

Multidisciplinary treatment for functional urological disorders with psychosomatic comorbidity in a tertiary pelvic care center—A retrospective cohort study

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Abstract

Background: Functional urological disorders are highly prevalent, frequently interrelated, and characterized by a chronic course and considerable treatment resistance. From our point of view, poor treatment outcomes are often attributable to underlying but undetected mental disorders.

Objective: To investigate the effect of integrated outpatient care by a urologist and a psychiatrist on the symptomatology of patients with functional urological disorders in a tertiary referral Pelvic Care Centre.

Setting: Retrospective observational cohort study in functional urological disorders in combination with psychosomatic co-morbidity. When treatment by a urologist alone was not sufficient, the suitability for a multidisciplinary approach was considered i) if there was a susceptibility for psychiatric comorbidity, ii) if diagnostic procedures did not reveal a treatable somatic cause, or iii) if multiple failed somatic treatments did not relieve complaints. Patients underwent urological treatments before, without reduction of complaints, no treatable somatic cause could be found after diagnostic procedures; or patients suffered from psychiatric comorbidity.

Method: Outcome was measured using patient global impression of improvement, hospital anxiety and depression scale (HADS), global assessment of functioning (GAF), and a health consumption questionnaire.

Results: A significant reduction in HADS-depression score was found ($p = 0.001$) after multidisciplinary treatment. The GAF score increased from 61 to 80, leading to no more than slight impairment in social, occupational, or school functioning. Patients reported their situation as better in comparison with before multidisciplinary treatment. An association was found between pelvic pain and anxiety ($p = 0.032$) and panic disorder ($p = 0.040$). Psychological trauma was found to be associated with depression ($p = 0.044$), with an

odds ratio of 2.93 (1.01–8.50). Psychological trauma coincided in 62.3% of patients with urological pain syndromes and in 83.3% with pelvic pain.

Conclusion: Overall results indicate that functional urological patients, previously refractory to urological treatment, benefit from an integrated care approach by urologists and psychiatrists. Explanation about the bladder–brain axis and the alarm falsification model enlightens understanding of urological and psychological contributions to functional syndromes and creates an opportunity for integrated care.

KEYWORDS

anxiety, bladder pain syndrome, chronic pelvic pain, depression, integrated care, mental disorders, overactive bladder

1 | INTRODUCTION

Functional urological disorders are of considerable individual and societal impact. These comprise overactive bladder (OAB) syndrome, urological pain syndromes, such as, bladder pain syndrome/interstitial cystitis (BPS/IC) and chronic pelvic pain syndrome (CPPS). The prevalence of functional urological syndromes is highly variable, due to a lack of unified diagnostic criteria. In the United States, estimated frequency varies between 3% and 43% for OAB in both men and women, 2.7%–6.5% for BPS and 8%–11.5% for CPPS.^{1,2} The prevalence of bladder pain symptoms in men approaches that in women, suggesting that this condition may be underdiagnosed in the male population.² It is hard to determine the sex distribution of CPPS, given that the characteristics are different and are not always comparable to each other. The impression is that men do more often suffer from CPPS, probably due to the history of defining this disease.²

The key symptoms of OAB are urinary urgency, usually with urinary frequency and nocturia, with or without urinary incontinence. Urgency is a compelling need to urinate being difficult to defer (pain, pressure, and discomfort).³

BPS is defined by the ICS as persistent or recurrent chronic pelvic pain, pressure, or discomfort perceived as being related to the urinary bladder accompanied by at least one other urinary symptom, such as urgent need to void or urinary frequency. A characterizing symptom is relief of bladder symptoms after voiding and increase of symptoms during bladder filling.^{4,5} Several neurogenic and peripheral organic pathways may also lead to pain sensation, due to increased sensitivity in the nervous system or in the bladder itself.⁶

CPPS is defined as persistent pain lasting longer than 6 months or recurrent episodes of abdominal/pelvic pain,

hypersensitivity, or discomfort often associated with urine elimination changes and sexual dysfunction in the absence of organic etiologies.^{7,8}

1.1 | Bladder–brain axis

Bladder function involves storage of urine continuously produced by the kidneys until this can be evacuated at an appropriate time and moment. In the bladder, sensation of filling, urge, and pain can be detected.⁹

Through the lateral spinal cord (initiation of micturition) or thoracolumbar cord (inhibition of micturition), the periaqueductal gray (PAG) records the bladder sensation, forwards this to several brain regions such as the lateral insula, preoptical cortex, anterior cingulate, back to PAG, and also to the pontine micturition center. This activates the voiding reflex. Initiation of micturition inhibits the sacral sphincter motor neurons in Onuf's nucleus, followed by activation of bladder and detrusor contraction, bladder neck opening, and sphincter relaxation. Integration of bladder, cerebral cortex, thalamus, and hypothalamus activity is mediated by the PAG, making this an important structure in the bladder–brain connection. This network consists of even more circuits. The anterior cingulate cortex, as part of the default mode network also relates to impulse control and decision making, and is stimulated during filling of the bladder and activated during the motivation phase to void.¹⁰ Besides, the parahippocampal cortex (tissue surrounding the hippocampus) may also be activated in patients with OAB. Given the amygdalae are closely situated to this region, the assumption is that the amygdalae are activated also, giving emotional, perceptual, or sensation input to voiding too.¹¹

