

EAU Guidelines on Chronic Pelvic Pain

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Abstract

Objectives: On behalf of the European Association of Urology (EAU) guidelines for diagnosis, therapy and follow-up of chronic pelvic pain patients were established.

Method: Guidelines were compiled by a working group and based on current literature following a systematic review using MEDLINE. References were weighted by the panel of experts.

Results: The full text of the guidelines is available through the EAU Central Office and the EAU website (www.uroweb.org). This article is a short version of this text and summarises the main conclusions from the guidelines on management of chronic pelvic pain.

Conclusion: A guidelines text is presented including chapters on prostate pain and bladder pain syndromes, urethral pain, scrotal pain, pelvic pain in gynaecological practice, role of the pelvic floor and pudendal nerve, general treatment of chronic pelvic pain and neuromodulation. These guidelines have been drawn up to provide support in the management of the large and difficult group of patients suffering from chronic pelvic pain.

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1. Introduction

“Chronic pelvic pain” is a non-malignant pain perceived in structures related to the pelvis. It can be difficult to manage because it is often impossible to identify the pathophysiological origin. Nociceptive pain must prove persistent or recurrent over six months before being described as chronic. If non-acute pain mechanisms are identified then the pain is considered chronic, irrespective of the time course. There is no

ideal classification for the conditions included in the set that constitutes chronic pain syndrome. The terms used in these guidelines follow the most recent recommendations for the terminology by the International Continence Society (ICS) [1], which are based on the Axial Structure of the International Association for the Study of Pain (IASP) classification (Table 1).

2. Prostate pain syndrome

Prostatitis is a poorly defined condition that encompasses the three elements, lower urinary tract

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Table 1
Classification of chronic pelvic pain syndromes

Chronic pelvic pain (new definition)	Pelvic pain syndrome (1)	Urological	Bladder pain syndrome (1)		Interstitial cystitis			
			Urethral pain syndrome (1)					
			Penile pain syndrome (new definition)					
			Prostate pain syndrome (Adapted from NIH (3))					
			Scrotal pain syndrome (1)	Testicular pain syndrome (new definition)				
				Post-vasectomy pain syndrome (new definition)				
		Epididymal pain syndrome (new definition)						
		Gynaecological	Endometriosis-associated pain syndrome (new definition)					
			Vaginal pain syndrome (1)					
			Vulvar pain syndrome (1)	Generalized vulvar pain syndrome (ISSVD 1999)				
				Localized vulvar pain syndrome (ISSVD 1999)	Vestibular pain syndrome (ISSVD 1999)		Clitoral pain syndrome (ISSVD 1999)	
		Anorectal	Proctalga fugax (2)					
			Anorectal pain syndrome (new definition)					
			Anismus					
	Neurological	Pudendal pain syndrome (new definition)						
	Muscular	Perineal pain syndrome (1)						
		Pelvic floor muscle pain syndrome (new definition)						
	Well-defined conditions that produce pain, examples include:	Urological	Infective cystitis					
			Infective prostatitis					
			Infective urethritis					
			Infective epididymo-orchitis					
		Gynaecological	Endometriosis					
		Anorectal	Proctitis					
			Haemorrhoids					
			Anal fissure					
		Neurological	Pudendal neuropathy					
Sacral spinal cord pathology								
Other		Vascular						
		Cutaneous						
		Psychiatric						

symptoms (LUTS), evidence of inflammation and involvement of the prostate. These features may exhibit varying degrees of involvement since the term primarily portrays a symptom set. The NIDDK system is the preferred classification identifying four major subtypes of disease [2] (Table 2). An EAU working group has suggested a practical classification that divides chronic prostatitis into chronic bacterial, in which a pathogen

