

Chronic pelvic pain of unknown origin may be caused by loose uterosacral ligaments failing to support pelvic nerve plexuses – a critical review

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Citation: Enache T, Bratila E, Abendstein B. Chronic pelvic pain of unknown origin may be caused by loose uterosacral ligaments failing to support pelvic nerve plexuses – a critical review. Cent European J Urol. 2020; 73: 506-513.

Article history

Submitted: Oct. 12, 2020

Accepted: Oct. 21, 2020

Published online: Dec. 14, 2020

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Introduction Chronic pelvic pain of unknown origin (CPPU) affects the quality of life (QoL) of up to 20% of women. The 2005 Cochrane Review, based on randomized controlled trials (RCTs), stated that the pathogenesis of CPPU is poorly understood and its treatment is empirical and ineffective. Totally ignored were the high cure rates from uterosacral ligament (USL) repair, the principal subject of this review.

Material and methods We carried out a review of literature on USL causation, diagnosis, and treatment of CPPU, selecting only the literature relevant to USL.

Results The first mention of CPPU being caused by lax USLs was in the pre-WWII German literature by Heinrich Martius. In 1993, CPPU was described as one of the 4 pillars of the posterior fornix syndrome (PFS- CPPU, urgency, nocturia, abnormal bladder emptying). Cure/improvement of CPPU was reported by widely geographically separated surgical groups using squatting-based pelvic floor exercises and by shortening and reinforcing USLs with tension tapes, literally a reverse transvaginal tape. Patients can potentially be cured either by native tissue ligament repair or in older women a posterior sling can be tested using a speculum test or even menstrual tampons.

Conclusions This technology, based on USL pathogenesis, which can be tested for potential cure, non-surgical or surgical, offers hope for women for a condition previously considered incurable. Chronic pelvic pain, bladder and bowel incontinence occur in predictable symptom groupings, which are associated with apical prolapse. USL repair, whether native tissue or (preferably) using a posterior sling has the potential to improve clinical practice, QoL for women and open new research directions.

Key Words: chronic pelvic pain of unknown origin ↔ Integral Theory ↔ pelvic floor disorders
↔ posterior fornix syndrome ↔ overactive bladder ↔ Allen-Masters syndrome

INTRODUCTION

The 2005 Cochrane Review summarized chronic pelvic pain as follows “Chronic pelvic pain (CPP) is common in women in the reproductive and older age groups and causes disability and distress. Often, investigation by laparoscopy reveals no obvious cause for the pain. As the pathophysiology of chronic pelvic pain is not well understood, its treatment is often unsatisfactory and limited to symptom relief. Currently the main approaches to treatment include

counseling or psychotherapy, attempts to provide reassurance by using laparoscopy to exclude serious pathology, progesterone therapy such as medroxyprogesterone acetate, and surgery to interrupt nerve pathways” [1].

The association between pain, depression, and psychological disturbance is well described [1–4].

The present trend for psychiatric evaluation and treatment appears to have arisen because of previous studies that showed a high correlation between chronic pelvic pain of unknown origin (CPPU) and

psychiatric disturbances [6]. Pelvic congestion as originally proposed by Beard is considered a major cause of CPPU [6]. Traditionally, hysterectomy has been recommended as a cure for chronic pelvic pain by a significant body of specialist opinions [7]. No pathogenic basis with reference to pain is described for this treatment.

Renowned institutions do not consider symptoms of chronic pelvic pain of unknown origin to be surgically curable [8]. Recent studies [9] confirm Heinrich Martius's 1938 assertion [10] that CPPU in which no obvious cause is evident is mainly caused by loose uterosacral ligaments; hence, it is potentially curable surgically by repairing such ligaments. This type of CPPU generally coexists with one or more symptoms of bladder and bowel dysfunctions that may occur even with minimal apical prolapse [10].

The work of Heinrich Martius [10] on the role of loose uterosacral ligaments in the causation of chronic pelvic pain were recently brought into light by Klaus Goeschen.