In that regard, Leue et al.¹² described the hypothetical bladder–gut–brain axis (BGBA). The concept can be used

as a foundation for common pathways of functional urological, gastrointestinal and affective disorders. Co-occurrence of functional disorders, on the one hand, and mood and anxiety disorders, on the other, are common and associated with greater symptom severity. Dysregulation of the BGBA can evolve into the direction of false alarm, provoking physical and emotional distress eventually resulting in psychiatric disorders, as well as bodily distress as functional somatic disorders. Alarm falsification refers to a burst of sensations and emotions instead of a normal response to neutral stimuli. Since, complex multidirectional interactions are likely to occur, given psychiatric disorders can have effects on the BGBA also. With more threat over time, vulnerability increases and resilience decreases leading to a greater symptom burden and defense reactions (i.e., urgency, voiding frequency, vomiting, and diarrhea—the symptoms of underlying functional disorders) as well as pain, anxiety, and decreased mood.¹²

1.2 | Affective problems

Hence, functional urological disorders are strongly associated with affective symptoms and have a negative impact on quality of life,¹³ which involve less effective coping strategies, social withdrawal, fear in daily life, and other psychological concerns.¹² Psychological distress is higher in patients with OAB and BPS, before and as a consequence of bladder symptoms.^{13,14} To date, the historical viewpoint of organ-centered diseases is increasingly questioned and current studies focus more on a spectrum of diseases or disease-related symptoms as a syndrome, a complexity phenotype. Different psychosocial factors are associated with OAB or CPPS and with other functional somatic syndromes, such as irritable bowel syndrome or fibromyalgia^{8,15–17} which even may be referred to as somatic symptom disorders. Accumulating evidence is generated in which psychosocial factors moderate disease severity and complexity, as well as persistence of symptoms and may even predict treatment response.^{18,19}

1.3 | Therapeutic approaches

Possible treatment strategies for functional urological disorders consist of behavioral interventions, pharmacological treatment, and invasive medical therapies, such as botulinum toxin A injections, sacral nerve stimulation, and to a lesser extent bladder augmentation or urine deviating techniques.^{20,21} Approximately, 40% of OAB

patients; however, do not achieve acceptable therapeutic benefit and are eventually refractory to treatment.¹⁵ Accordingly, the associations between urgency incontinence and both anxiety disorders and depression are established.¹³ However, the cross-sectional Norwegian HUNT study recently revealed that the use of a selective serotonin reuptake inhibitors (SSRI) did not influence associations between urgency incontinence and anxiety or depression.²² On the other hand, duloxetine improved bladder capacity in women with a mean daytime voiding interval of less than 2 h and detrusor over-activity or bladder capacity of less than 400 ml, compared with placebo.²³ Moreover, Urits et al.²⁴ reviewed cognitive behavioral therapy (CBT) in treatment of chronic pelvic pain, and a study of fluoxetine-use in men suffering from CPPS showed improvement of symptoms and quality of life.²⁵ Still, published results of multidisciplinary treatment including psychopharmacological or psychotherapeutic interventions in functional urological disorders are sparse.^{14,26} However, quality of life, patients' symptom perception and unmet clinical needs may profit from integrated care solutions in these patients. A major challenge concerning integrated care approaches comprises the selection of the right patient with functional urological complaints for these treatments and determination of the necessary steps to enable consultants' and patients' regarding shared decision making.

2 | AIM OF THE STUDY

Since 2010, a combined diagnostic evaluation and integrated treatment for functional urological disorders was launched by urologists and psychiatrists at our academic institution. When treatment by a urologist alone was not sufficient, the suitability for a multidisciplinary approach was considered i) if there was a susceptibility for psychiatric comorbidity, ii) if diagnostic procedures did not reveal a treatable somatic cause, or iii) if multiple failed somatic treatments did not relieve complaints.

The *objective* of the current study is to investigate the effect of integrated outpatient care by a urologist and a psychiatrist on the symptomatology of patients with functional urological disorders in a tertiary referral Pelvic Care Centre. The outcome assumption behind this approach was: If multidisciplinary treatment is effective, patients will visit less medical specialists and will have fewer consultations at general practitioners', accompanied with fewer visits concerning occupational care givers (physiotherapist, haptonomist, etc.) and/or treatment will lead to less symptom burden.

3 | METHODS

3.1 | Study design

This retrospective observational cohort study was approved by the University Hospital's Ethical Review Committee (local number: 2020-1637) and conducted in patients suffering from functional urological disorders in combination with suspected psychosomatic comorbidity. Anonymized data were collected from a multidisciplinary outpatient clinic (Departments of Urology and Psychiatry) during the past 5 years. Included patients received the following questionnaires after finishing treatment: hospitality anxiety and depression scale (HADS), OAB-questionnaire (OAB-Q) or interstitial cystitis symptom index and problem index (ICSI or ICPI) or National Institute of Health chronic prostatitis symptom index (NIH-CPSI) (depending on their diagnosis), and a health consumption questionnaire.^{27–32} Furthermore, a patient global impression of improvement and a degree of change were evaluated by telephone interview.

