transurethral ulcer resection with hydrodistention are available, we assessed the effects of such combined surgery for ulcerative IC.

**Materials and Methods:** Between June 2006 and June 2011, 87 female patients with IC who underwent transurethral resection with hydrodistention and were followed up for at least 12 months were included. Improvements in patients' voiding symptoms and pain were analyzed retrospectively by using a 3-day micturition chart and a 10-point visual analogue scale (VAS) before and after the operation. The global response assessment (GRA) was used to assess treatment satisfaction.

**Results:** The mean age of the 87 female patients was  $59.1 \pm 10.1$  years, and the mean follow-up period was  $26.7 \pm 14.4$  months. Mean maximum functional bladder capacity increased from  $168.4 \pm 92.4$  mL to  $276.3 \pm 105.4$  mL (1 month) and to  $227.3 \pm 91.7$  mL (12 months). The mean frequency of voiding decreased from  $17.2 \pm 8.5$  before to  $10.6 \pm 5.3$  after (1 month) surgery; however, it increased again to  $13.3 \pm 4.8$  at 12 months. The 10-point VAS score decreased from  $9.1 \pm 0.8$  to  $1.2 \pm 0.3$  (1 month); however, it increased again to  $2.5 \pm 0.4$  (3 months),  $3.2 \pm 0.4$  (6 months), and  $5.3 \pm 0.5$  (12 months) ( $p < 0.001$ ). Symptom improvement based on the GRA was observed in 83 of the 87 patients (95.4%) at 1 month and in 55 of 87 patients (63.2%) at 12 months.

**Conclusions:** Transurethral resection with hydrodistention is an effective treatment option for ulcerative IC because it provides improvements in voiding symptoms and pain.

**Keywords:** Interstitial cystitis; Treatment outcome

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## INTRODUCTION

Interstitial cystitis (IC) is a disease accompanied by voiding symptoms such as increased frequency, nocturia, and urgency as well as pain in the bladder. Because the clinical and physiological causes of IC are not clearly understood and no effective treatments have been developed, various therapies have been used to treat the condition. IC is categorized into ulcerative and nonulcerative types. The ulcerative type, with the classic Hunner ulcer, is associated with high levels of pain. Surgical treatment for the ulcerative type consists of bladder augmentation or replacement us-

ing the small intestine and transurethral endoscopic surgery, which preserves the bladder. Endoscopic treatments used for IC include transurethral ulcer resection and hydrodistention. Surgical therapy is attempted more frequently for ulcerative IC than for nonulcerative IC because conservative treatments including oral drug administration and intravesical drug instillation have a less marked effect at improving symptoms and increasing bladder capacity, which is reduced because of fibrosis of the surrounding tissues around the ulcer. The effects of ulcer resection by transurethral endoscopy were reported in the 1970s. Kerr reported improved symptoms after performing an ul-

cer resection in one patient in 1971 [1], and Greenberg et al. [2] reported improved symptoms and reduced recurrence using the same method for 28 patients in 1974. However, evaluation of the effects and risk factors of transurethral ulcer resection is difficult because few cases have been reported.

Hydrodistention is used to diagnose and treat patients with IC. Several reports of its use for the treatment, but not the diagnosis, of IC are available. In 1978, Sehn [3] performed hydrodistention in patients with IC and reported an improvement in symptoms. However, the effectiveness of hydrodistention treatment in patients with IC is controversial because of a variable success rate of 18% to 77% and the limited duration of its effects.

Because no reports of the simultaneous performance of both transurethral ulcer resection and hydrodistention are available, we investigated the effectiveness of this combined treatment at improving voiding symptoms, pain, and the quality of life of patients with ulcerative IC.

## MATERIALS AND METHODS

### 1. Patients

A total of 109 female patients with ulcerative IC underwent transurethral resection and hydrodistention simultaneously from June 2006 to June 2011. Ulcerative IC was confirmed by cystoscopy in the outpatient clinic. Of the 109 female patients, 87 (79.8%) with a greater than 12-month follow-up were included. Of the 87 female patients who underwent surgery, 64 (73.6%) received nonsurgical treatment in another hospital; 53 (60.9%) and 11 (16.1%) received oral and intravesical drug instillation, respectively. In 14 of the remaining 23 patients (16.1%), oral treatment (e.g., with pentosan polysulfate sodium [PPS] or amitriptyline) was performed first in our hospital, and 9 patients (10.3%) received surgical treatment immediately for multiple ulcer lesions and severe pain.