In 2015, Goeschen mentioned that Heinrich Martius published papers in which he stated that backaches are provoked by damaged suspending or supporting ligaments of the pelvic organs. Therefore, the paired 'Ligamenta rectouterina', which are connected via paraproctium to the bony sacrum and in general are termed 'plica or ligamenta sacrouterina' or 'uterosacral ligaments' (USL), are placed in the centre of numerous pathophysiological considerations [11]. The first mention of USL causation of CPPU was in 1993, when Petros and Ulmsten independently described CPPU as being caused by lax uterosacral ligaments as part of the 'posterior fornix syndrome' (CPPU, nocturia, urgency, abnormal emptying with increased post-void residual urine) [12]. Subsequently, CPPU in PFS also involves vulvodynia, lower abdominal pain, and low sacral backache. More recently, obstructed defecation and faecal incontinence were also included in PFS. They reported a significant cure rate of CPPU and other posterior fornix symptoms following repair of the uterosacral ligaments. In the 1996 ANZJOG, Petros reported CPPU in many young nulliparous women, some of whom were admitted as emergencies because of the severity of the pain. All without exception had normal laparoscopic findings [13]. At 3 months, 85% of patients' symptoms improved following plication of the USLs and 70% at 12 months.

The modern definition of chronic pelvic pain that is accepted by the International Association for the Study of Pain (ISAP) is the one constructed and used by the European Association of Urology (EAU) guideline: 'Chronic pelvic pain is chronic or persistent pain perceived in structures related to the pelvis

of either men or women. It is often associated with negative cognitive, behavioral, sexual, and emotional consequences as well as with symptoms suggestive of lower urinary tract, sexual, bowel, pelvic floor or gynecological dysfunction' [14].

Messelink's view on management is enlightened [14], especially in light of the commonly held view [5] that the cause of CPPU is psychological (Figure 1). He stated that chronic pelvic pain requires an integral approach, based on the principles of non-organ based terminology and pain mechanisms, provided by a team of experts with the patient at the best place on the discussion table. Moreover, he also mentioned that pelvic pain is quite a private subject and that physicians are the guests and the patient is the host who lets them look into her life. In addition, that is what makes caring for patients with pelvic pain, based on an integral approach, so special. At the same time, Messelink also stated that chronic pelvic pain is a rather young area of interest in the world of pain. He considers it an area changing quite rapidly. He sees pain in the pelvic area primarily as pain that needs to be addressed. Moreover, physicians have to realize that patients with pelvic pain have to deal with changes in voiding, defecation, and sexual functioning. This makes every pelvic pain patient unique for the caregiver. An open-minded

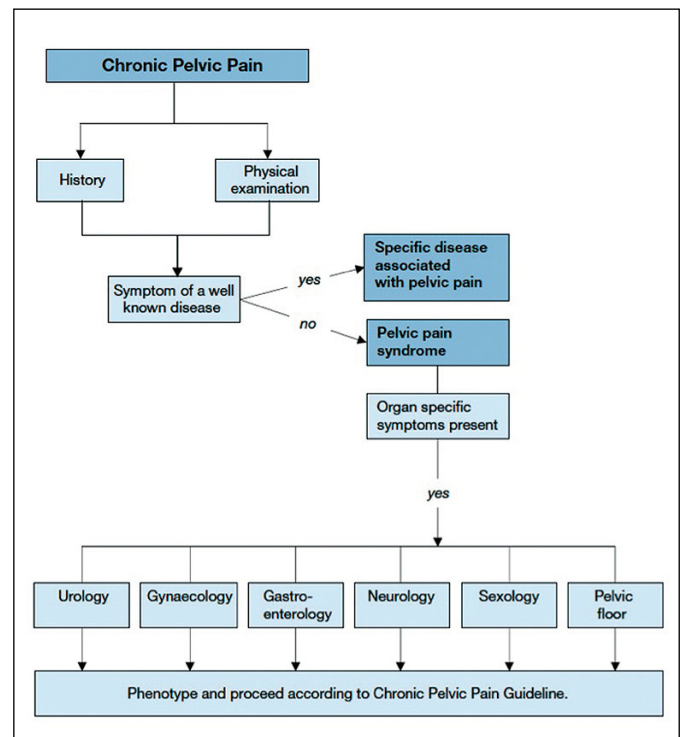


Figure 1. EAU Guideline Chronic Pelvic Pain, 2016. Source: Messelink B. *Perspective Pelviperineology*. 2017; 36: 67-70 (published with permission).

approach of listening in an atmosphere in which a patient feels heard, is the basis for all that is said, taught, and discussed about chronic pelvic pain [14] (Figure 1).