3.2 | Study population

Patients diagnosed with OAB syndrome and urological pain syndromes were included by two urologists, according to the ICS criteria. Based on the diagnostic and statistical manual of mental disorders, fifth edition (DSM-5) criteria, psychiatric evaluation including history and mental status examination was performed by a psychiatrist.³³ The included patients previously underwent, either one or multiple urological treatments, without reduction of complaints, or had no treatable somatic cause after diagnostic procedures or were suspected for psychiatric comorbidity. In these cases, a multidisciplinary treatment approach by an urologist and a psychiatrist was offered. Exclusion criteria were: age below 18 years, pregnancy, or insufficient available data before or after multidisciplinary treatment. We did not exclude any somatic disorders. The patients underwent multidisciplinary treatment, and were consecutively referred to a psychologist or psychiatrist in their region of living or back to their general practitioner.

3.3 | Measurements

Medical history and complaints were collected from patients' medical charts and measurements were performed before and after the multidisciplinary treatment. Measurements after treatment were collected through

questionnaires. Data collection from the electronic patient file system (System Analysis Program) and statistical analysis were carried out by an independent researcher and a research assistant. Patient data were retrospectively analyzed, without randomization, in a noncontrolled pre–post comparison.

Before and after multidisciplinary treatment, patients completed the HADS questionnaire.²⁷ A score below 7 excluded depression or anxiety disorder. Scores between 8 and 10 indicated a possible depression or anxiety disorder, and above 11 was indicative for a suspected depression or anxiety disorder. If a new psychiatric disorder such as anxiety, panic, or depressive disorder was diagnosed by the psychiatrist, according to DSM-5 criteria.³³ At first and last presentation, the psychiatrist scored the global assessment of functioning (GAF).²⁸ GAF is a generic scoring system for the severity of illness in psychiatric conditions and gives a global measurement of patients' mental health, rating psychological, social and occupational functioning. At least, patients scored the patient global impression of improvement and the degree of change ranging from 0 (very much worse) to 10 (very much better).²⁹ The urological symptoms questionnaires OAB-Q, ICSI/ICPI, and NIH-CPSI were also used at the follow-up assessment to evaluate symptom burden and quality of life.^{27–32}

3.4 | Multidisciplinary urological and psychiatric treatment

All patients received psychoeducation about the bladder–brain axis and the alarm falsification model.¹² Successive treatment regimens consisted of prescribing SSRIs (e.g., sertraline, escitalopram) in affective conditions or serotonin noradrenalin reuptake inhibitors (SNRIs) (e.g., duloxetine) in affective conditions with chronic pain, augmented with atypical antipsychotics (e.g., quetiapine), and/or psychotherapy (CBT, acceptance and commitment therapy, etc.), if indicated.

3.5 | Statistical analysis

All statistical analyses were performed with IBM SPSS Statistics for Windows, version 25 (IBM Corp). Patient characteristics were evaluated by median, with an interquartile range if values were not normally distributed. Patient characteristics and associations between urological and psychological/psychiatric symptoms were evaluated by Pearson χ^2 test. Effect of treatment, measured by, for example, HADS and GAF scales were calculated by Wilcoxon signed ranked test.

4 | RESULTS

A total number of 77 patients were selected for the study, 67 completed a patient global impression of improvement (PGI-I) score, the degree of change evaluation by telephone questionnaire and were evaluated. The urological, HADS, and health consumption questionnaires were completed by 55 patients. Before multidisciplinary treatment, 47 patients filled in the HADS with a median time of 2.4 months (1.2, 5.1) between the HADS and participation in the multidisciplinary treatment. Median time between first urological consultation and multidisciplinary consultation was 3.9 months (1.9, 13.1). Duration of treatment (i.e., starting point of the

multidisciplinary consultation) and time of final consultation at the urologist was 11.2 months (5.6, 24) and for the final consultation at the psychiatrist 9.4 months (4.7, 15.5). Data from the questionnaires was collected for 23.3 months (5.5, 36.7) after the last urological consultation, and 25.4 months (12, 37.3) after the last psychiatric consultation. Outliers were excluded from time analysis if a Z-score was above or below three times standard deviation, and when patients visited the multidisciplinary consultation once.