Table 2
Classification of prostatitis according to NIDDK/NIH

I.	Acute bacterial prostatitis (ABP)
II.	Chronic bacterial prostatitis (CBP)
III.	Chronic pelvic pain syndrome (CPPS)
	A. Inflammatory CPPS: WBC in semen/EPS/voided bladder urine-3 (VB3)
	B. Noninflammatory CPPS: no WBC semen/EPS/VB3
IV.	Asymptomatic inflammatory prostatitis (histological prostatitis)

has been demonstrated, and culture-negative disease, where inflammation is found microscopically in the absence of an identified pathogen [3]. In 5 to 10% of cases, prostatitis is shown to have a bacterial aetiology. In the remaining proportion the symptoms have been attributed to “Chronic non-bacterial prostatitis”, “Prostadyndia” or “Chronic prostatitis associated with chronic pain syndrome”. The latter is defined as discomfort or pain in the pelvic region with negative culture of specimens and insignificant numbers of white blood cells in prostate-specific specimens including semen, expressed prostatic secretions and urine collected after prostatic massage. There is neither overt renal tract disease nor evidence of urethritis, other inflammation, urogenital cancer, urethral stricture or neurological disease. The aetiology and pathogenesis of this larger group of patients is extremely speculative and therefore the new term “Prostate pain syndromes” seems more appropriate.

The diagnosis rests on a clinical history, symptoms evaluation, examination and analysis of urine and prostate-specific specimens. Commonly, a course of antibiotics is used as a therapeutic test rather than a diagnostic response.

2.1. Medical treatment

Current treatment is directed at symptom management to improve life quality and the involvement of pain management services. Benefit may be wrought by alpha blockers [4–6], muscle relaxants [7,8] and antibiotics [9–14]. Patients who effect a response to antibiotics should be maintained on such for at least six weeks. Should a relapse occur, continuous low-dose antimicrobial treatment should be used [7].

Although analgesics are given to most patients, efficacy data are sparse [7]. Other options have been advocated but need justification through evidence. These include non-steroidal anti-inflammatories (NSAID), immunotherapy [15], 5-alpha-reductase inhibitors [16,17] and anticholinergics [7].

2.2. Interventional treatments

Various physical therapies have been claimed to improve symptoms although rigorous efficacy data are lacking. Heat therapy as microwave energy applied trans-urethral or trans-rectal has been reported to induce favourable effects in some patients [18,19]. Surgical treatment is limited to circumstances where another indication exists [20,21].

3. Bladder pain syndrome (Interstitial cystitis)

The collective term “Interstitial cystitis” includes a variety of conditions most commonly identified by symptoms. The classical ulcer disease (Hunner’s ulcer) is found in as few as 10% up to 50% of cases [22,23]. The diagnostic criteria described by the NIDDK [24] were formulated for research purpose and reach a diagnosis through exclusion, inappropriate in clinical care (Table 3). Since symptoms invariably define the clinical condition the term “Painful bladder syndrome” or “Bladder pain syndrome” is more apposite.

The prevalence of bladder pain syndrome is between 5 and 16 per 100,000 of the population [25–27] although higher prevalence up to 0.5% have been reported. The aetiology is not known. No bacterial or viral cause for bladder pain syndrome has been found despite the use of sophisticated detection methods. Many hypotheses have been proposed, the more popular including mast cell activation [23], defects in the urothelial glycosaminoglycan (GAG) coating [28,29] autoimmune disease [30,31], toxic agents [32] and neuroendocrine-immune interactions [33, 34]. None of these hypotheses have been tested properly and have invalid status.

Table 3

Research definition of interstitial cystitis described by NIDDK Workshop on IC, 28–29 August 1987 [24]

Automatic inclusions

- Hunner’s ulcer

Positive factors

- Pain on bladder filling relieved by emptying
- Pain (suprapubic, pelvic, urethral, vaginal or perineal)
- Glomerulations on endoscopy
- Decreased compliance on cystometrogram

