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Diagnostic and therapeutic efficacy of urinary bladder hydrodistension in patients with bladder pain syndrome

Dijagnostička i terapijska efikasnost hidrodistenzije mokraćne bešike kod bolesnika sa sindromom bolne bešike

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Abstract

Background/Aim. Interstitial cystitis (IC)/bladder pain syndrome (BPS) is a condition with recurring discomfort or pain in the urinary bladder and the surrounding pelvic region without an identifiable disease. The aim of this study was to assess hydrodistension as a diagnostic and treatment procedure in patients with BPS. **Methods.** This prospective study included 45 patients who underwent cystoscopy with hydrodistension. The mean values for 24-hr voiding frequency, maximal voided urine volume, average voided urine volume, and minimal voided urine volume originated from the frequency volume chart. The values were compared between the time before hydrodistension and one, three, and six months after that. **Results.** By comparing the initial data and data in all three follow-up periods (after one, three, and six months), the statistical significance ($p < 0.046$) was found, and that: for 24-hr voiding frequency, it was 19.64 ± 3.56, 9.42 ± 1.71, 9.58 ± 1.45, and 12.2 ± 2.79, respectively; then, for the minimal voided urine volume ($p < 0.03$), it was 59.11 ± 23.72 mL, 114.89 ± 4.09 mL, 112.44 ± 100.86 mL, and 89.00 ± 29.45 mL, respectively; for an average voided volume ($p < 0.04$), it was 105.33 ± 18.29 mL, 186.89 ± 23.14 mL, 186.44 ± 21.44 mL, and 155.78 ± 30.78 mL, respectively. There was no significant statistical difference ($p < 0.1$) regarding the maximal voided urine volume between initial and follow-up interval data: 196.89 ± 43.68 mL, 312.89 ± 54.59 mL, 316.00 ± 49.47 mL, 266.67 ± 53.17 mL, respectively. **Conclusion.** Our results demonstrate that hydrodistension is a reliable diagnostic and therapeutic procedure.

Key words:
cystitis, interstitial; cystoscopy; diagnosis; treatment outcome; urinary bladder; urination disorders; urine.

Apstrakt

Uvod/Cilj. Intersticijski cistitis (IC)/sindrom bolne bešike (SBB) je stanje ponavljajuće nelagodnosti ili bola u mokraćnoj bešici i okolnom karličnom regionu bez prepoznatljive bolesti. Cilj rada bio je da se kod bolesnika sa SBB proceni značaj hidrodistenzije kao dijagnostičke i terapijske procedure. **Metode.** Prospektivnom studijom obuhvaćeno je ukupno 45 bolesnika podvrgnutih cistoskopiji sa hidrodistenzijom. Srednje vrednosti za parametre učestalost 24-časovnog mokrenja, zapremina maksimalno izmokrenog urina, zapremina prosečno izmokrenog urina i zapremina minimalno izmokrenog urina dobijene su iz „dnevnika mokrenja“. Ove vrednosti su upoređivane između vremena pre hidrodistenzije i jedan, tri i šest meseci posle toga. **Rezultati**. Poređenjem početnih podataka i podataka iz sva tri perioda praćenja (posle jedan, tri i šest meseci) utvrđena je statistički značajna razlika ($p < 0,046$), i to: za 24-časovnu učestalost mokrenja, bila je 19,64 ± 3,56, 9,42 ± 1,71, 9,58 ± 1,45 i 12,2 ± 2,79, redom; zatim, za minimalnu zapreminu urina ($p < 0,03$), bila je 59,11 ± 23,72 mL, 114,89 ± 4,09 mL, 112,44 ± 100,86 mL i 89,00 ± 29,45 mL, redom; za prosečnu zapreminu mokrenja ($p < 0,04$), bila je 105,33 ± 18,29 mL, 186,89 ± 23,14 mL, 186,44 ± 21,44 mL i 155,78 ± 30,78 mL, redom. Nije bilo statistički značajne razlike ($p < 0,1$) za vrednosti maksimalne zapremine izmokrenog urina između početnih i kontrolnih intervala: 196,89 ± 43,68 mL, 312,89 ± 54,59 mL, 316,00 ± 49,47 mL, 266,67 ± 53,17 mL, redom. **Zaključak.** Rezultati našeg istraživanja ukazuju na to da je hidrodistenzija pouzdana dijagnostička i terapijska procedura.

