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ORIGINAL ARTICLE

Long-term follow-up after cystectomy for bladder pain syndrome: pain status, sexual function and quality of life

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Abstract

Purpose To assess the long-term complications, pain status, sexual function and quality of life after cystectomy for bladder pain syndrome (BPS).

Methods We retrospectively reviewed functional variables for 35 patients (34 women/1 man, 67 ± 9 years old) who underwent cystectomy due to BPS since 1993 in our department. Cystectomy was offered to patients with BPS refractory to conservative treatments. Six cystectomies with ileal conduit (17.1%) and 29 supratrigonal cystectomies with enterocystoplasty (82.9%) were performed. Prospectively, patients completed questionnaires on pain [BPIC-SS, visual analogue scale (VAS) for pain], health-related quality of life (EQ-5D) and sexual function (FSFI; 2–36), rated satisfaction with surgery (0–10) and reported whether they would undergo the same surgery again.

Results Mean follow-up was 107 ± 83 months. In two (5.7%) patients, pain persisted and in one patient (2.8%) pain recurred after 20 months. Significant improvements in daytime and nighttime frequency and bladder capacity were observed postoperatively. 21 patients completed questionnaires. Mean BPIC-SS was 7.5 ± 8.4, mean VAS score 2.5 ± 2.8. 14 (66.7%) patients reported no problems related to pain on the EQ-5D, similar to our regional reference population. 13 (61.9%) patients had sexual intercourse after surgery, ten of them without pain. Mean FSFI score was 9.5 ± 9. Satisfaction with surgery was 8.8 ± 1.7 and 20 (95.2%) patients would undergo the same surgery again.

Conclusion Pain persistence or recurrence after cystectomy for BPS is infrequent. Quality of life related to pain is similar to that in the general population and patients can resume sexual activity without pain.

Keywords Pelvic pain · Cystitis · Interstitial · Cystectomy · Quality of life

Introduction

Bladder pain syndrome (BPS) is the occurrence of persistent pain perceived to be related to the bladder, accompanied by other urinary symptoms, when other confusable diseases are excluded [1]. BPS represents a debilitating disease which affects mental health and quality of life [2], disrupts the patient's patterns of social and sexual behaviour and requires treatment during the patient's lifetime [3].

Most treatments focus on reducing BPS symptoms, starting with conservative measures such as dietary changes, oral agents or intravesical instillations [4]. However, the therapeutic response to such treatments is often brief, relapse is common, and some patients develop refractory symptoms [5], for which a surgical approach is the only option. Approximately, 10% of patients with BPS are candidates for surgical treatment [6]. Reconstructive surgeries are used as

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the last resort because of their invasiveness and irreversibility. Supratrigonal cystectomy followed by enterocystoplasty (SC-EC) represents the most favoured continence-preserving technique: it has been shown to be effective in terms of pain relief [7] and is the most widely used reconstructive procedure. However, long-term follow-up reports on the outcomes of reconstructive surgeries regarding not only pain relief but also sexuality and quality of life are lacking. Our aim was to assess the long-term functional results, pain status, sexuality and quality of life after cystectomy for refractory BPS.

