Chronic Pelvic Pain

PD Dr. med. Daniel S. Engeler

Department of Urology
Interdisciplinary Pelvic Floor Centre
Kantonsspital St. Gallen
Switzerland

daniel.engeler@kssg.ch

1

Chronic pelvic pain: What are we talking about

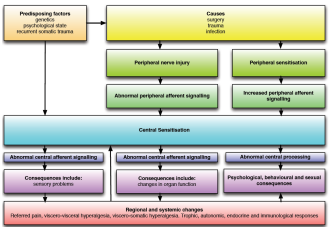
2

CPP Introduction

- In the past: focus on periphery (inflammation, infection)
- Animal and clinical research: many of the mechanisms based within the CNS
- Peripheral stimulus may initiate -> self-perpetuation as a result of CNS modulation

3

Pain and the Brain



© European Association of Urology

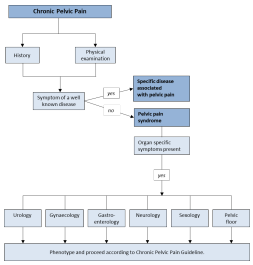
4

Visceral vs Somatic

	Visceral	Somatic
Stimuli	Stretching Distension Poorly localized	Mechanical Well localized
Summation	Magnifying pain	Modest increase pain
Referred pain	Common	Rare
Innervation	Unmyelinated C-fibres, thin Aδ fibers	Wide range of fibers
Primary afferent physiology	Intensity coding	Two fibre coding

5

Algorithm



EAU Guidelines on CPP

6

Kantonsspital St.Gallen

Chronic Pelvic Pain

Definition of a Pain Syndrome

- Chronic pelvic pain syndrome is the occurrence of chronic pelvic pain
  - when there is no proven infection or other obvious local pathology that may account for the pain.
  - It is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract, sexual, bowel or gynaecological dysfunction.

EAU Guidelines on CPP

7

Kantonsspital St.Gallen

Chronic Pelvic Pain

The pain syndromes

Subdivision	End-organ as pain syndrome as identified from Hx, Ex, Ix
Urological	Prostate, Bladder, Scrotal, Testicular, Epididymal, Penile, Urethral, Postvasectomy
Gynaecological	Vulvar, Vestibular, Clitoral, Endometriosis associated, CPPS with cyclical exacerbations, Dysmenorrhoea
Gastrointestinal	Irritable bowel, chronic anal, intermittent chronic anal
Peripheral nerves	Pudendal
Sexological	Dyspareunia, pelvic pain with sexual dysfunction
Psychological	Any pelvic organ
Musculo-skeletal	Pelvic floor muscle, abdominal muscle, coccyx

EAU Guidelines on CPP

8

Kantonsspital St.Gallen

Chronic Pelvic Pain

Treatment Rationale for Chronic Pelvic Pain

9

Kantonsspital St.Gallen

Chronic Pelvic Pain

First Step:
Explain to the Patient what Chronic Pain is

- He/She has to be informed about the nature of chronic pain
  - Not just a symptom of disease
  - Chronic pain as a "Disease in its own right" (IASP)
  - Peripheral and central sensitisation
  - Psychological components

Engeler DS et al. Eur Urol 2013

10

Kantonsspital St.Gallen

Chronic Pelvic Pain

Second Step: Discuss Realistic Treatment Aims

- Complete cure is only rarely reached
  - Chronic pain should be relieved to a level patients can accept to live with
    - e.g. Pain of a VAS 6-7 to VAS 2-3
- Try to target associated problems
  - e.g. micturition problems, erectile dysfunction

Engeler DS et al. Eur Urol 2013

11

Kantonsspital St.Gallen

Chronic Pelvic Pain

Third Step: Phenotype Targeted Therapy

UPOINT description	Suggested therapies
Urinary	
NIH CPSI urinary score >4	Antimuscarinics
Obstructive voiding symptoms	α-Blockers
Bothersome urgency, frequency, and/or nocturia	
Elevated postvoid residual	
Psychosocial	
Clinical depression	Counselling
Evidence of maladaptive coping	Cognitive behavioural therapy
Anxiety/stress	Antidepressants
	Anxiolytics/pain
Organ specific	
Specific prostate tenderness	α-Blockers
Leukocytosis in prostatic fluid	5-α-Reductase inhibitors
Haematospermia	Physiotherapy
Extensive prostatic calcification	Prostate massage
Infection	
Gram-negative bacilli or enterococci localized to prostatic fluid	Antimicrobials
Documentation successful response to antimicrobial therapy	
Neurologic/systemic conditions	
Evidence of central or central sensitization	Neuromodulators
Pain beyond pelvic	Specific therapies for associated conditions
Irritable bowel syndrome	
Fibromyalgia	
Chronic fatigue syndrome	
Tenderness of skeletal muscles	
Palpable tenderness and/or painful muscle spasm or trigger points in abdomen and/or pelvic floor	Focused pelvic physiotherapy
	General physiotherapy
	Exercises