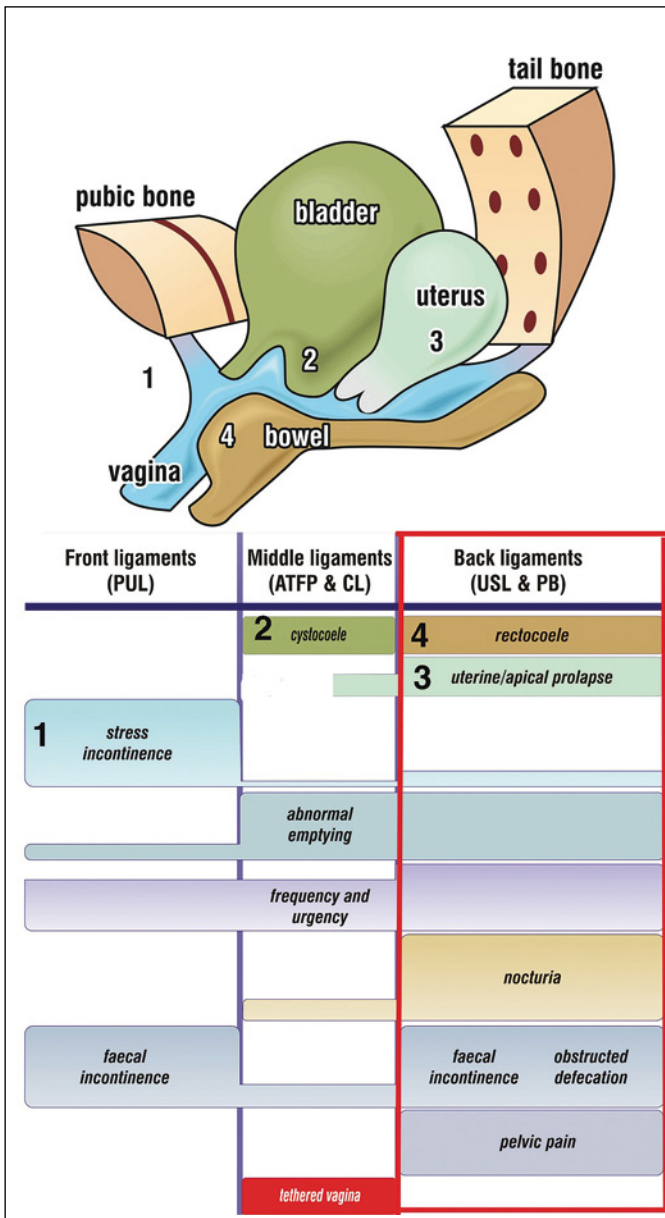


Figure 2. The Pictorial Diagnostic Algorithm – co-occurrence of pain with bladder and bowel symptoms with USL damage. The size of the bar correlates broadly with the site and probability of symptom causation. The posterior zone (red rectangle) indicates the symptoms associated with uterosacral (USL) ligament looseness. These occur in predictable groupings (red rectangle). The main ligaments are indicated in capital letters: PUL ‘pubourethral ligament’, (front ligaments); ATFP ‘arcus tendineus fascia pelvis’, CL ‘cardinal ligament’ (middle ligaments); USL ‘uterosacral ligament’, PB ‘perineal body’ (back ligaments).

Messelink’s statement “The patient with chronic pelvic pain deserves an integral approach [14] crystallizes the essence of this review, that CPPU in females is usually associated with other symptoms which have their origin in loose USLs” ‘back ligaments’? (Figure 2), which also serves as the guideline for diagnosis and management (Figure 2) [10, 12].

MATERIAL AND METHODS

We carried out a review of literature on USL causation, diagnosis, and treatment of CPPU, selecting only the literature relevant to USL. The literature outlines the failure of society and the medical profession to recognize the devastating effects of CPPU on patients’ lives. Moreover, we analyzed a study of Kurdoglu et al. regarding the short-term results of changes concerning the urinary tract symptoms after robot-assisted laparoscopic uterosacral ligament suspension (RALUSLS) and sacrocolpopexy (RALSC) [39].