Materials and methods

We retrospectively assessed the clinical records of patients who had undergone a reconstructive surgery for refractory BPS since 1993 in our department. BPS was considered in patients with persistent pain, pressure or discomfort perceived to be related to the bladder, accompanied by other urinary symptoms such as persistent urge to void or frequency when a urinary tract infection and other confusable diseases had been excluded [1]. Diagnostic assessment included a medical history and physical examination with particular attention to transvaginal palpation of the bladder trigone and pelvic muscles to rule out pelvic floor muscle dysfunction (myofascial pain) [8], urine analysis, bladder diary, urodynamics and cystoscopy under anaesthesia with bladder biopsy. Reconstructive surgery was offered to BPS patients with a positive biopsy according to the ESSIC criteria [1] when conservative treatments had failed. Conservative treatments included oral analgesic drugs (gabapentin, pregabalin) and pentosan polysulfate sodium as first-line treatments, intravesical instilations (dimethyl sulfoxide, hyaluronic acid) as second-line treatments, and bladder hydrodistension, intradetrusor botulinum toxin injection or Hunner's ulcer (HU) transurethral ressection as third-line treatments. Moreover, all related risks and benefits of the surgery, including the possibility of pain persistence or recurrence, the irreversibility of the procedure and the risk of complications, were extendedly discussed with the patient. Oral analgesics were maintained until the time of surgery and then gradually withdrawn. Surgery consisted in SC-EC with ileum except in patients proven to be incapable of performing bladder self-catheterisation, when a cystectomy with ileal conduit (C-IC) was preferred. All surgeries were conducted through an open approach and were performed by the same two specialized urologists (CE, CG). Supratrigonal cystectomy consisted in an excision of the bladder wall leaving in situ the minimum amount possible of bladder mucosa in the bladder neck and around the trigonal area. The neobladder was conducted in a Studer fashion with double detubularisation and sutured to the remaining trigone and bladder neck with a running absorbable suture. In those patients to whom an ileal conduit was performed, a simple cystectomy was conducted and the proximal urethra closed with absorbable sutures. Vaginal wall was preserved in all cases, thus no vaginal reconstruction was needed. After bladder catheter removal, patients were instructed to flush the neobladder once per day with 50 ml of saline solution to remove mucus. Relative rest was recommended to patients for 1 month, when they were counselled to restore their normal activities. Follow-up consisted in periodic clinical visits to assess pain status, the need for adjuvant analgesic treatment and to rule out complications, which were classified according to the Clavien-Dindo (CD) classification [9]. Further investigations included bladder diary, blood test, ultrasound scan and urodynamics. Patients with a post-void residual urine greater than 150 ml were instructed to self-catheterise. Cystoscopy during follow-up was performed in patients with self-reported pain persistence or recurrence and in those who were under bladder self-catheterisation.

The statistical program IBM® SPSS® v.22.0 (IBM Corp., Armonk, NY, USA) was used for data analysis. The Shapiro–Wilk test was used to assess the normality of distribution of continuous variables. The postoperative and postoperative results were compared using the Student's t test for paired samples for variables with a normal distribution (daytime frequency and functional bladder capacity) and the paired-sample Wilcoxon test for variables with a non-normal distribution (nighttime frequency and cystometric bladder capacity). Postoperative results after SC-EC were compared to those after C-IC using the Fisher's exact test. A value of $p < 0.05$ was considered significant. To compare severity of morbidity, complications were grouped into CD ≤ 2 and CD > 2.

In a second phase, we prospectively assessed bladder pain, sexuality and health-related quality of life using the validated questionnaires bladder pain/interstitial cystitis symptom score (BPIC-SS) [10], female sexual function index (FSFI) [11] and EQ-5D 3L and 5L [12], respectively. The BPIC-SS consists of eight items related to the urge to urinate, urinary frequency and bladder pain and pressure; on the last of these items the patient is requested to rate the pain from 0 (no pain at all) to 10 (worst possible pain) as a visual analogue scale (VAS). A total score ranging from 0 to 38 is created by summing all eight item scores [10]. The FSFI is a non-condition-specific questionnaire with 19 questions addressing different sexual dimensions (desire, arousal, lubrication, orgasm, satisfaction and pain). After summing the weighted results for each dimension, a total score from 2 to 36 is obtained [11]. The EQ-5D consists of five questions covering five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression [12]. In the 3L version, each dimension has three levels (no problems, some problems and extreme problems) while in the 5L version each dimension has five levels (no problems, slight

problems, moderate problems, severe problems and extreme problems) [12]. The responses to the different dimensions have no arithmetic properties but form a five-digit number. Every combination of digits corresponds to a single index value from 0 to 1, obtained in accordance with a particular set of weights based on representative samples of the general population of a particular country [13]. Additionally, both versions record the respondent's self-rated health on a vertical VAS from 0 = "best imaginable health state" to 100 = "worst imaginable health state" (EQ VAS) [12]. Country- and region-specific (Catalonian) population norms are available for the EQ VAS and for every EQ-5D-3L dimension [13]. Finally, patients completed a satisfaction questionnaire ("How satisfied are you with the outcome of your treatment?") on an ordinal scale from 0 to 10 and answered the "yes/no" question "Would you undergo the surgery again if you had the pain you had before?". Questionnaires were administered in a clinical visit. According to our institution policy, all patients gave written permission for data collection and permission from our institution's ethical board was obtained.

Results

35 reconstructive surgeries were performed, 29 SC-EC (82.9%) and 6 C-IC (17.1%), in 34 women and 1 man. Characteristics of patients included in the study and operative outcomes are shown in Table 1.