Automatic exclusions

- <18 years old
- Benign or malignant bladder tumours
- Radiation cystitis
- Tuberculous cystitis
- Bacterial cystitis
- Vaginitis
- Cyclophosphamide cystitis
- Symptomatic urethral diverticulum
- Uterine, cervical, vaginal or urethral cancer
- Active herpes
- Bladder or lower ureteral calculi
- Waking frequency < five times in 12 hours
- Nocturia < two times
- Symptoms relieved by antibiotics, urinary antiseptics, urinary analgesics (for example phenazopyridine hydrochloride)
- Duration <12 months
- Involuntary bladder contractions (urodynamics)
- Capacity >400 cc, absence of sensory urgency

Bladder pain syndrome is diagnosed on the basis of symptoms, examination, urine analysis and cystoscopy with hydro-distension and biopsy. All patients describe pain, urinary frequency and nocturia. The pain, which is sometimes extreme, typically increases with bladder filling and is located suprapubically. This may radiate to the groins, vagina, clitoris, penis, rectum or sacrum and it is relieved by voiding although it soon returns [24].

Classical ulcer disease and bladder pain syndrome demonstrate different clinical presentations and age distributions [35]. They can be discriminated non-invasively and respond differently to treatment. Classical ulcer disease is a destructive inflammation which in some patients leads to contracted, fibrotic bladders and upper tract outflow obstruction. This progression does not occur in non-ulcer bladder pain syndrome. The two conditions differ in their histopathology, immunology and neurobiology [23].

Classical ulcer disease displays reddened mucosal areas often associated with small vessels radiating towards a central scar, sometimes covered by a small clot or fibrin deposit [35]. The scar ruptures with increasing bladder distension with a characteristic “waterfall” type of bleeding. There is a strong association between classical ulcer disease and reduced bladder capacity under anaesthesia [23,35]. Non-ulcer disease displays a normal bladder mucosa at initial cystoscopy. The development of glomerulations after hydro-distension is a diagnostic sign still lacking evidential authority.

Biopsies help to support the clinical diagnosis of classical ulcer disease and to exclude carcinoma *in situ* and tuberculous cystitis [36]. Several tests, for example the measurement of potassium chloride permeability have been proposed but evidence is meagre. The

Table 4

Level of evidence and grade of recommendation

Level	Type of evidence
1a	Meta-analysis of randomized trials
1b	At least on randomized trial
2a	One well-designed controlled study without randomization
2b	One other type of well-designed quasi-experimental study
3	Non-experimental study (comparative study, correlation study, case reports)
4	Expert committee, expert opinion
Grade	Basis for recommendation
A	Clinical studies of good quality and consistency including at least one randomized trial
B	Well-conducted clinical studies without randomized trials
C	Absence of directly applicable clinical studies of good quality

O’Leary Sant symptom index [37] aids diagnosis and helps to measure outcome.

3.1. Medical treatment

The treatment of bladder pain syndrome has yet to be defined from evidence. Tables 4–6 summarise the current literature on this subject.

4. Urethral pain syndrome

Urethral pain syndrome is diagnosed in patients presenting with dysuria, with or without frequency, nocturia, urgency and urge incontinence in the absence of evidence of urinary infection.

It is germane that the methods typically used to identify urinary infection are extremely insensitive and some patients may have genuine infection that has not been recognised. Modern automated laboratory methods will not detect colony counts below 10^4 colony

Table 5

Medical treatment of IC

	Level of evidence	Grade of recommendation	Comment
Analgesics	4	C	Indications limited to cases awaiting further treatment
Corticosteroids	3	C	Corticosteroids not recommended as long-term treatment
Hydroxyzine	2b	B	Standard treatment
Cimetidine	1b	A	Preliminary data so far
Amitriptyline	1b	B	Standard treatment
Sodium PPS	1a	A	Standard treatment
Antibiotics	1b	A	Limited role in the treatment of IC
Prostaglandins	3	C	Insufficient data on IC, adverse effects
L-arginine	1b	C	Effect in IC uncertain
Immunosuppressants	3	C	Insufficient data on IC, adverse effects
Oxybutynin	3	C	Limited indication in IC
Tolterodine	3	C	Limited indication in IC
Gabapentin	3	C	Preliminary data so far
Suplatast tosilate	3	C	Preliminary data so far
Quercetin	3	C	Preliminary data so far