### 2. Preoperative evaluation

A medical history was recorded and a physical examination, which included urinalysis, urine culture, urine tuberculosis polymerase chain reaction, *Mycoplasma* culture, urine cytologic analysis, uroflowmetry, cystoscopy, a 3-day micturition chart, and a 10-point visual analogue scale (VAS), was performed preoperatively. Patients who previously underwent radiation treatment for cancer, previously underwent urological surgery, were incontinent, had a urinary tract infection within the past 3 months, or had bladder cancer or urinary stone disease were excluded from the study.

### 3. Surgical techniques

A resectoscope was used to perform a transurethral resection for ulcer lesions while the patient was under spinal or general anesthesia, and hydrodistention was then performed twice. Bleeding after transurethral resection was controlled by electrical cauterization before hydrodisten-

tion (Fig. 1). The continuous flow of the resectoscope was used to prevent excessive bladder filling and bladder rupture. In addition, only the bleeding site was treated locally to prevent bladder contracture during electric cauterization. For hydrodistention, a saline solution was instilled 80 cm above the location of the bladder after transurethral ulcer resection and cauterization, and the bladder was distended to 400–600 mL (mean:  $480 \pm 74.5$  mL first and  $530.6 \pm 70.3$  mL later) at a rate of 40 mL/min. After a waiting period of < 10 minutes, the operation was completed by removing the saline solution and inserting a urinary catheter.