Ključne reči:
cistitis, intersticijalni; cistoskopija; dijagnoza; lečenje, ishod; mokraćna bešika; mokrenje, poremećaji; mokraća.

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Introduction

In the past, due to the absence of a commonly accepted definition for the condition affecting urinary bladder, confusion arose in defining and understanding patients' complaints. In 1808, Philip Syng Physick, a pioneer in medicine, was the first to mention bladder pain syndrome (BPS). This condition remained unnamed until 1987 when the National Institute for Diabetes and Digestive and Kidney Diseases introduced the term interstitial cystitis (IC) [1, 2].

In 2002, painful bladder syndrome (PBS)/BPS was defined by the International Continence Society (ICS) as "the complaint of suprapubic pain related to bladder filling, accompanied by other symptoms such as increased daytime and nighttime frequency, in the absence of proven urinary infection or other obvious pathology" [3]. Additionally, the European Society for the Study of IC/BPS (ESSIC) and its definition were incorporated in the nomenclature proposed by the International Consultation on Incontinence in 2010 [4, 5].

The estimated prevalence of BPS adds up to 0.06–20.0%, with a female predominance of 10 : 1 [6]. This discrepancy in available data can be explained by the fact that diagnosis of BPS is mainly determined by a reverse process of eliminating confusable diseases and excluding criteria and diagnostic procedures. Hydrodistension, initially reported by Bumpus [7] in 1930 and followed by Hand [8] in 1949, is widely accepted as a diagnostics tool included in guideline algorithms presented by relevant associations involved in treating BPS [4, 6, 9–11]. Besides that, hydrodistension is also performed as a treatment in managing BPS, which is of increased significance since other treatment options are often unavailable [12]. The aim of this study was to analyze the results of hydrodistension in 45 examined patients with BPS by determining the efficacy of hydrodistension as a diagnostic and therapeutic procedure.

Methods

Patients

This prospective study included 45 patients who underwent cystoscopy with hydrodistension as a diagnostic and treatment procedure for BPS at the Clinic for Urology, Military Medical Academy, Belgrade, Serbia, from April 2013 to January 2018. The study was conducted according to the Declaration of Helsinki and the protocol was approved by the local Ethics Committee. All patients signed a consent form.

Patients with a history of chronic pelvic pain (discomfort, pressure, burning sensation) in a period longer than six months, accompanied by bladder filling and an urge to void or increased frequency of urination were enrolled. The preoperative evaluation consisted of previous medical history, clinical examination, urine and urine culture analyses, abdomen and pelvis minor ultrasound with post-void residual urine measurement, as well as a 72-hr frequency volume chart (FVC).