NIH CPSI = National Institutes of Health Chronic Prostatitis Symptom Index; UPOINT = Urinary, Psychosocial, Organ specific, Infection, Neurologic/systemic, and Tenderness.
Exclude patients with clinical category 3 or 2 prostatitis.
Adapted from Nickel and Shoskes [36].

Adapted from Nickel JC et al. Current Urol Rep 2009; 10:307-12 in Engeler DS et al. Eur Urol 2013; 64:431-9.

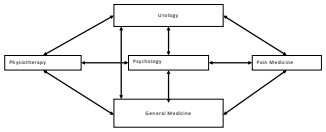
12

Kantonsspital St.Gallen

Chronic Pelvic Pain

Forth Step: Early Interdisciplinary Management of CPPS

- Like for the management of other chronic pain a holistic approach by a multidisciplinary team is recommended



13

Kantonsspital St.Gallen

Chronic Pelvic Pain

Do Not Repeat: Negative Diagnostic Tests or Ineffective Therapy

- The chance is very low that repeat diagnostics will lead to any new results or change management
- Repeating ineffective therapy puts the patient to a higher risk of adverse effects and leads to higher cost
  - Almost always it won't work better the second time
    - e.g. multiple antibiotic use leads to resistance
  - Sometimes repeating ineffective therapy gives a wrong psychological signal to the patient
    - e.g. "there must be some persisting bacteria causing the chronic pain"

14

Kantonsspital St.Gallen

Chronic Pelvic Pain

An example

Clinical Management of Bladder Pain Syndrome/Interstitial Cystitis (BPS/IC)

15

Kantonsspital St.Gallen

Chronic Pelvic Pain

BPS/IC: Diagnosis

1) Patient selection
   - Chronic (>6 months) pelvic pain, pressure or discomfort perceived to be related to the urinary bladder
   - Accompanied by at least one other urinary symptom (persistent urge to void or frequency)
2) Exclusion of confusable diseases
   - Medical history, physical, urinalysis/urine cultures, PSA (>40y), uroflowmetry, post-void residual
   - Cystoscopy/Bladder-Bx
3) Classification/phenotyping

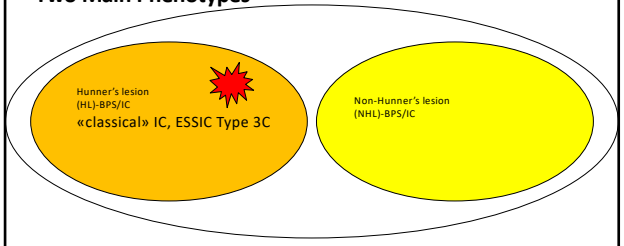
Von de Merwe JP, Nordling J, et al. Eur Urol 2008; 53:60-7

16

Kantonsspital St.Gallen

Chronic Pelvic Pain

Two Main Phenotypes



17

Kantonsspital St.Gallen

Chronic Pelvic Pain

Why are the Phenotypes Important?

Because they MAKE THE DIFFERENCE

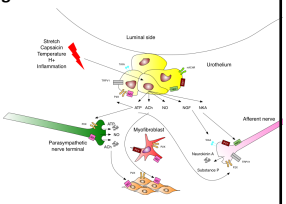
- Aetiology/pathophysiology
- Epidemiology
- Clinical and pathological features
- Response to treatment
- Complications

18

Kantonsspital St.Gallen | Chronic Pelvic Pain

Peripheral Changes in BPS:
Interconnection between physiological Urge and Pain

- Changes in chemical communication between urothelium and capsaicin sensitive C-fibre afferents may be responsible for afferent sensitisation
- Silent fibers (50-90%) become active
- Intensity coding of afferent fibers – increase in sensation leads finally to pain
  - Urge ➔ Pain