Table 6

Intravesical, interventional, alternative and surgical treatment of Interstitial cystitis

	Type of evidence	Nature of recommendation	Comment
Intravesical anesthetics	3	C	
Intravesical pentosanpolysulfate (PPS)	1b	A	
Intravesical heparin	3	C	
Intravesical hyauronic acid	3	C	
Intravesical dimethyl sulfoxide (DMSO)	1b	A	
Intravesical Bacillus Calmette-Guérin (BCG)	1b	Not recommended beyond clinical trials	Data contradictory
Intravesical clorproctin	3	Not recommended	Obsolete
Intravesical vanilloids	1b	Not recommended beyond clinical trials	Insufficient data on IC
Bladder distension	3	C	
Electromotive drug administration (EMDA)	3	B	
Transurethral resection (TUR), coagulation and LASER	n.a.	A/B	Hunner's ulcers only
Nerve blockades/epidural pain pumps	3	C	For crisis intervention, effect on pain only
Sacral neuromodulation	3	B	Not recommended beyond clinical trials
Bladder training	3	B	Patients without pain
Manual and physical therapy	3	B	
Diet	3	C	
Acupuncture	3	C	Data contradictory
Hypnosis		No data	
Psychological therapy	3	B	
Surgical treatment	n.a.	A	Ultima ratio, experienced surgeons

n.a. = not applicable

forming units per ml (cfm/ml) of urine, when in the presence of symptoms an appropriate diagnostic threshold should be 10^2 cfm/ml. Nearly one third of acutely dysuric women with urinary infection caused by *Escherichia coli*, *Staphylococcus saprophyticus* or *Proteus spp.* have mid-stream urine colony counts in the range 10^2 to 10^4 cfm/ml [38–40].

Urethral trauma arising from intercourse may cause pain and dysuria. Women with pelvic floor dysfunction describe the symptoms as do postmenopausal women.

5. Scrotal pain syndrome

Acute scrotal pain includes torsion of the testis and appendices and requires immediate diagnostic and therapeutic attention. In contrast, chronic scrotal pain is a symptom that has lasted at least six months. It can be unilateral or bilateral, continuous or intermittent.

In order to clarify the diagnosis, each component of the scrotum should be palpated and, if possible the site of the pain should be localised. A digital rectal examination is mandatory and the integrity of the pelvis and spine should be checked. It is essential to perform ultrasonography of the scrotal contents to seek for lesions within the testicular parenchyma and epididymis. Ultrasound should also include examination of the prostate, upper urinary tract and bladder. The urine should be analysed. MRI and CT scans are optional

[41]. The differential diagnoses to consider include chronic epididymitis, painful cystic lesions, sequelae following trauma or orchitis or pain referred from prostatitis, prostate cancer, anorectal disorders or distal ureteric stones.

5.1. Medical treatment

The first-line treatments in chronic epididymitis are antibiotics and nonsteroidal anti-inflammatory drugs. Patients with extragenital disease are treated according to the cause. Patients without identifiable lesions have to be treated conservatively, using antibiotics and methods for managing chronic pain. It is not unusual to be unable to find an explanation for chronic scrotal pain.

If microcalcifications are identified in the testes during the assessments, the patients should be followed up, not because the calcifications have anything to do with the symptoms but because there is a slight chance of the development of testicular cancer [42].

5.2. Surgical treatment

A surgical procedure will cure an average of 50% of patients with an identifiable intrascrotal lesion [43–46], with superior results from painful hydrocoel, spermatoceol and varicoceol. Surgery is also the method of choice in chronic epididymitis associated with recurrent urinary infection and urethral stricture, in this specific case to ablate the stricture. Postvasectomy pain, like chronic epididymitis or sperm granuloma

may also be accessible to surgical management. Post-hernia repair orchalgia with presumed nerve entrapment will require surgical exploration when all other means have failed. In patients with chronic orchalgia where no cause has been found surgery may be contemplated but the results are not good [43]. Favourable results have been reported from microsurgical testicular denervation [47].