Hydrodistension procedure

The cystoscopy with hydrodistension was carried out in an inpatient setting under general anesthesia. This low-pressure, short-duration hydrodistension is one of the most common treatments in BPS. Prior to the procedure, all patients were administered a single-dose antibiotic prophylaxis. They were placed in a dorsal lithotomy position. The bladder was filled through a 26 French (Fr) size electro resectoscope with 30° Hopkins® optic, using urologic irrigating solutions containing sorbitol (27 g/L) and mannitol (5.4 g/L) with an infusion height of 80 cm above the symphysis level (80 cm H_2O) without any additional pressure applied. The electroresectoscope was used for better visibility and less leakage during the procedure. The filling was terminated when the bladder capacity of 500 mL of the irrigating solution was achieved or when visible leakage occurred around the cystoscope. This was maintained for around 3 min, and the bladder was drained by assessing the bleeding through the color of the irrigation fluid. The volume of the drained fluid was measured, and the maximal bladder capacity was presented. Following the hydrodistension, the bladder was filled again to around two-thirds of its capacity for optimal vision and inspection of the bladder mucosae (anterior, posterior, lateral bladder walls and base of the bladder) to visualize the presence of glomerulations or even Hunner's ulcer. Glomerulations are commonly defined as small submucosal hemorrhages or petechial bladder bleedings. Hunner's lesion, previously known as Hunner's ulcer, represents a localized hyperemic part of the bladder mucosae and submucosae with central scaring surrounded by tiny blood vessels in a radiated fashion. It can be seen following cystoscopy with hydrodistension. Cystoscopic findings were classified as grade 0 – normal mucosa; grade I – petechiae in at least two quadrants; grade II – considerable submucosal bleeding (ecchymosis); grade III – diffuse global mucosal bleeding; grade IV – mucosal disruption, with or without bleeding/oedema. According to the ESSIC group classification, different types of BPS are defined. BPS types are defined using two symbols. The first one represents cystoscopic findings (1 – normal; 2 – glomerulations grade II or III; 3 – Hunner's lesion with or without glomerulations), while the second stands for the biopsy results (X – not performed; A – normal; B – inconclusive; C – inflammatory infiltrates). Our study defined BPS types as 1X, 2X, and 3X since no biopsy was performed during the cystoscopy and hydrodistension. An indwelling urinary catheter 16 Fr was left overnight, and all patients were discharged the following day.

The evaluation following cystoscopy with hydrodistension was conducted in an outpatient setting for one, three, and six months, respectively. This assessment included a urine culture and a 72-hr FVC, intended to record the volumes voided (VV), as well as the time of each visit to the toilet, both during the day and night. It aimed to determine the therapeutic effect of hydrodistension by analyzing FVC parameters. We examined the voiding frequency, as well as minimal, average, and maximal VV. These parameters were

then compared with the ones from FVC before hydrodistension.

Prior to the cystoscopy with hydrodistension, all patients were given detailed instructions about the procedure itself and what was planned to be performed.

Statistical analysis

Descriptive statistics, including mean, standard deviation, and median, were calculated for each variable using Statistical Package for the Social Sciences (SPSS) version 29.0 with significance set at $\alpha = 0.05$. The normality of the data distribution was assessed using the Kolmogorov-Smirnov test implemented in SPSS. We applied the Friedman test to compare multiple related samples, and the Wilcoxon signed-rank test was performed for pairwise comparisons between associated samples. Differences between independent samples were assessed using the Mann-Whitney *U* test in SPSS. The Chi-square test (χ^2) was utilized to analyze categorical variables, with the likelihood ratio employed to assess goodness-of-fit. The Spearman correlation coefficient was computed to examine the relationship between non-normally distributed variables. Factor analysis with varimax rotation was performed to explore underlying patterns or dimensions within the dataset. The value of $p < 0.05$ was considered significant for all tests.

Results

The study included 45 patients. The average age was 57.78 (29–82) years. The baseline patient characteristics are presented in Table 1. Out of the 45 monitored patients, 40 (88.8%) were female and 5 (11.2%) were male. According to the ESSIC group classification of BPS, 2 (4.4%) patients were marked as type 1X, 41 (91.2%) as 2X, and 2 (4.4%) patients as 3X (Table 1, Figure 1).

Table 1

Demographic characteristics of the patients with BPS and their grades of BPS including the ESSIC dysfunction without biopsy

Parameters	Values
Age, years	57.78 (29–82)
Gender	
female	40 (88.8)
male	5 (11.2)
ESSIC classification	
1X	2 (4.4)
2X	41 (91.2)
3X	2 (4.4)

BPS – bladder pain syndrome; ESSIC – European Society Study of Interstitial Cystitis.
1X – normal without glomerulations; 2X – 2- and 3-grade glomerulations; 3X – Hunner's ulcers.
All values are given as numbers (percentages) except age which is given as median (range).