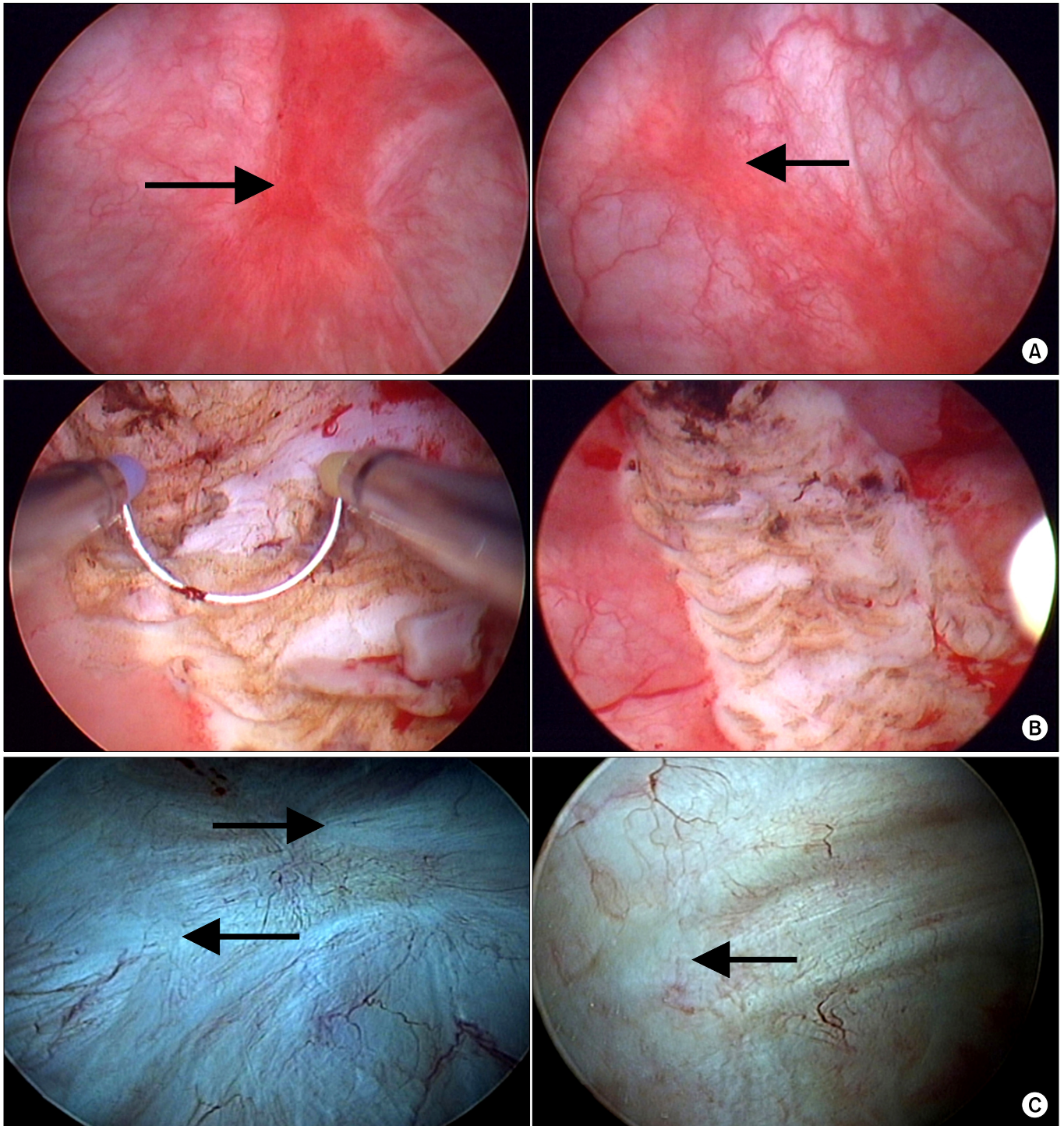
### 4. Postoperative follow-up

The patients completed the 3-day micturition chart and the GRA both before and 1 and 12 months after the operation. The 10-point VAS scale was assessed before and 1, 3, 6, and 12 months after the operation. The changes in maximum functional bladder capacity, in frequency of voiding, and in patient satisfaction from before to after the operation were determined and compared. The level of change in pain experienced by the patients was also assessed;  $p < 0.05$  (paired t test) was considered statistically significant. IBM SPSS ver. 18.0 (IBM Co., Armonk, NY, USA) was used for the statistical analysis. A score of -3 on the GRA was considered markedly worse, -2 moderately worse, -1 slightly worse, 0 no change, 1 slightly improved, 2 moderately improved, and 3 markedly improved. A score of 1 or greater indicated symptom improvement. A cystoscopy was performed 12 months after the operation to check for recurrence of ulcers.

## RESULTS

The mean age of the 87 female patients with ulcerative IC was  $59.1 \pm 10.1$  years, and the mean duration of follow-up was  $26.7 \pm 14.4$  months (range, 12 to 53 months). The mean duration of symptoms was  $30.6 \pm 23.7$  months. The mean number of ulcers on cystoscopy was  $4.2 \pm 1.8$ . On the 3-day micturition chart, the maximum functional bladder capacity before the operation was  $168.4 \pm 92.4$  mL, and the mean frequency of voiding was  $17.2 \pm 8.5$ . In addition, the mean 10-point VAS score before the operation was  $9.1 \pm 0.8$ , which indicated that patients were in severe pain (Table 1).

The 3-day micturition chart showed that the maximum functional bladder capacity increased from  $168.4 \pm 92.4$  mL before the operation to  $276.3 \pm 105.4$  mL at 1 month and to  $227.3 \pm 91.7$  mL at 12 months after the operation ( $p < 0.001$ ). The mean frequency of voiding decreased significantly from  $17.2 \pm 8.5$  before the operation to  $10.6 \pm 5.3$  at 1 month after the operation and to  $13.3 \pm 4.8$  at 12 months after the operation ( $p < 0.001$ ). Both the maximum functional bladder capacity and mean frequency of voiding improved after the operation, but the degree of improvement decreased over time (Table 2). The mean 10-point VAS score decreased significantly from  $9.1 \pm 0.8$  before the operation to



**FIG. 1.** Typical appearance of a bladder ulcer lesion before and after surgery. (A) Cystoscopic appearance of ulcerative interstitial cystitis (arrow: ulcer lesion). (B) Transurethral resection of ulcer lesion. (C) Cystoscopic appearance of ulcer lesion (arrow: scar formation) at 12-month follow-up.