Further, we analyzed the possibility that chronic pelvic pain is caused by Allen-Masters syndrome [41]. The differences between the Allen-Masters syndrome (AMS) and posterior fornix syndrome (PFS) are the following: for AMS – pelvic congestion, pelvic pain, menstrual disturbances, dyspareunia, fatigability, pain during intercourse, sore back, causes muscle damage at birth, and for PFS – urge, frequency, nocturia, abnormal emptying with increased post-void residual urine, chronic pelvic pain (includes AMS descriptions but also vulvodynia, lower abdominal pain, low sacral backache) and, more recently, obstructive defecation and fecal incontinence, causes USL laxity (often with only minor prolapse) failing to support nerve plexuses in USLs – age, birth, hysterectomy related sometimes congenital.

Pelvic congestion and menstrual disturbances have not been described in PFS. Also, these symptoms can be cured or improved by shortening and reinforcing the lax USLs.

RESULTS

Petros and Goeschen underlined that the cause of chronic pelvic pain of unknown origin originated from the S2-S4 sacral plexus and Th11-L2 Frankenhauer plexus, both of which are supported by the uterosacral ligaments (USL) and near their insertion into the cervical ring [13, 15].

Regarding the diagnosis of CPPU [9], USL caused pain can occur in the following forms: persistent abdominal pain in the lower part of the body, often unilateral (Th11-L2); low sacral pain (S2-S4); paraurethral pain and tenderness (S2-S4); introital, perineal

pain (vulvodynia) (S2-S4); dyspareunia (S2-S4) and postcoital pain (Th11-L2); asthenia; irritability.

Petros [13] wrote a classic description of the pain “In its acute state of manifestation, the pain was invariably severe, frequently one-sided, situated low in the right or left iliac fossa, usually relieved on lying down, frequently relieved by insertion of a ring pessary, reproducible on palpating the cervix and displacing it posteriorly with the patient in the supine position. Although the pain was chronic in nature, it varied considerably from time to time as concerns intensity. Almost all patients complained of tiredness and irritability by the end of the day. The symptom of deep dyspareunia was not often volunteered. The pain only occurred on deep penetration, or in specific positions. Frequently the patient complained of a constant lower abdominal pain the day after intercourse. Again, palpation of the cervix generally reproduced the pain experienced during intercourse.”

As far as the association of other symptoms is concerned, as an important diagnostic feature for CPPU, of particular importance to the diagnosis of USL causation of chronic pelvic pain, is the association of other symptoms, in particular, symptoms of overactive bladder, urge, frequency, nocturia.

Even if the relationship of CPPU to bladder and bowel symptoms is well known [8], substantial cure rates related to these conditions by uterosacral ligament repair provided further proof of a causal relationship with USL laxity [9, 11, 12, 13, 16–24, 26–30, 31–34] adding to conclusions from clinical, radiological and urodynamically controlled studies [26, 35–38]. However, this relationship was never quantified until a study of 611 patients by Liedl et al., which repaired cardinal and uterosacral ligaments with tissue fixation system (TFS) minislings [34], (Figure 3).

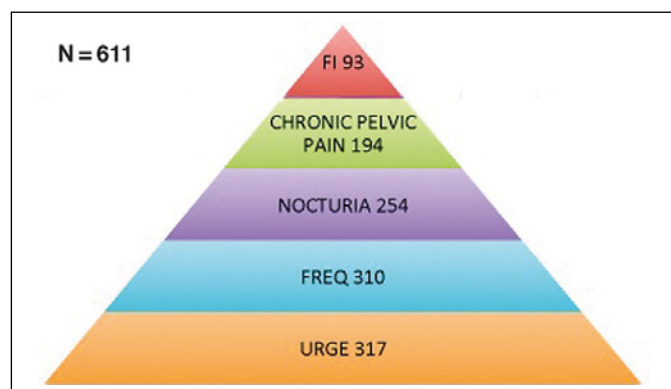


Figure 3. The Pelvic Symptom probability pyramid – Symptoms occur in predictable groupings. The relationship of symptoms within this grouping of 611 patients who had cardinal/uterosacral ligament laxity is expressed as a pyramid. Published with permission of the authors Liedl et al. [34].