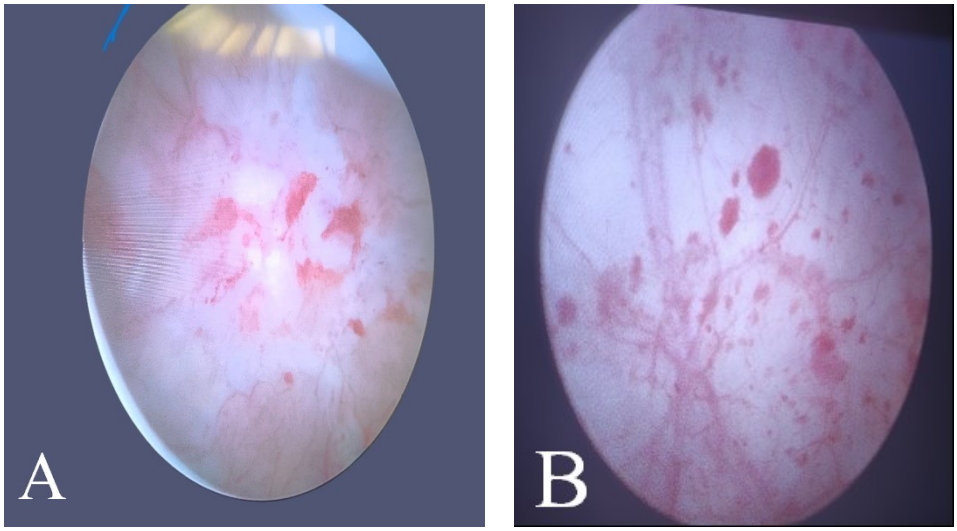

Fig. 1 – Cystoscopic findings of two patients that were marked as 3X according to the criteria of the European Society for Study of Interstitial Cystitis group classification of bladder pain syndrome (without biopsy performed show); A) Hunner's ulcer; B) grade 2 glomerulations.

FVC parameters, including the preoperative assessment and follow-up intervals, are presented in Table 2. The statistical analysis has reiterated a statistical significance ($p < 0.05$) by comparing the initial frequency and the frequency in all three follow-up periods (Table 2, Figure 2). The same has been confirmed when contrasted with minimal VV and the same parameter in all three follow-up periods (Figure 3). Comparison of the initial average VV with the same FVC parameters at one, three, and six months confirmed the statistical significance (Figure 4). However, no statistical difference was found when comparing the initial maximal FVC VV with the same parameter in the follow-up intervals (Figure 5).

Table 2

Frequency volume chart (FVC) parameters of examined patients with bladder pain syndrome

Parameters	Initial	Follow-up (months)			
		1	3	6	*p*-values
Frequency (24 hrs)	19.64 ± 3.56	9.42 ± 1.71	9.58 ± 1.45	12.2 ± 2.79	< 0.046
Maximal VV (mL)	196.89 ± 43.68	312.89 ± 54.59	316.00 ± 49.47	266.67 ± 53.17	< 0.100
Average VV (mL)	105.33 ± 18.29	186.89 ± 23.14	186.44 ± 21.44	155.78 ± 30.78	< 0.040
Minimal VV (mL)	59.11 ± 23.72	114.89 ± 4.09	112.44 ± 100.86	89.00 ± 29.45	< 0.030

VV – voided volume. All values are given as mean ± standard deviation.
Note: initial means before hydrodistension.