Table 1 shows the demographic characteristics indicating group differences in incontinence prevalence for OAB syndrome ($p = 0.026$) and in pelvic pain for pain syndromes ($p = 0.030$). In OAB syndrome, urgency was

TABLE 1 Demographic characteristics

Number of patients/ diagnoses (N)	Total		Overactive bladder syndrome		Urological pain syndromes	
	N (%)	Missing data (N)	N (%)	Missing data (N)	N (%)	Missing data (N)
Primary complaint	77 (100)		29 (37.7)		48 (62.3)	
Age in median (range)	54 (27–78)		52 (27–73)		57 (27–78)	
Gender (male/female)	31/46		10/19		21/27	
Frequency	47 (61)		17 (58.6)		30 (62.5)	
Urgency	50 (64.9)		22 (75.9)		27 (56.3)	
Incontinence	29 (37.7)		16 (55.1)		12 (25)	
Pain during filling phase of the bladder	39 (50.6)		11 (37.9)		28 (58.3)	
Pelvic pain	57 (74)		17 (58.6)		40 (83.3)	
Globus sensation (throat)	10 (17.9)	21	4 (13.8)	8	6 (12.5)	13
Epigastric complaints	20 (35.5)	19	5 (17.2)	7	15 (31.3)	12
Palpitations	15 (25.8)	19	6 (20.7)	9	8 (16.7)	9
Chest pain	14 (24)	19	5 (17.2)	9	9 (18.8)	10
Dizziness complaints	16 (27.5)	19	6 (20.7)	7	10 (20.8)	12
Fibromyalgia	14 (19.2)	4	8 (27.6)	2	6 (12.5)	2
Irritable bowel syndrome	24 (32)	2	8 (27.6)	1	16 (33.3)	1
Psychological trauma in the past ^a	24 (32)	2	8 (27.6)	1	16 (33.3)	1
Anxiety disorder	13 (16.9)		6 (20.7)		6 (12.5)	
Panic disorder	14 (18.2)		7 (24.1)		7 (14.6)	
Depression disorder	20 (26)		6 (20.7)		14 (29.2)	
Total psychiatric diagnoses pretreatment ^b	47		19		27	
Psychiatric diagnosis during consultation ^b	47		17		30	
No psychiatric comorbidity	8 (10.4)		2 (6.9)		6 (12.5)	

^aTraumas: Mental abuse, sexual abuse, or physical abuse.

^bDiagnoses: Anxiety disorder, panic disorder, or depression disorder.

present in 75.9% of the patients and frequency in 58.6%, while urgency existed in 56.3% and frequency in 60.2% in urological pain syndromes patients. This difference was not significant ($p = 0.050$ and $p = 0.811$). Psychosomatic complaints, such as globus sensation or others showed a normal distribution. Patients often experienced different traumas during different periods of a lifetime, including emotional abuse and neglect as well as physical maltreatment or even sexual abuse. Given the multiple facets of frequently repeated traumatization, we did not differentiate between types of trauma, since it was not possible to specify a trauma course in relation to urological complaints retrospectively in most of the patients. Anxiety disorders consist of panic disorder and general anxiety disorder. In the case that panic attacks were associated with a traumatic event, the attack did not appear with further symptoms of a posttraumatic stress disorder (PTSD), such as flashbacks or nightmares. Hence, no PTSD was diagnosed. The numbers for anxiety disorders, panic disorder, and depression were the numbers of confirmed diagnoses by a psychiatrist in all patients, and patients could have, for example, anxiety disorders and depressive disorder at the same time. In total, 49 patients were previously diagnosed with a panic or anxiety disorders (otherwise) or depression in their medical history ($n = 32$) or were currently suffering from these disorders ($n = 17$). Of these patients, 23 did not complete the HADS questionnaire.

An association was found between pelvic pain and anxiety ($p = 0.032$) and panic disorders ($p = 0.040$). Odds ratios were 0.22 (0.06–0.76) for anxiety disorders and 0.26 (0.08–0.87) for panic disorders. An even stronger association was found between these variables in the group of urological pain syndromes ($p = 0.001$ in both groups). For anxiety disorders the odds ratio was 0.02 (0.00–0.18) and for panic disorders 0.03 (0.00–0.24). A psychological trauma in the past was associated with a depressive disorder ($p = 0.044$), with an odds ratio of 2.93 (1.01–8.50). Of the patients with a psychological trauma in the past, 62.3% had urological pain syndromes and 83.3% suffered from pelvic pain.

Table 2 shows the number of urological treatments, patients had been subjected to before participating in the multidisciplinary approach. Twenty-two patients (28.6%) were referred by the general practitioner, 9 patients (11.7%) by another specialism consultant, 44 patients (57.1%) by another nonacademic hospital urologist, and 2 patients (2.6%) by another academic hospital urologist. Several urological treatments were applied before the multidisciplinary treatment participation. Table 3 displays, among others, the frequency of being treated by a psychiatrist or psychologist elsewhere before multidisciplinary treatment, although it was not always evident

which therapy they had undergone a priori. Figure 1 illustrates the multidisciplinary treatment approach and shows that 71.4% of patients started with antidepressants (SSRIs or SNRIs) and atypical antipsychotics were augmented in 22.8% of the cases to achieve maximum therapeutic benefit (i.e., augmentation strategy). Matching the tables with the flowchart (Figure 1), one patient had no psychiatric comorbidity but still started with antidepressants, which explains the differences in numbers between tables and flowchart. Figure 2 provides an overview of prescribed medication during multidisciplinary treatment.