$1.2 \pm 0.3$  at 1 month after the operation. The degree of pain increased gradually from  $2.5 \pm 0.4$  at 3 months after the operation to  $3.2 \pm 0.4$  at 6 months and to  $5.3 \pm 0.5$  at 12 months after the operation, but remained improved compared with before the operation (Fig. 2). The change in the 10-point VAS score at all time points before and after the operation

was significant. The mean score for all patients on the GRA at 1 month after the operation was  $2.1 \pm 0.9$ . A score of 1 was assigned by 9 patients (10.3%), 2 by 47 patients (54.0%), and 3 by 27 patients (31.0%), which indicated that symptoms improved in 83 patients (95.4%) with a score  $\geq 1$ . Two patients had no change in symptoms (score, -1), and another

er two had worse symptoms (score, -2). The mean GRA score for all patients 12 months after the operation was  $1.0 \pm 1.3$ . A score of 1 was assigned by 16 patients (18.4%), 2 by 31 patients (35.6%), and 3 by 8 patients (9.2%), which indicated that symptoms improved in 55 patients (63.2%). Twenty-six patients had no change, whereas six had worse symptoms (Table 3). No recurrence of ulcers was found in 36 patients (41.4%) by cystoscopy performed at 1 year; 10 of these patients remained in remission for up to 3 years with no symptoms. Recurrence of ulcers in new areas and in surgical margins was found in 35 patients (40.2%). Ulcers only in new areas were found in 9 patients (10.3%), and ulcers only in surgical margins were found in 7 patients (8.0%). Bladder perforation occurred in two patients intraoperatively, and bladder diverticulum was observed in three cases postoperatively.

## DISCUSSION

IC is a chronic disease, the etiology of which is unclear. Patients with IC typically complain about voiding symptoms, such as frequency and urgency, and pain in the lower abdomen when the bladder is full. IC was first defined by Hunner in the early 1900s; thus, the typical lesion detected by cystoscopy is called Hunner ulcer [4]. Hunner initially asserted that the best treatment for IC is partial cystectomy of the ulcer lesion by opening the abdomen [5]. However, this method does not result in a good long-term treatment outcomes; therefore, many physicians have opposed its use [6,7]. Subsequently, a variety of therapeutic approaches have been attempted, including oral drug ad-

ministration, intravesical drug instillation, and surgical treatment [8]; however, no effective treatment has yet been developed. Fall et al. [9] analyzed and reported the evidence level and recommendation grade of various treatment methods in an IC study published between 2003 and 2007 [9]. According to this study, oral administration of PPS, amitriptyline, hydroxyzine, and cyclosporine A had a recommendation grade of A based on clinical studies of good quality and consistency that included at least one randomized trial. Intravesical instillation of PPS and dimethyl sulfoxide were the A-grade treatment recommendations. The evidence level for surgical treatment could not be determined, because a randomized controlled clinical trial of both transurethral ulcer resection and cauterization could not be conducted because of ethical issues. However, these two methods have been described to have a treatment recommendation grade of A/B, which indicates well-conducted clinical studies with or without randomized trials. Hydrodistention was reported to have a treatment recommendation grade of C; i.e., no experimental studies or applicable clinical studies of good quality were available [9].

Surgical treatment is categorized as open surgery (e.g., bladder augmentation and bladder replacement using the small intestine) and endoscopic surgery. The success rate of ileocystoplasty ranges from 25% to 100%, but few cases have been reported and long-term follow-up is rare [10,11]. However, restoration of normal urination after this type of surgery can be problematic, and it can cause dysuria seri-

**TABLE 1.** Baseline characteristics of female patients undergoing transurethral ulcer resection with hydrodistention

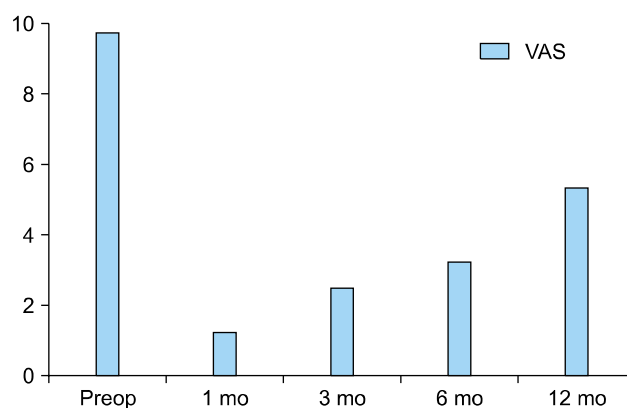
Parameter	Value
Age (y)	$59.1 \pm 10.1$
Follow-up period (mo)	$26.7 \pm 14.4$ (12-53)
Ulcers	$4.2 \pm 1.8$
Maximum FBC (mL)	$168.4 \pm 92.4$
Frequency	$17.2 \pm 8.5$
10-Point VAS	$9.1 \pm 0.8$
Symptom duration (mo)	$30.6 \pm 23.7$

Values are presented as mean  $\pm$  standard deviation (range). Maximum FBC, maximum functional bladder capacity; VAS, visual analogue scale.