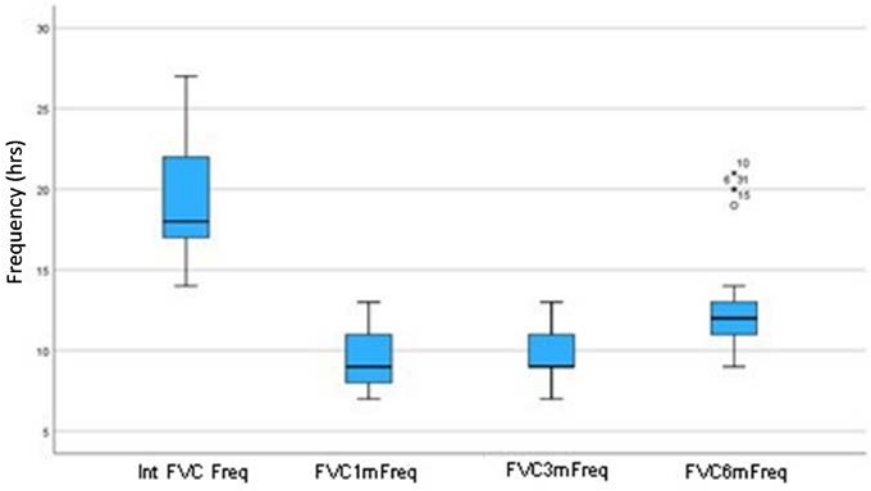

Fig. 2 – Frequency volume chart – 24-hr frequency.
Int – initial; Freq – frequency; m – months.
Note: The numbers above the 6-month value indicate the number of patients whose monitored values individually deviated from the range.

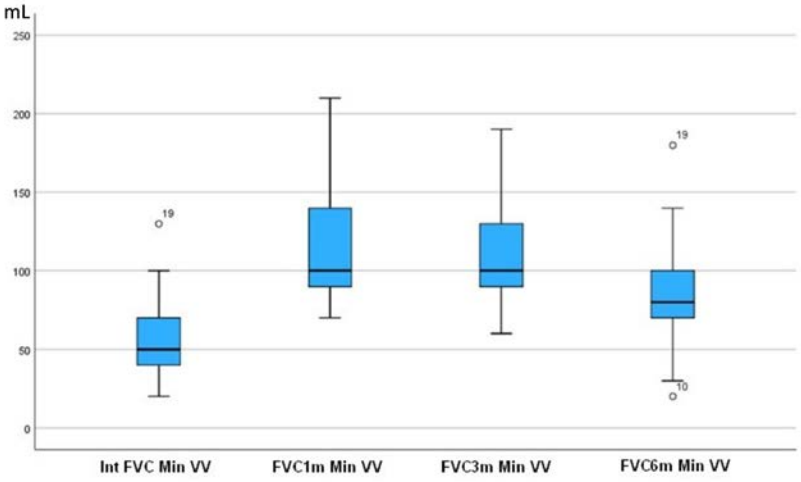

Fig. 3 – Frequency volume chart (FVC) – minimal voided volume (Min VV).
Int – initial; Freq – frequency; m – months.
Note: The numbers above the initial value and above and below 6-month value indicate the number of patients whose monitored values individually deviated from the range.