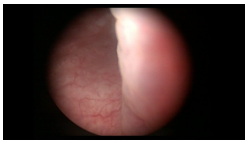
Sun Y, et al. J Urol 2001;166:1951–1956

19

Kantonsspital St.Gallen | Chronic Pelvic Pain

Rigid cystoscopy under general anaesthesia

- Reddend mucosal areas with small vessels radiating toward a central scar ➔ Hunner's lesion

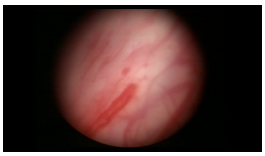


20

Kantonsspital St.Gallen | Chronic Pelvic Pain

Rigid cystoscopy under general anaesthesia

- Tears and oozing of blood (waterfall bleeding) after distention

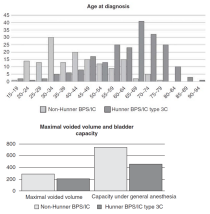


21

Kantonsspital St.Gallen | Chronic Pelvic Pain

Phenotypic Differences

Feature	HL-BPS/IC	NHL-BPS/IC	P
Mean Age [y]	62	42	<0.001
Mean voided volume [ml]	206	289	<0.001
Mean bladder capacity under anaesthesia [ml]	459	743	<0.001



Logadottir Y, Fall M, et al. Scand J Urol Nephrol 2012; 46:365-70

22

Kantonsspital St.Gallen | Chronic Pelvic Pain

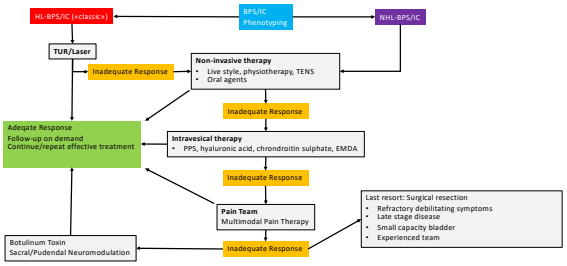
Treatment Rationale

- Similar basic approach
  - BPS/IC should be treated as a chronic pain syndrome
  - Patient information and expectations important
  - Early involvement of a pain team
  - Holistic approach
- Specialized treatment differs between phenotypes

23

Kantonsspital St.Gallen | Chronic Pelvic Pain

Treatment Algorithm



24

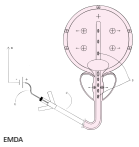
Non-invasive/Conservative Therapy

- Treatment should be tailored to the individual patient and phenotype
- Live style/behavioural changes
- Physiotherapeutic approaches targeting pelvic pain and pelvic floor dysfunction
- Psychological interventions directed at pain itself or adjustment to pain
- Oral medical therapy
  - Amitriptylin
  - Pentosane polysulfate

25

Intravesical Instillations

- In use for about 25 years
- For local anaesthesia or GAG-layer replenishment
- Different compounds and regimens (on and off-label use) including local anaesthetics, heparin, pentosane polysulfate, hyaluronic acid, chrondroitin sulphate
- Electromotive Drug Administration (EMDA) may be used for better penetration
- Overall only weak recommendation for their use but should be tried before proceeding to more invasive treatment options



Madersbacher H, et al. Neurourol Urodyn 2013; 32:9-18
Fontanella UA, et al. BJU 1997; 79: 414-20

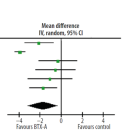
26

Intradetrusor Botulinumtoxin A

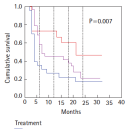
Forest plot of changes in pelvic pain (VAS)

Study or subgroup	BTX A Mean	BTX A SD	BTX A Total	Control Mean	Control SD	Control Total	Weight	Mean difference IV, random, 95% CI
Akiyama 2015	−2.2	2	18	−0.1	2.1	16	17.3%	−2.10 [−3.48, −0.72]
Gao 2015	4.2	1.7	66	8.1	1.2	58	20.1%	−3.90 [−4.41, −3.39]
Kayan 2012	5.8	2.4	15	6.1	2.8	17	15.5%	−0.30 [−2.10, 1.50]
Kao 2009 100U	2.97	1.99	29	3.52	3.07	12	15.2%	−0.55 [−2.43, 1.33]
Kao 2009 200U	2.47	2.1	15	3.52	3.07	11	14.3%	−1.05 [−3.15, 1.05]
Kao 2015	−2.6	2.8	40	−0.9	2.2	20	17.6%	−1.70 [−3.00, −0.40]
Total (95% CI)			**183**			**134**	**100.0%**	**−1.73 [−3.16, −0.29]**