A simulated operation is a clinical assessment technique for assessing whether a particular ligament is causing a particular symptom [37].

It must be performed with a bladder sufficiently full to provoke stress or urgency in the supine position. For example, supporting the middle part of urethra on one side (pubourethral ligament ‘PUL’) controls urine loss on coughing and indicates that the cause is a lax PUL.

The aim of ‘simulated operation’ technique: posterior zone is to support the lax uterosacral ligaments. The patient should always be tested with a full bladder. The bottom half of a bivalve speculum is placed very gently in the posterior vaginal fornix, and the percent diminution of urge or pain symptoms is annotated. Alternatively, a tampon can be gently inserted into the posterior fornix. In patients with pelvic pain, gentle pressure on the cervix or hysterectomy scar by an examining finger generally reproduces that pain.

Using the speculum method, Wu Q et al., demonstrated relief of suburethral tenderness on mechanical support of the posterior vaginal fornix [37].

In order to confirm USL origin of pain, the following clinical tests are performed: Bornstein test [36], surgical and non-surgical treatment.

The Bornstein test to check for origin of chronic pelvic pain was first applied in 2005 to challenge the hypothesis that the causation of vulvodynia may not be from the vulva itself, but from laxity in the uterosacral ligaments. It has been subsequently successfully applied to patients with interstitial cystitis. During the Bornstein local anesthetic (LA) test technique, the lower half of a bivalve speculum is inserted into the vagina. Then, the cervix or hysterectomy scar are visualized, gently grasped with Allis forceps, and then gently stretched towards the introitus. USLs are located by digital palpation. A 21-gauge needle attached to a 10 ml syringe loaded with 1% xylocaine is inserted through the vaginal mucosa to a depth of 1.5 cm at 4 and 8 o’clock in a position just lateral to the uterosacral ligaments (USLs). A total of 5 ml of 1% xylocaine are injected on each side. After the elapse of 5 minutes, the patient is checked to see if sensitivity is relieved. The Bornstein test is a valuable clinical and research tool for assessing whether chronic pelvic pain has its origins in the nerve plexuses of the uterosacral ligaments [36].

Regarding surgical treatment, CPP can predominantly be treated by shortening and reinforcing USLs so they can support the Frankenhauser and aacral nerve plexuses. If there is sufficient collagen (e.g. in younger women), a simple plication [13] may improve up to 85%, at least initially [13]. For post-menopausal women with deficient collagen,

Table 1. Signs and symptoms (pelvic pain, nocturia, urge incontinence, frequency, faecal incontinence, apical prolapse) at baseline and after 12 months in patients operated by infracoccygeal sacropexy (PIVS) or tissue fixation system (TFS).

	Number of patients with symptom or condition/total patients (%)				Confidence interval of difference between proportions*		Probability (two-tailed)**	
	pre-PIVS	pre-TFS	post-PIVS	post-TFS	pre-PIVS vs. pre-TFS	post-PIVS vs. post-TFS	pre-PIVS vs. pre-TFS	post-PIVS vs. post-TFS
Pelvic pain	405/809 (50)	194/611 (31)	131/809 (16)	46/611 (7)	0.13 to 0.23	0.06 to 0.12	<0.0001	<0.0002
Nocturia	286/809 (35)	254/611 (41)	59/809 (7)	77/611 (7)	0.011 to 0.11	0.021 to 0.085	0.017	0.0008
Urge/Urge incontinence	322/809 (40)	317/611 (52)	100/809 (12)	51/611 (8)	0.069 to 0.17	0.007 to 0.071	<0.0002	0.015
Frequency	233/549 (42)	310/611 (51)	48/549 (9)	55/611 (9)	0.025 to 0.14	-0.03 to 0.035	0.0047	0.87
Faecal Incontinence	69/324 (21)	93/532 (17)	17/324 (5)	34/532 (6)	-0.015 to 0.094	-0.023 to 0.042	0.167	0.49
Apical prolapse	809/809 (100)	611/611 (100)	56/809 (7)	63/611 (10)	-0.006 to 0.005	0.0047 to 0.064	"	0.022