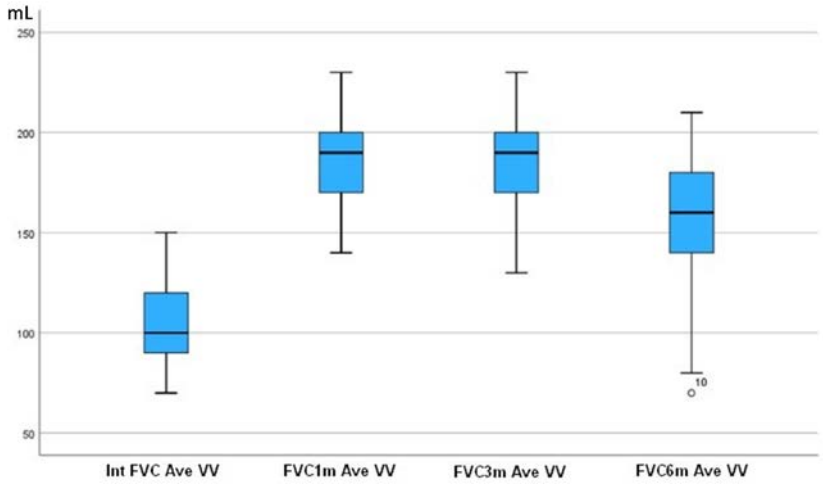

Fig. 4 – Frequency volume chart (FVC) – average voided volume (Ave VV).
Int – initial; Freq – frequency; m – months.
Note: The number below 6-month value indicates the number of patients whose monitored values individually deviated from the range.

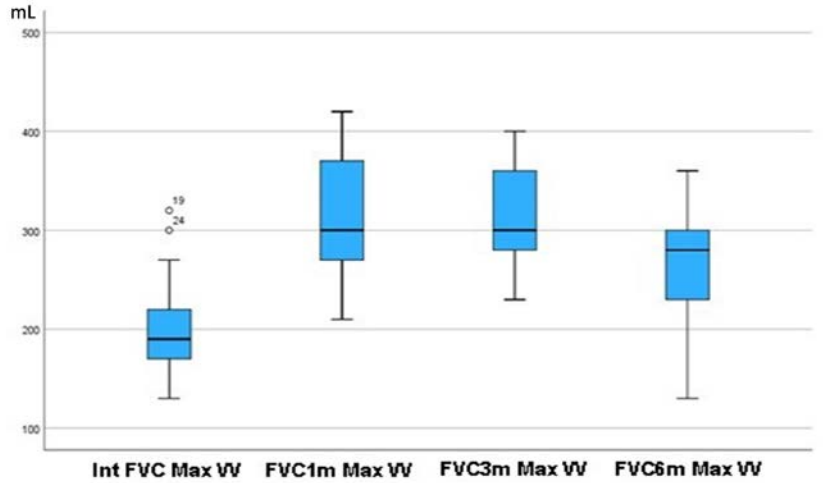

Fig. 5 – Frequency volume chart (FVC) – maximal voided volume (Max VV).
Int – initial; Freq – frequency; m – months.
Note: The numbers above the initial value indicate the number of patients whose monitored values individually deviated from the range.

In the monitored group of patients, symptoms failed to improve in all monitored follow-up intervals, in two patients with 1X and six patients with 2X following hydrodistension. Therefore, the treatment outcome by hydrodistension was favorable in 37 (82.22 %) patients in the first two periods. Eight more patients suffered from an unfavorable increase in symptoms after six months. The overall positive treatment outcome was favorable in 29 (64.44 %) patients at the end of the monitored intervals.

Discussion

BPS/PBS/IC is a chronic condition that may significantly impact patients' quality of life. BPS is a clinical diagnosis pertaining to pain symptoms in the bladder and pelvis, including other predominant urinary symptoms such as urgency and frequency. As previously mentioned, hydrodistension is broadly accepted as a diagnostics tool incorporated in guideline algorithms presented by relevant associations. According to the ESSIC criteria, evidence of positive signs of hydrodistension at cystoscopy is a prerequisite for diagnosing BPS [4].

Hydrodistension itself can be performed with or without concomitant bladder biopsies. The guidelines view this issue differently, including the necessity of performing them. It should be noted that bladder biopsies have not been routinely performed in the United States of America. Consequently, we have aligned with that view [9]. Therefore, we tend to perform hydrodistension as a single diagnostic procedure without concurrent biopsies. There is no difference in the baseline demographics in our study compared to the published data. This applies to the female/male ratio. According to the ESSIC criteria in our research, 41 (91.2%) diagnosed patients had 2X (2- and 3-grade glomerulations), 2 (4.4%) had