**TABLE 2.** Paired outcome results of posttransurethral ulcer resection with hydrodistention

Parameter	Initial	1 Month (n=87)	12 Months (n=87)	p-value
Maximum FBC (mL)	$168.4 \pm 92.4$	$276.3 \pm 105.4$	$227.3 \pm 91.7$	< 0.001
Frequency	$17.2 \pm 8.5$	$10.6 \pm 5.3$	$13.3 \pm 4.8$	< 0.001
10-Point VAS	$9.1 \pm 0.8$	$1.2 \pm 0.3$	$5.3 \pm 0.5$	< 0.001

Values are presented as mean  $\pm$  standard deviation. Maximum FBC, maximum functional bladder capacity; VAS, visual analogue scale.



**FIG. 2.** Changes in 10-point visual analogue scale (VAS) scores after transurethral ulcer resection with hydrodistention. Preop, preoperation.

**TABLE 3.** Changes in the global response assessment (GRA) score after transurethral ulcer resection with hydrodistention

Postoperation	GRA							Total	Mean±SD
	-3	-2	-1	0	1	2	3		
1 Month (n)	0	1	1	2	9	47	27	87	2.1±0.9
12 Months (n)	2	3	1	26	16	31	8	87	1.0±1.3

SD, standard deviation.

-3, markedly worse; -2, moderately worse; -1, slightly worse; 0, no change; 1, slightly improved; 2, moderately improved; 3, markedly improved.

ous enough to require self-catheterization [12]. Cystectomy with an ileal conduit and continent diversion is considered a “last resort” when other treatments fail [13]. Thus, it is recommended that patients seriously consider alternative treatments.

Transurethral surgery, laser resection using cystoscopy, and therapeutic hydrodistention have been reported to preserve the bladder. Peeker et al. [14] performed transurethral ulcer resection in 103 patients with IC and reported symptom improvement in approximately 90% of these patients. In that study, remission was defined as no symptoms for > 3 years on average, and remission was achieved in 40 patients (38.9%). This study was the result of follow-up in the majority of subjects in the analysis, the findings of which were consistent with those of a previous small-scale study of transurethral ulcer resection in patients with IC [1,2]. However, bladder contracture occurred after transurethral ulcer resection in 22 patients (21.4%), of whom 14 (63.6%) experienced bladder contracture within 2 years [14]. Thus, bladder contracture is caused by fibrosis of bladder tissue, and transurethral ulcer resection may be a risk factor, although it is unclear whether bladder contracture is caused by disease progression or is a result of transurethral ulcer resection. Little information is available about bladder perforation or bladder diverticulum as side effects of transurethral resection for ulcerative IC; however, it is believed that excessive resection can lead to such complications. In this study, bladder perforation occurred in two patients and bladder diverticulum occurred in three patients, in whom resection was deep and functional bladder capacity was < 200 mL because of fibrosis. Thus, caution should be exercised when resecting ulcers around the bladder dome site or the ureteral orifice, where the bladder capacity is small. Both patients who experienced bladder perforation were treated only with Foley catheters.

Rofeim et al. [15] performed ulcer resection using a neodymium-doped yttrium aluminum garnet laser in 24 patients with IC. Symptoms remained improved for approximately 19 months in 13 patients (54%), and symptoms recurred in 11 patients (46%) after an average of < 8 months.

The treatment effect is believed to be due to removal of ulcers using transurethral endoscopy or a laser. The mechanism of action has not been determined, but Fall [16] argues that transurethral ulcer resection improves the symp-

toms of patients with IC by removing nerve terminals activated during the inflammatory response. Thus, complete removal of the ulcerative lesion enhances the effect of transurethral ulcer resection. However, identification of the border before removal of the ulcers is difficult. When checking the resectoscope to identify ulcerative lesions, it is also difficult to clearly identify the border of an ulcer because of bleeding in the ulcer lesion and bladder mucosa from bladder filling.