One complication occurred after C-IC (pelvic hematoma, CD1) and seven after SC-EC (one wound infection, CD1; one urinary fistula, CD1; four non-febrile urinary tract infections, CD2; and one bleeding episode requiring surgical revision, CD3b). Neither frequency nor severity of complications was significantly different between both groups (p 0.58 and p 0.875, respectively). All specimens' pathological reports were consistent with preoperative biopsy.

Mean (SD) follow-up was 107 (83) months. During follow-up, two complications were detected after C-IC: one incisional hernia not requiring further treatment (CD1) and one uretero-ileal stenosis requiring ureteral catheter placement (CD3a); while five complications were detected after SC-ED: one incisional hernia (CD1), one enterocutaneous fistula managed conservatively (CD1), one vesicoureteral reflux causing recurrent pyelonephritis (CD2), one incisional hernia that required surgical repair (CD3b) and one intestinal obstruction due to postoperative adherences (CD3b). Neither frequency nor severity of complications was significantly different between both groups (p 0.344 and p 0.714,

Table 1 Characteristics of patients included in the study and operative outcomes

	All patients (N = 35)	SC-EC (N = 29)	C-IC (N = 6)
Men N (%)/women N (%)	1 (2.9%)/34 (97.1%)	1 (3.4%)/28 (96.6%)	0 (0%)/6 (100%)
Age at symptom onset (years) mean ± SD	60.5 ± 10.1	58.4 ± 9.1	72.8 ± 6.5
Age at surgery (years) mean ± SD	67 ± 9	64.5 ± 8.7	79 ± 3.8
Time from symptom onset to reconstructive surgery (years) mean ± SD	5.9 ± 4.1	6.1 ± 4.1	5 ± 4.1
Body mass index (kg/m^2) mean ± SD	25.8 ± 3.8	26.1 ± 4.1	24.8 ± 2.6
Irritable bowel syndrome N (%)	3 (8.6%)	3 (10.3%)	0 (0%)
Fibromyalgia N (%)	1 (2.8%)	1 (3.4%)	0 (0%)
Depression N (%)	8 (22.8%)	7 (24.1%)	1 (16.7%)
Previous pelvic surgery N (%)	8 (22.8%)	6 (20.7%)	2 (33.3%)
Previous BPS treatment N (%)	35 (100%)	29 (100%)	6 (100%)
Oral drugs N (%)	35 (100%)	29 (100%)	6 (100%)
Intravesical instillation N (%)	32 (91.4%)	26 (89.6%)	6 (100%)
Hunner's ulcer resection N (%)	22 (62.8%)	19 (65.5%)	3 (50%)
Hydrodistension N (%)	26 (74.3%)	21 (72.4%)	5 (83.3%)
Botulinum toxin N (%)	11 (31.4%)	10 (34.5%)	1 (16.7%)
Hunner's ulcer at cystoscopy N (%)	4 (11.4%)	3 (10.7%)	1 (16.7%)
Operative time (min) mean ± SD	320 ± 61	320 ± 51	325 ± 103
Bleeding (ml) mean ± SD	590 ± 646	520 ± 481	920 ± 1117

Continuous variables are expressed as mean ± standard deviation and qualitative variables as number and percentage

C-IC cystectomy with ileal conduit, *SC-EC* supratrigonal cystectomy with enterocystoplasty, *SD* standard deviation

respectively). 17 patients (48.6%) required at least one bladder self-catheterisation per day during follow-up due to post-void residual urine.

Postoperative results of bladder diary and urodynamic parameters are shown in Table 2. Three patients presented with mild stress urinary incontinence during follow-up after SC-EC, two of them were already incontinent before surgery and the other one developed de novo urinary incontinence.

Among 35 patients, in two patients (5.7%) bladder pain persisted after SC-EC, requiring further treatment with oral analgesics, with persistence of pain in both cases. Two patients reported persistence of pelvic pain after SC-EC, with physical exploration suggestive of a myofascial syndrome as the cause of pain. One patient (2.8%) reported pain recurrence 20 months after SC-EC, requiring treatment with oral analgesics with no pain relief at the end of follow-up. Cystoscopy was conducted in all patients with pain persistence or recurrence showing no Hunner's ulcers at the remaining bladder mucosa. No cases of bladder pain persistence or recurrence were detected after C-IC (p 0.682 and p 0.829, respectively).