1X (normal without glomerulations), and 2 (4.4%) had visible Hunner's ulcers during hydrodistension. Besides visible glomerulations or Hunner's ulcers, mucosal bleeding after distension could be seen [13]. By definition, Hunner's ulcers were first reported by Guy L. Hunner [14] in 1915 as single or multiple erythematous mucosal patches, often accompanied by small vessels in a radiating fashion surrounding a central scar. According to current guidelines, fulguration is one of the treatment options for resolving Hunner's ulcers that are refractory to treatment by intravesical instillation solutions. These guidelines propose level of evidence C recommendation ("well-conducted case-control cohort studies with a low risk of bias and a moderate probability that the relationship is causal") or fulguration in instances with visible Hunner's ulcers at hydrodistension [15]. We have, therefore, conducted fulguration in all our patients with registered Hunner's ulcer lesions during cystoscopy with hydrodistensions.

The underlying principles for patients with BPS imply a decrease in their debilitating symptoms, improving their quality of life, and encouraging realistic patient expectations. Optimal management should involve multimodal behavioral, physical, and psychological techniques and proceed stepwise, starting with the most conservative one. Different grades of recommendation for all treatments of bladder hydrodistension and transurethral fulguration of Hunner's lesions have been discussed as the third-line option for treating BPS following the failure of the second-line therapies [10].

Having said this, we ought to emphasize that most patients were referred to our hospital without a defined condition. However, they were treated using the first- and second-line options without significant improvements. Different means can be used to assess symptoms before and following hydrodistension, such as validated symptom scores, O'Leary-Sant IC Symptom Index and the IC Problem Index and the Pelvic Pain and Urgency/Frequency Scale [16].

One of the available assessment tools is FVC, which evaluates the overall frequency, minimal, average, and maximal VV in 24 hrs. BPS patients typically have lower VV and higher voiding frequency than asymptomatic patients. Therefore, using an FVC is recommended for the initial evaluation. The recommended FVC is a three-day (72 hrs) FVC and we decided to apply it in our study. ICS defines median functional bladder capacity as the median maximum VV in everyday activities (as *per* FVC) [12, 17]. The initial frequency in our study was consistent with published data. Following hydrodistension, there is a significant decrease in frequency in all three monitored intervals, especially after one and three months. Regarding average FVC VV, there was a substantial increase in volume in all post-hydrodistension analyzed intervals ($p < 0.04$). The same was confirmed by comparing the initial and post-hydrodistension minimal FVC VV in all follow-up intervals ($p < 0.03$). No statistical significance was determined when comparing the initial maximal VV with values registered in the follow-up periods.

Since the symptoms failed to improve in all monitored follow-up intervals, the treatment outcome by hydrodistension was favorable in 37 (82.22%) patients in the first two periods. After six months, even eight more patients had additional symptoms. The overall positive treatment outcome was favorable in 29 (64.44%) patients at the end of the monitored intervals. This is higher than in available published data where a decrease in symptoms at three months following hydrodistension is registered in 53.8% of patients and in 25% of them at six months [18, 19].

Conclusion

Our results conclude that hydrodistension is a straightforward, broadly accepted, safe diagnostics procedure with low complication rates. Additionally, it is a therapeutic procedure providing significant symptomatic relief, with the possibility of repetition, should it be needed. Together, these results help reiterate/confirm that hydrodistension is a valuable diagnostic and therapeutic procedure with significant benefits for patients with severe BPS/PBS/IC. Unfortunately, the predictors of symptom response to hydrodistension have not been clearly identified. Our study considered some aspects of hydrodistension as a diagnostic and therapeutic procedure for the management of BPS/PBS/IC. Our ongoing research will enable us as providers to identify patients who are most likely to benefit from the procedure and potentially improve the treatment outcomes in those patients who suffer from this debilitating condition.

Conflict of interest

The authors declare no conflict of interest that could influence the work reported in this paper.

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