Heterogeneity: Tau² = 2.61; Chi² = 35.78, df = 5 (P < 0.00001); I² = 86%
Test for overall effect: Z = 2.35 (P = 0.02)



Treatment success



Treatment
HD
Botox 100U+HD
Botox 200U+HD

- BTX A → Neuromuscular transmission, Afferents?
- Several studies available (incl. RCTs and SR/MAs)

Conclusions

- Intravesical BTX injections might offer significant improvement in bladder pain symptoms, daytime urination frequency, and MCC for patients with refractory BPS/IC

Kuo HC, et al. BJUI 2009;104:657-62
Wang J, et al. Med Sci Monit 2016; 22:3257-67

27

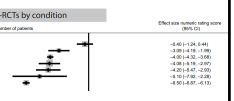
Neuromodulation

Systematic Reviews on Published Data on Outcome of SNM in BPS/IC

Published data on the outcome of sacral neuromodulation for BPS/IC

References	Subtypes	Pts	Pts	Duration of Tests Follow-up	% Success PN	% Success 2 Elements Analysis	% Permanent Implant	Mean Max Follow-up	Treatment Success/ Major Impact
Maher et al.[27]	Global PM 2.0	15	1.0-3 Days	6	—	—	—	—	—
Chai et al.[28]	Stage PM 3.0	9	5 Days	Not available					
Peters KM, Rev Urol 2003 & 100	PNE + stages 3.0	20	2 Weeks	10 (4-22)	90 (14/16)	87	—	—	Pain statistically improved in 70% + markedly improved in 30%
Zermann[29]	Stage PM 3.0 + similar stages 3.0	35	4 Days	40	34/35	97 (33/34)	80	14	Mean reduction in VAS pain scores by 72%
Zermann et al.[30]	Stage 3.0	12	Not available	—	—	—	—	—	
Chelimsky, RC, Urology 2005	Stage 3.0	15	Not available	—	—	—	Not available	14	Reduction in Groups Distress Inventory, 43% mean decrease in postintervent scores (p < 0.05)
Peters et al.[31]	Pudendal or S3 stimulation	22	1 Week	—	—	—	77	9	Mean VAS pain score decreased 49% (vs 3%&6.5% for PNE)
Powell and Kinder[32]	PNE + stages 3.0	35	1-3 Wks	40 (12-83)	31.5 (10/15)	56	60	10	Mean reduction in VAS pain by 75%, 65% free of pain scores
Hachiya et al.[33]	Stage 3.0	10	Not available	—	50	50	57	12	Mean reduction in VAS pain scores by 50%
Siepmann and Al-Zahrani[34]	Global PM 3.0	19	3-7 Days	67	—	—	50	60	Long-term success in 73%

B Forestplot of non-RCTs by condition



Conclusions

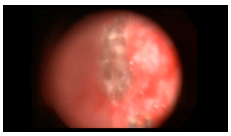
- Promising results of small series, but overall insufficient evidence to determine the role of SNM → Larger prospective trials with long-term evaluation needed
- SNM may be a treatment option in cases where reversible functional problems exist and noninvasive therapy was ineffecive

Marcelissen T et al. J Urol 2011; 186:387-93
EAU CPP Guideline panel SR, Cottrell AM,Engeler DS et al Eur Urol Focus 2019 Oct 18

28

HL-BPS/IC: Laser Coagulation/Resection

- Larger series for transurethral resection or laser coagulation of Hunner's lesions exist
- Symptom improvement in a high proportion of patients up to three years
- Can be repeated



Kerr WS. J Urol 1971; 105:664
Peeker R, et al. Urogynecol J Pelvic Floor Dysfunct 2000;11:290-5
Rofeim O, et al. J Urol 2001; 166:134

29

Cystectomy

- Different techniques
  - Supratrigonal cystectomy with augmentation (HL-BPS/IC), subtrigonal cystectomy with orthotopic neobladder, cystectomy + ileal conduit
- Last resort, but may be very relieving for the patient with irreversible bladder dysfunction ("organ failure")
- Only for experienced team

30

Conclusions

- Managing patients with CPP remains a chalenge
- It is important to look at it as a PAIN SYNDROME
- Explain to the patient what CPP is
- Adapt treatment to the phenotype
- Whenever possible: Use multimodal and interdisciplinary/interprofessional approaches

31