20 patients returned the questionnaires after SC-EC, with mean age at follow-up 76.3 ± 8.8, and 1 after C-IC, aged 80. The mean total BPIC-SS after SC-EC was 7.9 ± 5.7 and 0 after C-CI, while the mean for the last BPIC-SS item (VAS) was 2.6 ± 2.8 after SC-EC and 0 after C-IC. Satisfaction with surgery was 8.7 ± 1.7 after SC-EC and 10 after C-IC. 19 out of 20 patients (95%) after SC-EC and the one after C-IC reported that they would undergo surgery again. 13 patients (61.9%) had had vaginal intercourse after SC-EC, ten of them without pain. Four patients were still sexually active at follow-up. Patient after C-IC had not reassumed sexual activity due to reasons not related with pain. Mean results for the different postoperative FSFI dimensions are shown in Table 3. Mean (SD) EQ-5D index value was 0.78 (0.21) after SC-EC and 0.93 after C-IC. Mean (SD) EQ VAS was 66.8 (24) after SC-EC and 84 after C-IC, while mean EQ VAS for the local (Catalonian) reference general population and for the local reference population older than 75 years are 72.3 and 54.4, respectively [13]. Results for the EQ-5D-3L dimensions and comparisons with local general population reference values are shown in Table 4.

Table 3 Results for each FSFI dimension and total score

Dimension	All patients (N = 21)	SC-EC (N = 20)	C-IC (N = 1)
Desire (1.2–6)	2.8 ± 1	2.8 ± 1.1	3.6
Arousal (0–6)	0.7 ± 1.6	0.7 ± 1.7	0
Lubrication (0–6)	0.8 ± 1.8	0.8 ± 1.8	0
Orgasm (0–6)	0.7 ± 1.8	0.8 ± 1.8	0
Satisfaction (0–6)	3.5 ± 1.2	3.5 ± 1.3	2.8
Pain (0–6)	1 ± 2.3	1.1 ± 2.4	0
Total (2–36)	9.5 ± 9	9.6 ± 9.2	6.4

Values are mean ± SD

C-IC cystectomy with ileal conduit, *SC-EC* supratrigonal cystectomy with enterocystoplasty, *SD* standard deviation

Discussion

In this study, we assessed functional outcomes after cystectomy for BPS as well as bladder pain, sexual function and quality of life after a long-term follow-up. Our results suggest that bladder capacity and urinary frequency significantly improve after surgery. Pain persistence or recurrence is infrequent after surgery, most patients who reassume sexual activity do not experience pain during intercourse and quality of life of these patients is similar to that in our reference population.

First reports on the results of enterocystoplasty for the treatment of refractory interstitial cystitis date back to the 1950s [14, 15]. Since then, several case series studies have shown pain relief after this procedure [6, 16] as well as improvement in bladder capacity and urinary frequency [6, 17]. To our knowledge, the largest series to date was that published by Kim et al. [6] in 40 patients with BPS. In that study, 20% of patients presented persistence of pain after surgery [6]. Persistence of pain may be related to the residual bladder wall [6], requiring further local treatment or even urinary conduit formation [18]. In our series, although not statistically different, all pain persistence or recurrences appeared after SC-EC while none of them after C-IC. However, small case series assessing the

Table 2 Postoperative results of bladder diary and urodynamic parameters, compared with preoperative values in patients who underwent a supratrigonal cystectomy with enterocystoplasty

Variable	Preoperative	Postoperative	p value
Daytime frequency mean ± SD	21 ± 12	10 ± 4	0.02[a]
Nighttime frequency median (IQR)	5 (3–7.7)	2.2 (1–4)	0.01[b]
Functional bladder capacity (ml) mean ± SD	152 ± 76	289 ± 102	0.01[a]
Cystometric bladder capacity (ml) median (IQR)	122 (81–181)	292 (196–370)	< 0.001[b]

IQR interquartilic range, *SD* standard deviation

[a]Student's t test for paired samples

[b]Wilcoxon test for paired samples

Table 4 Results of EQ-5D-3L responses and comparisons with the local (Catalonian) reference general population

Dimension	Response	All patients ($N=21$)	SC-EC ($N=20$)	C-IC ($N=1$)	Reference population (%)
Mobility	No problems	13 (61.9)	12 (60)	1 (100)	83.1
	Some problems	7 (33.3)	7 (35)	0	16.9
	Extreme problems	1 (4.8)	1 (5)	0	
Self-care	No problems	15 (71.4)	14 (70)	1 (100)	93
	Some problems	5 (23.8)	5 (25)	0 (0)	7.0
	Extreme problems	1 (4.8)	1 (5)	0 (0)	
Usual activities	No problems	11 (52.4)	10 (50)	1 (100)	87.6
	Some problems	7 (33.3)	7 (35)	0 (0)	12.4
	Extreme problems	3 (14.3)	3 (15)	0 (0)	
Pain/discomfort	No problems	14 (66.7)	13 (65)	1 (100)	67.1
	Some problems	7 (33.3)	7 (35)	0 (0)	32.9
	Extreme problems	0 (0)	0 (0)	0 (0)	
Anxiety/depression	No problems	17 (81)	16 (80)	1 (100)	80.5
	Some problems	4 (19)	4 (20)	0 (0)	19.5
	Extreme problems	0 (0)	0 (0)	0 (0)	