Only 2.6% of the patients were not compliant to the multidisciplinary therapy, signified by no-show at follow-up after integrated consultation. The integrated approach led to the following results, as presented in Tables 2 and 3. No difference is noticed in both groups ($p = 0.219$) in the HADS-anxiety score before and after the multidisciplinary treatment. However, a significant 2-point reduction in the HADS-depression score is found ($p = 0.001$). The GAF score increased to the category 71–80, which indicates no more than slight impairment in social, occupational, or school functioning.²⁹ Patients reported their situation as a little better (PGI = 3 [median]) in comparison with before multidisciplinary treatment, with a degree of change of 7, on a scale of 1–10. Dividing groups according to treatment, a significant decrease in HADS-depression score is seen in the psychotherapeutic consultation group ($p = 0.028$) and no change in the other groups. Moreover, no other differences in results could be revealed when classifying groups based on treatment. No significant reduction could be found in use of pain medication (paracetamol, nonsteroidal anti-inflammatory drugs, pregabalin, tramadol, or other opioids) after multidisciplinary treatment ($p = 0.051$). Although the opiate use has been halved in the pain group.

5 | DISCUSSION

To our knowledge, this is the first observational cohort study on integrated psychosomatic treatment of functional urological disorders with psychosomatic comorbidity. The current study reveals a pre–post comparison before and after multidisciplinary treatment by urologist and psychiatrist. A significant reduction in HADS-depression scores was observed, and the GAF shows an improvement in functioning. Furthermore, at follow up only a slight impairment in social, occupational, or school functioning (e.g., temporarily failing behind in schoolwork) had remained, indicating that earlier treatment refractoriness was redressed.²⁸ The PGI-I revealed that the situation of patients is improved with a

TABLE 2 Urological therapies before and after multidisciplinary treatment

Disease Therapy	Overactive bladder syndrome N (%)		Urological pain syndromes N (%)		Total N (%)	
	Before	After	Before	After	Before	After
Pelvic floor physiotherapy	20 (69)	5 (17.2)	26 (54.2)	11 (22.9)	46 (59.7)	16 (20.5)
Clean intermittent self catheterization	4 (13.8)	1 (3.4)	5 (10.4)	0	9 (11.7)	1 (1.3)
Tined lead procedure	4 (13.8)	1 (3.4)	4 (8.3)	2 (4.2)	8 (10.4)	3 (3.9)
Sacral neuromodulator	1 (3.4)	0	1 (2.1)	2 (4.2)	2 (2.6)	2 (2.6)
Laser coagulation	1 (3.4)	1 (3.4)	11 (22.9)	5 (10.4)	12 (15.6)	6 (7.8)
Botox injection	3 (10.3)	0	8 (16.7)	1 (2.1)	11 (14.3)	1 (1.3)
Bladder infusion	3 (10.3)	0	14 (29.2)	1 (2.1)	17 (22.1)	1 (1.3)
Cystectomy and suprapubic catheter	0	0	0	1 (2.1)	0	1 (1.3)
Urethral stricture treatment (urethroplasty)	0	0	0	2 (4.2)	0	2 (2.6)
Neural block (via another pain discipline)	0	0	0	1 (2.1)	0	1 (1.3)
Testis removal incl. prosthesis	0	0	0	1 (2.1)	0	1 (1.3)
Transobturator tape	3 (10.3)	0	1 (2.1)	0	4 (5.2)	0
Percutaneous tibial nerve stimulation	4 (13.8)	0	6 (12.5)	0	10 (13)	0
Dissection of n. genitofemoralis	0	0	0	2 (4.2)	2 (2.6)	0
Medication						
Anticholinergics	22 (75.9)	3 (10.3)	28 (58.3)	8 (16.7)	50 (64.9)	11 (14.3)
B3-adrenoceptoragonists	17 (58.6)	2 (6.8)	22 (45.8)	14 (29.2)	39 (50.6)	16 (20.8)
Maintenance dose antibiotics	7 (24.1)	0	18 (37.5)	4 (8.3)	25 (32.5)	4 (5.2)
A1 blockers	8 (27.6)	1 (3.4)	14 (29.2)	0	22 (28.6)	1 (1.3)
5a reductase inhibitors	2 (6.9)	1 (3.4)	2 (4.2)	0	4 (5.2)	1 (1.3)
Oxybutinine (transcutaneous)	6 (20.7)	0	9 (18.8)	1 (2.1)	15 (19.5)	1 (1.3)
Estriol (local vaginal)	1 (3.4)	0	10 (20.8)	4 (8.3)	11 (14.3)	4 (5.2)
Pain medication ^a	6 (20.7)	5 (17.2)	18 (37.5)	13 (27.1)	24 (31.2)	19 (24.7)
Tramadol or stronger opioids	2 (6.9)	5 (17.2)	10 (20.8)	5 (10.4)	12 (15.6)	10 (13)

^aConsisting any of the following medications: Paracetamol, nonsteroidal anti-inflammatory drugs, tramadol, lyrica, and opioids.

degree of change of 7 (from 0 [very much worse] to 10 [very much better]).²⁹ Together with the quality-of-life score of 7 (ranging from 0 to 10) this confirms the positive effect of the integrated approach in our functional bladder syndrome cohort. The present study showed an optimal adherence to the therapy with near maximum compliance. It is estimated that the first contact with the psychiatrist in combination with the urologist, combined with a balanced explanation of the combined therapy, along both the psychological and the somatic track, is likely to be responsible for this. Although, a selection bias does exist, as there are patients with a suspicion of comorbidity, but who did not want to be seen by a psychiatrist.