6. Pelvic pain in gynaecological practice

Pelvic pain presenting to the gynaecologist will feature a remedial cause in approximately 70% of cases, leaving 30% unexplained [48]. Clues to the aetiology are provided by the history, including the nature, frequency and site of the pain, precipitating factors, effect of the menstrual cycle, a record of sexually transmitted diseases, vaginal discharge and sexual trauma. Abdominal and pelvic examination will exclude gross pathology as well as demonstrating the site of any tenderness. Vaginal and endocervical swabs may identify pathogens. Cervical cytology screening is advised. Pelvic ultrasound should always be used, MRI where indicated. Laparoscopy is the most useful invasive investigation [49,50].

Primary dysmenorrhoea begins with the onset of ovulatory menstrual cycles and tends to decrease following childbirth. Secondary dysmenorrhoea suggests a pathological process such as endometriosis and pelvic infection.

Endometriosis is suggested by a history of secondary dysmenorrhoea and often dyspareunia, with reduced uterine mobility, and sometimes adnexal masses. The bladder, ureter and bowel may be involved. Endometriosis may be halted, but not cured, by hormone treatment. The best surgical results are achieved laparoscopically in specialist centres. Despite extensive surgery, pain may persist.

Chronic pelvic pain may arise from gynaecological malignancy or childbirth-related injuries. It is essential to consider pain associated with urinary and gastrointestinal disease.

7. Pelvic floor and pudendal nerve

The pelvic floor has three functions; support, contraction and relaxation. Underactive pelvic floor muscles result in urinary and faecal incontinence and pelvic organ prolapse. Overactive muscles may result in high outflow resistance producing low urinary flow rates, obstructed defaecation and dyspareunia [51,52].

Pelvic floor overactivity is thought to be a major factor contributing to chronic pelvic pain. The cycle usually starts with increased muscle tension which may arise from several causes. Pelvic floor muscle overactivity results in several symptoms including pain which in turn causes anxiety and distress that aggravate and perpetuate the muscle contraction.

Pudendal nerve entrapment leading to chronic compression of the pudendal nerve arise pelvic floor anomalies. It can result in a perineal pain located either anteriorly in the vagina and vulval region, or posteriorly in the anorectal region. It is suggested by a one-sided, burning sensation, exacerbated by unilateral rectal palpation which may be associated with delayed pudendal motor latency on the painful side. Pain associated with denervation and reinnervation may be caused by many lesions of the pelvic organs other than dysfunction of the pelvic floor muscles.

Magnetic resonance imaging (MRI) is the investigation of choice to show both neural tissue and surrounding structures. The examination should include scrutiny of the anatomy along the course of the pudendal nerve.

Improvement in pelvic floor muscle function can be achieved by pelvic floor education, including such techniques as pelvic floor relaxation and biofeedback.

7.1. Psychological factors in chronic pelvic pain

Psychiatric disorders may be involved in some cases of chronic pelvic pain including somatisation and somatoform disorders. These are characterised by physical symptoms that cannot be accounted for by a general medical condition, the effect of a substance or mental disorder. They cause clinically significant distress and impairment [53].

Somatisation is an avoidance coping strategy. Childhood physical and sexual abuse are strongly associated with later somatisation [54], including chronic pelvic pain. When no reasons for chronic pelvic pain have been identified it is important to ask about physical and sexual abuse when taking the history because of the consequences for the therapy chosen. On the other hand, chronic pelvic pain must not be used to stigmatise patients as being abused when no such history is forthcoming.

Depression is a state of significantly decreased emotional, psychological and social functioning with neurovegetative symptoms lasting at least two weeks. A subclinical depression is often overlooked in both men and women and can worsen or prolong chronic pelvic pain [55].

8. General treatment of chronic pelvic pain

8.1. Analgesia

Clinical trial evidence is signally lacking in this field. Whilst paracetamol should be considered for mild pain, research is needed to define its role in chronic pelvic pain [56]. There are very few data on the use of NSAIDs and even less on COX2 selective drugs with studies focused on dysmenorrhoea. However, this subject is inchoate and lack of data should not necessarily be seen as indicative of futility.