As the proportion of people reporting severe problems is usually very low in general population surveys, the sum of the proportions reporting level 2 and level 3 problems is used [13]. Values are *N* (%)

C-IC cystectomy with ileal conduit, *SC-EC* supratrigonal cystectomy with enterocystoplasty

role of subtrigonal cystectomy [19] or cystectomy with urethrectomy [20] failed to find significant differences in comparison with supratrigonal cystectomy. Additionally, other groups have reported pain relief after an ileal conduit without cystectomy [21, 22].

Some authors have suggested that supratrigonal cystectomy is effective in patients who present with HU, whereas patients with non-ulcer disease obtain less benefit from this surgery [23, 24]. In our series, HU were detected preoperatively in only four patients. However, all but three patients reported no pain related to the bladder after surgery, BPIC-SS results were low and satisfaction with surgery was high, suggesting that patients without HU also benefit from this treatment. On the other hand, it has been shown that up to 87% of patients with BPS may present pelvic floor muscle dysfunction [25] which may persist after cystectomy. Thus, we consider an accurate physical examination to be crucial in ensuring proper selection of patients in whom the bladder is the origin of pelvic pain before cystectomy.

BPS has negative sexual consequences, leading to decreased interest in sexual interactions and to painful sensations during intercourse in 60–90% of patients [26]. Few studies address sexual function after cystectomy in these patients [26, 27]. Elzevier et al. [26] observed that 12 out of 15 patients were sexually active after a cystectomy for BPS, although dyspareunia could occur during follow-up. In our series, 13 patients had been sexually active after surgery, ten of them without pain during intercourse. Low FSFI results could be explained by the fact that only four patients were sexually active at the time of follow-up. However, only in three patients the presence of pain was the cause of sexual inactivity. Interestingly, the dimension of the FSFI with the highest score was "satisfaction", which reflects overall sex life [11].

BPS is also associated with impaired quality of life, which may result in depression, anxiety, insomnia and fatigue [28]. We used the EQ-5D questionnaire as we considered it of interest to compare quality of life in BPS patients after cystectomy with reference values of the general population in our region. Self-rated health results on the EQ VAS were lower in patients of our series than in the general reference population. However, mean age of patients in our series at follow-up was 77 years and results on the EQ VAS were higher than in the reference population older than 75 years. On the other hand, the proportion of patients reporting no problems related to pain or discomfort was high and similar to the reference population, even when comparison was made with the general population and not only with those aged above 75 years. Overall, our results suggest that quality of life is not greatly impaired by pain after surgery.

Cystectomy for treating BPS is not exempt of complications. In our series, eight (22.8%) complications occurred during the postoperative period and seven (20%) were detected during follow-up, four of them requiring surgical treatment. Although SC-EC and C-IC constitute two different surgical techniques, we failed to find any significant differences between the frequency or severity of complications between the two techniques.

Our study has some limitations. First, a limited number of patients were included, primarily because SC-EC is indicated only in very carefully selected cases. The fact that not all patients completed questionnaires, could lead to the misdiagnosis of pain recurrences. However, the mean follow-up time of patients who did not complete questionnaires was 90 ± 62 months, thus we would not expect further changes in the pain status in these patients. Second, the study had a retrospective design, but the mean follow-up of almost 9 years, the longest published, allowed us to detect complications when present. Third, we did not obtain questionnaires before treatment, again due to the retrospective design. However, bladder pain, sexuality and quality of life after surgery were assessed in a prospective fashion. To our knowledge, this is the first study to address not only bladder pain but also specifically sexuality and quality of life after reconstructive surgery for BPS.

Conclusion

Pain persistence or recurrence after cystectomy for bladder pain syndrome is infrequent. Many patients resume sexual activity without pain after surgery. Pain-related quality of life is similar to that in the reference general population. However, it is associated with significant morbidity and an accurate selection of candidates is therefore imperative.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Statement of human rights All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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