The urological questionnaires consisted of the OAB-Q, ICSI/ICPI, or CPSI/CPPI questionnaires (depending on the urological syndrome) and were used to investigate the burden of urological symptoms after multidisciplinary treatment (Table 4).³⁴ Thus, urological testing delivered a cross-sectional observation after integrated care. With the interpretation of the results, one has to bear in mind the high treatment refractoriness of our population, 59.7% were referrals from other specialists. The scores indicate that patients had moderate complaints in general, and that pain was only moderate after integrated care as well. Furthermore, BPS patients receiving the O'Leary-Sant symptom (ICSI)

TABLE 3 Psychiatric/psychological therapies before and after multidisciplinary treatment

Disease Therapy	Overactive bladder syndrome N (%)		Urological pain syndromes N (%)		Total N (%)	
	Before	After	Before	After	Before	After
Cognitive behavior therapy (CBT)	3 (10.3)	5 (17.2)	6 (12.5)	7 (14.6)	9 (11.7)	12 (15.6)
Psychotherapy (not specified)	4 (13.8)	7 (24.1)	4 (8.3)	7 (14.6)	8 (10.4)	14 (18.2)
Psychotherapy (e.g. CBT, ACT, talk therapy)	9 (13.8)	12 (41.4)	11 (20.8)	14 (29.2)	20 (22.1)	26 (33.8)
Talk therapy	2 (6.9)	0	1 (2.1)	0	3 (3.9)	0
EMDR	1 (3.4)	0	2 (4.2)	0	3 (3.9)	0
Mindfulness	2 (6.9)	0	3 (6.3)	0	5 (6.5)	0
Meditation	1 (3.4)	0	1 (2.1)	0	2 (2.6)	0
Treated by another psychiatrist or psychologist (in the past)	16 (55.2)	–	21 (43.8)	–	37 (48.1)	–
Medication						
SSRI	5 (17.2)	17 (58.6)	8 (16.7)	21 (43.8)	13 (16.9)	38 (49.5)
SNRI	0	6 (20.7)	2 (4.2)	15 (31.3)	2 (2.6)	21 (27.3)
TCA	3 (10.3)	0	11 (22.9)	1 (2.1)	14 (18.2)	1 (1.3)
Atypical antipsychotics	0	5 (17.2)	1 (2.1)	12 (25)	1 (1.3)	17 (22.1)
Follow up						
Follow up by general practitioner	–	11 (37.9)	–	16 (33.3)	–	27 (35.1)
Follow up by their own psychiatrist	–	5 (17.2)	–	5 (10.4)	–	10 (13)
Referred to another psychiatrist	–	1 (3.4)	–	5 (10.4)	–	6 (7.8)

Abbreviations: ACT, acceptance and commitment therapy; EMDR, eye movement desensitization and reprocessing; SNRI, serotonin noradrenalin reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressants.

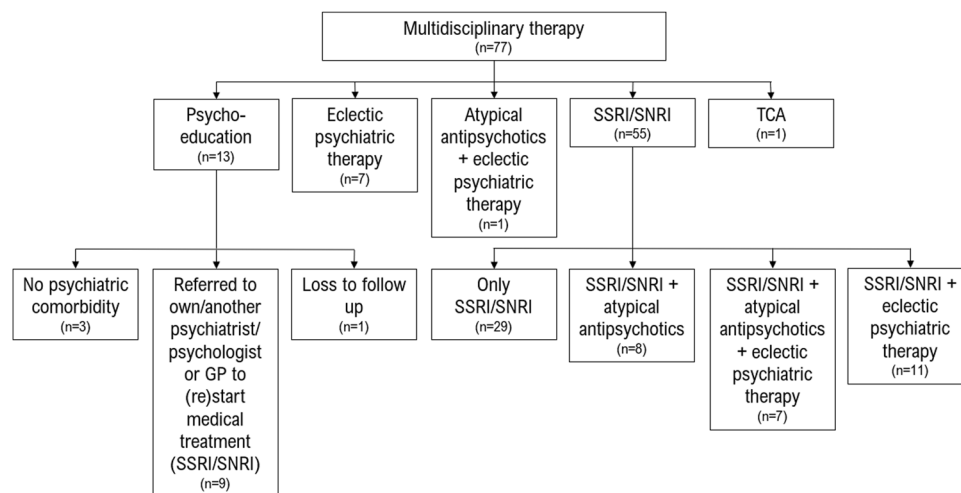


FIGURE 1 Flowchart multidisciplinary treatment approach. SNRI, serotonin noradrenalin reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressants

Overview of medication use in number of patients

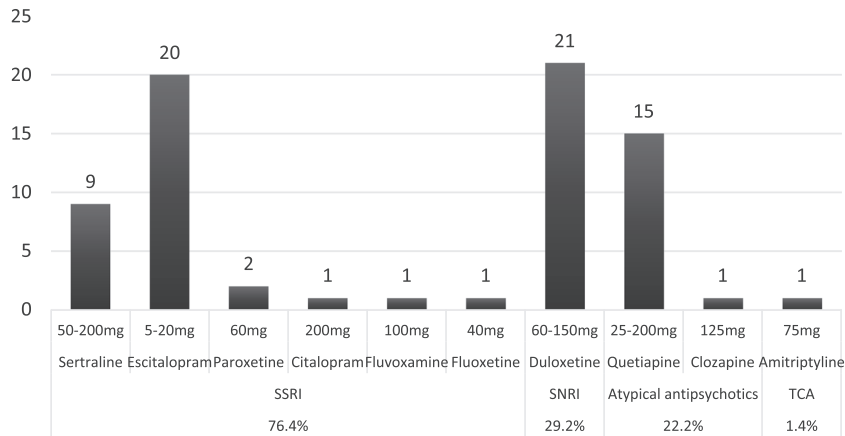


FIGURE 2 Overview of medication use. SNRI, serotonin noradrenalin reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressants

TABLE 4 Results of multidisciplinary treatment (groups divided according to urological syndromes)

	Before start of multidisciplinary treatment ^a		After multidisciplinary treatment		<i>p</i> *
HADS-A					
OAB	6 [4.5,11.5]	(<i>n</i> = 21)	8.5 [4, 10.25]	(<i>n</i> = 18)	0.554
BPS/CPPS	7 [4.75,10.25]	(<i>n</i> = 26)	6 [5, 9]	(<i>n</i> = 37)	0.081
Total	7 [5, 11]	(<i>n</i> = 47)	6 [5, 9]	(<i>n</i> = 55)	0.219
HADS-D					
OAB	5 [2.5, 9]	(<i>n</i> = 21)	4.5 [1.75, 6.5]	(<i>n</i> = 21)	0.046
BPS/CPPS	8.5 [5.75,11]	(<i>n</i> = 26)	6 [2, 10]	(<i>n</i> = 37)	0.006
Total	7 [4, 11]	(<i>n</i> = 47)	5 [2, 9]	(<i>n</i> = 55)	0.001
GAF scale					
OAB	61 [51, 61]	(<i>n</i> = 29)	80 [65.5, 90]	(<i>n</i> = 29)	0.001
BPS/CPPS	51 [51, 61]	(<i>n</i> = 48)	75 [70, 90]	(<i>n</i> = 48)	0.001
Total	51 [51, 61]	(<i>n</i> = 77)	80 [70, 90]	(<i>n</i> = 77)	0.001
PGI-I					
OAB			3 [2, 4]	(<i>n</i> = 23)	
BPS/CPPS			3 [1.25, 4]	(<i>n</i> = 44)	
Total			3 [2, 4]	(<i>n</i> = 67)	
Degree of change					
OAB			6 [5, 7]	(<i>n</i> = 23)	
BPS/CPPS			7 [5, 8]	(<i>n</i> = 44)	
Total			7 [5, 8]	(<i>n</i> = 67)	
Quality of life					
OAB			7 [6, 8]	(<i>n</i> = 17)	
BPS/CPPS			7 [6, 8]	(<i>n</i> = 36)	
Total			7 [6, 8]	(<i>n</i> = 53)	

TABLE 4 (Continued)

Before start of multidisciplinary treatment ^a	After multidisciplinary treatment	<i>p</i> [*]
OAB-q: symptom bother	19 [13.25, 36.75]	(<i>n</i> = 16)
HRQoL	54.5 [39.5, 75]	
Total	73 [54.75, 93.75]	
ICSI	10 [6, 13.5]	(<i>n</i> = 25)
ICPI	10 [3, 13]	
Total	18 [9, 27]	
NIH-CPSI	15 [8.25, 19.25]	(<i>n</i> = 16)

Abbreviations: BPS, bladderpain syndrome; CPPS, chronic pelvic pain syndrome; GAF, global assessment of functioning; HADS-A, hospitality anxiety and depression scale-anxiety; HADS-D, hospitality anxiety and depression scale-depression; HRQoL, health-related quality of life; ICPI, interstitial cystitis problem index; ICSI, interstitial cystitis symptom index; NIH-CPSI, National Institute of Health chronic prostatitis symptom index; OAB-q, overactive bladder-questionnaire; PGI-I, patient global impression of improvement.

^aFirst/second urological consult or first multidisciplinary consult.

^{*}Significance $p < 0.05$ (Pearson χ^2 test).

and problem index (ICPI) demonstrated that BPS patients were still suffering from their functional complaints. However, dividing the scores into symptom index and problem index indicated that patients may have learned to cope with their symptoms, in view of a lower problem index compared to the symptom index.