Non-selective, low potency NSAIDs should be used first and are most likely to be helpful when the pain has an inflammatory component. More potent NSAIDs should be used only when low-potency drugs have failed to be helpful. COX2 selective drugs are an alternative to non-selective drugs in patients with an increased risk of gastric complications such as those over 65 years of age, receiving prolonged, high-dose therapy, taking other medications that may induce gastrointestinal bleeding or with a previous history of gastrointestinal problems. NSAIDs should be taken with food and, if appropriate, gastric protective agents. The benefits of the NSAIDs must outweigh the risks. All NSAIDs are contraindicated in active gastrointestinal ulceration/bleeding and renal disease and may seriously exacerbate asthma and produce fluid retention. If stronger analgesics are needed, NSAIDs may be continued because of their synergistic action with opioids in controlling pain [57,58].

Opioids have a role in chronic non-malignant pain [59] but their use in urogenital pain is not well studied. All other reasonable treatments must have been tried and failed. The addictive nature of opioid medication means that various safeguards must be followed and the decision to instigate long-term opioid therapy should be made by an appropriately trained specialist in consultation with another physician, preferably the patient's primary care doctor. Morphine is the first-line drug unless there are contraindications or special indications for another drug. The drug should be prescribed in a slow-release form.

The neuropathic analgesics; tricyclic antidepressants or anticonvulsants may be more helpful in patients with nerve injury or central sensitisation. Serotonin reuptake inhibitors are less effective than tricyclic antidepressants. In some countries gabapentin is licensed for use in chronic neuropathic pain and is said to produce a more natural sleep state at night than the antidepressants [60]. Many practitioners no longer use carbamazepine because of its potentially serious side effects.

The N-methyl-D-aspartate (NMDA) receptor complex is an important channel for development and maintenance of chronic pain. The NMDA antagonist, ketamine may be helpful in nerve injury or central sensitisation [61], opioid-resistant pain [62] and intractable pelvic cancer pain. Ketamine is highly addictive and great care is required if a patient is to be managed at home on parenteral ketamine.

A change in the number, distribution and type of sodium channels can result in altered mechanosensitivity, thermosensitivity and chemosensitivity [63]. Thus low plasma doses of the sodium channel blocker, lidocaine have been used to reduce neuropathic pain and sensory phenomena without any effect on nociception [64,65]. Infusions must be performed by trained practitioners. A single infusion may have benefit for several months. The oral analogue, mexiletine may be helpful in similar circumstances.

8.2. Nerve blocks

These specialist procedures may be performed for diagnostic reasons and therapeutic benefit. Nerve blocks should be performed as part of a pain management package and not in isolation. Neurolytic blocks are rarely indicated for benign processes and to proceed with one may induce terrible consequences.

8.3. Transcutaneous electrical nerve stimulation (TENS)

Surface electrical nerve stimulation relieves pain by stimulating myelinated afferents and thereby activating segmental inhibitory circuits. Urinary frequency may also be reduced. Continuous stimulation seems preferable for treating pain. The maximum tolerable intensity just below the pain threshold should be used. The frequencies used vary widely from 1 to 100 Hz. Clinical experience suggests starting with the higher frequencies as the best option. The standard recommendation has been 0.5 to 2 hours treatment twice daily. In bladder pain syndrome suprapubic, vaginal-anal and tibial nerve sites have been tested using TENS, all with some success. The outcome is better in classical ulcer disease [66,67].

8.4. Sacral neuromodulation

Sacral root is based on the observation that electrical stimulation of sacral nerves modulates neural reflexes in the pelvis. It may benefit patients with refractory motor urge incontinence, urinary retention, chronic pelvic pain, neuropathic pain and complex regional pain syndromes as well as bladder pain syndrome and refractory pelvic floor dysfunction and pelvic pain [68–70].

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