Electric cauterization and resection are the two methods available for ulcer removal. Generally, ulcers are distributed widely when they are in the acute phase, which makes complete resection problematic. In such cases, cauterization is performed, which can result in ulcer remnants as a result of incomplete resection. Nevertheless, Payne et al. [17] reported that 4 of 14 patients with ulcerative IC who underwent transurethral resection experienced recurrence of symptoms, but symptoms improved in all 4 patients after resection of the recurrent lesions. Thus, complete resection of ulcers is important to prevent recurrence of ulcerative IC. Regular follow-up and a cystoscopy to excise ulcers are recommended if symptoms are present.

Besides transurethral ulcer resection, some studies have performed hydrodistention to improve symptoms of ulcerative IC. Animal experiments indicate that hydrodistention causes damage to submucosal nerves and improves symptoms, such as pain and frequency of voiding [18]. According to Kim et al. [19], hydrodistention in patients with IC relieves pain for about 4.4 months, which is consistent with the results of a study on hydrodistention by Ottem and Teichman [20]. In addition, Propert et al. [21] and Sant and LaRock [22] reported that only 20% of patients experience symptom improvement for an average of 6 months after a single hydrodistention procedure. Thus, one hydrodistention treatment in patients with IC is limited in its effect on long-term pain relief and efficacy.

As a bladder-preserving surgery for ulcerative IC, transurethral ulcer resection has the disadvantage of recurrence of ulcers and bladder contracture due to fibrosis of bladder tissues, whereas hydrodistention is limited in terms of the duration of symptom improvement. Therefore, we perform transurethral ulcer resection for long-term symptom improvement in patients with ulcerative IC and secondarily perform hydrodistention to prevent bladder contracture caused by transurethral ulcer resection, to ex-

pand the existing functional bladder capacity, and to relieve pain. During transurethral ulcer resection, excessive bladder filling and bladder perforation are prevented by maintaining continuous flow, and the bleeding site is cauterized only locally to prevent bladder contracture during electric cauterization. Maintaining continuous flow helps to secure the sight during surgery and facilitates complete resection of ulcers by reducing bleeding in the ulcer lesions. Because hydrodistention at high pressure (>80–100 cmH<sub>2</sub>O) and of long duration (>10 minutes) has no advantages, it is generally performed at 80 cmH<sub>2</sub>O for <10 minutes [23,24]. We perform transurethral ulcer resection and hydrodistention simultaneously to compensate for the drawbacks of each method. In this study, 87 patients were followed up for a mean of 26.7±14.4 months (range, 12–53 months). The mean maximum functional bladder capacity, the mean frequency, and the mean VAS scores were improved 1 year after treatment. No ulcers recurred for at least 1 year in 36 patients (41.4%), 10 of whom (27.8%) remained in remission for 3 years. A diagnostic method that identifies lesions by overfilling the bladder is occasionally used in patients with ulcerative IC, but the surgical approach can be difficult as a result of excessive bleeding in the ulcer lesion. Thus, it is important to not overfill the bladder during transurethral ulcer resection and to perform a complete resection to prevent lesion recurrence.

Peeker et al. [14] reported that the remission (≥3 years) rate after transurethral resection for ulcerative IC was 34.5%. In our study, the remission (≥1 year) rate after combination treatment for IC was 41.4%. The duration of follow-up in these two retrospective studies differed, but we believe that this study showed good efficacy of combination treatment. A limitation of our study was the absence of direct control groups, such as patients who underwent single hydrodistention or transurethral ulcer resection. However, we conducted a new trial of treatment for ulcerative IC and were able to indirectly compare outcomes of single endoscopic surgery with combination therapy in other reports. A prospective controlled study that includes long-term follow-up of randomized subjects is needed to confirm our findings and to establish the overall efficacy of transurethral ulcer resection in combination with hydrodistention for the treatment of ulcerative IC, which will facilitate the development of internationally standardized surgical methods.

## CONCLUSIONS

Our findings indicate that simultaneous transurethral ulcer resection and hydrodistention as bladder-preservation surgery without opening the bladder increased the functional maximum bladder capacity and reduced the frequency of voiding and pain. With regard to ulcerative IC, for which no effective treatment is yet available and the treatment success rate is low, transurethral ulcer resection in combination with hydrodistention may be an effective therapeutic alternative, not only to relieve pain but

also to improve voiding symptoms.

## CONFLICTS OF INTEREST

The authors have nothing to disclose.

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