The definitions of OAB syndrome and urological pain syndromes are based on symptom presentation and descriptive in nature instead of nosology driven.^{3,35} In that regard, focusing on our demographic characteristics, a remarkable finding is the subtle difference concerning the presence of urgency, frequency, and psychosomatic complaints in the OAB- and urological pain populations. These baseline characteristics have led to the assumption that OAB syndrome and urological pain syndromes do have more in common than we might realize, indicating that we may consider to treat them as one syndrome. This is in line with the literature since it has been described that frequency-urgency syndromes may contain OAB, IC/BPS, CPPS, and nonbacterial cystitis.³⁶

In this selected refractory OAB, BPS, and CPPS cohort including patients who are assumed to have psychiatric comorbidity, an association between pelvic pain and anxiety and more specifically with panic disorder has been recognized. It is well established that co-occurrence of functional disorders, on the one hand, and mood and anxiety disorders on the other, are common and associated with greater symptom severity.¹² Lane et al.³⁷ described the competition between emotional and physical pain recently. This implies that, patients with childhood adversity (e.g., physical, sexual, emotional, and verbal abuse or neglect) might pay more

attention to physical pain, which may reduce the experienced intensity and awareness of affective distress arising from their social disturbances. In our study, we found that 83.3% of the 24 patients (31.2%) who experienced a psychological trauma suffered from pelvic pain. These patients may experience more physical pain compared to emotional pain or may search for a physical explanation of their pain that might have been caused by their abusive emotional distress earlier in life. On the other hand, no significant correlation was found between psychological trauma and pelvic pain ($p = 0.236$), possibly be due to our small sample size. Overall, our findings are in line with the literature. Meltzer-Brody et al.³⁸ showed that women with CPPS have high rates of physical and sexual abuse. Moreover, history of prior abuse or trauma is associated with treatment refractory CPPS, and, therefore, treatment of CPPS should include an integrated multidisciplinary approach.³⁸ In addition, an association between psychological trauma and depression is confirmed in our cohort, with an odds ratio of 2.93. This association is well known and can be explained by the fact that patients who suffer from childhood adversity are more vulnerable to affective disorders.³⁹ In terms of causation, chronic stress can increase the risk of disease pathology and may result in hyperalgesia in individuals predisposed to functional urological diseases.⁴ Vrijens et al.¹³ described the association between affective symptoms and the new onset of OAB symptoms in depressive patients. Resulting in a positive association between the co-occurrence of OAB syndrome and depression, and to a lesser extent between co-occurrence of OAB syndrome and anxiety.¹³ Moreover, CPPS patients with a greater number of pain locations tend to have more

depression, anxiety and worse quality of life, reflecting a severity or complexity phenotype. However, the direction of this association remains unclear.^{8,20}

Hence, an integrated multidisciplinary approach in complex functional urological syndromes always has to be considered if underlying psychopathology is suspected or patients are refractory to fragmented urological treatment.

6 | LIMITATIONS

Almost all patients had multiple urological treatments before referral, without reduction of complaints. Furthermore, the multidisciplinary treatment was offered by the urologist if a psychiatric comorbidity was suspected. Patients were treated in our tertiary referral Pelvic Care Centre, meaning that selection bias is unavoidable. The selected population results in a small sample size, but still with enough importance to analyze. Data were collected retrospectively and not all patient files contained all included questionnaires. Urological questionnaires were not available before multidisciplinary treatment, which makes interpretation of the posttreatment urological questionnaires difficult. The lack of completed HADS questionnaires before the first consultation may have led to lower HADS scores, since it is even likely that patients were reluctant to complete these questionnaires due to their psychiatric disorder and the possible stigma around it.^{40,41}

7 | CONCLUSION

The current cohort study shows the results of the multidisciplinary, both urologic and psychiatric, treatment of patients with treatment refractory functional urological disorders or suspected psychiatric comorbidity. The overall results indicate that these patients may benefit from an integrated care approach. Explanation and education by the two specialists at the same time about the brain–bladder axis and the alarm falsification model enlightens the psychological and functional part of their syndromes. The positive effect of this integrated approach for treatment is confirmed by a decrease in psychological symptom scores and a positive impact on psychosocial outcome. Further prospective comparative research is required on a larger scale to confirm our encouraging results. Concerning future research, it would be of interest to compare psychopharmacological and psychotherapeutic interventions in well matched patient cohorts prospectively and in a more standardized manner. Especially with regard to

psychotherapy we suggest a more detailed evaluation of the relationship between the type of intervention and the effectivity in a multimodal (psychological and somatic) fashion.

AUTHOR CONTRIBUTIONS

Vera van Knippenberg, Carsten Leue, Desiree Vrijens, and Gommert van Koeveringe contributed to the design and implementation of the research, to the analysis of the results, and to the writing and reviewing of the manuscript.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

ETHICS STATEMENT

The study protocol was approved by the Regional Committee on Medical Research Ethics at Maastricht Universitair Medisch Centrum, Maastricht (Number: 2020-1637).

DATA AVAILABILITY STATEMENT

Due to the retrospective nature of this study, participants of this study did not specifically agree for their data to be shared publicly, given the fact that patients of the MUMC all know and agree at start of the diagnostics or therapeutic approach that their anonymized clinical and cost data might be part of scientific evaluation.

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