* No continuity correction; ** Z-test comparing PIVS vs. TFS, before or after surgery (www.vassarstats.net); PIVS – posterior intravaginal sling

there is a very high failure rate with USL plication by 12 months, up to 80% according to data from Shkapura (personal communication 2018). In contrast, Inoue reported 79% cure of pelvic organ prolapse at 5 years using a posterior TFS sling [16]. Because the original reason for ligament looseness is a decrease in its structural collagen, the surgical repair of ligaments ideally should follow the principle of neo-ligament repair [25], which is the basis of the midurethral sling: a thin strip of tape is inserted precisely in the position of the damaged ligament; it is tensioned to restore the length of the ligament; the tissue reaction from the tape creates new collagen to reinforce the damaged ligament, thereby restoring structure and function. Two established operations apply this principle, the infracoccygeal sacropexy (or posterior intravaginal sling – PIVS) and the tissue fixation system (TFS) USL repair. Both have reported cure rates between 70% and 85% at 12 months [9, 11, 12, 13, 16–22, 24, 26–31, 33, 34]. A comparison of the two slings with regards to CPP was performed by Wagenlehner et al. (Table 1).

Non-surgical treatment [23] using a 3-month squatting-based pelvic floor regime (4 surgery visits) has been found to materially improve younger women with CPPU and indeed, other related symptoms (Table 2).

According to a study by Kurdoglu et al., performed on existing and de novo lower urinary tract symptoms (LUTS), pelvic pain, and bowel function following robot-assisted laparoscopic uterosacral ligament suspension (RALUSLS) and sacrocolpopexy (RALSC), data collected were evaluated and symptoms were compared between patients undergoing RALUSLS and RALSC. The results showed no significant difference in background characteristics, except for parity, which was high in the RALUSLS group, with patients experiencing significant resolution of uri-

Table 2. Fate of individual symptoms*

Symptom	>50%
Stress incontinence (n = 69)	57 (82%)
Urge incontinence (n = 44)	33 (68%)
Frequency only (n = 12)	10 (83%)
Nocturia (n = 32)	29 (90%)
Pelvic pain (n = 17)	13 (76%)

*Most patients had overlapping symptoms, n – prevalence of the symptom

nary urgency and frequency, urge and mixed incontinence, and pelvic pain, whereas in the RALSC group, there was significant resolution of nocturia, mixed incontinence, pelvic pain, and dyspareunia [39].

Moreover, based on a study by Allen and Masters in 1955, mentioning that pain is associated with traumatic labour, Braun et al. reported 3 cases of patients diagnosed with Allen-Masters syndrome [40], which is a phenomenon related to traumatic labor [41]. Typical findings in laparoscopy include deep and congested Douglas pouch, peritoneal tears in the posterior leaf of the broad ligament with asymmetrical USL in some cases. Patients who are included in this category of syndrome usually present with the following symptoms: pelvic pain, menstrual disturbances, dyspareunia, fatigability, pain during intercourse and sore back. A pessary ring, placed for 2 weeks under the cervix and resulting in pain relief is a positive predictor for the syndrome [41].

DISCUSSION

Women with pelvic organ support or suspension deficiencies most often present after a long period of suffering, often accompanied by failed treatment attempts. Pain can be so severe that these patients may experience psychiatric disorders. Some even

mentioned suicide attempts. Invariably, laparoscopy is negative in these cases, which further supports the idea for physicians that the pathologic substrate is psychogenic [2, 6, 13] (Figure 4). This is a great tragedy, as pain can be significantly improved or even healed by repairing USLs [2, 12].

Chronic pain can induce asthenia and irritability, decrease of libido and the appearance of marital stress with depression, all of which, in another context, can be interpreted as psychological associations or even considered psychosomatic causes [2, 13].

In this context, Petros [13] revealed that the deficiency of the non-myelinated nerve endings supporting connective tissue, whose trajectory is along the uterosacral ligaments, could be the cause of lower abdominal or sacral pain. The pressure exerted on these nerves can induce deep dyspareunia.

Regarding the anatomical pathways to pain causation, the following hypotheses have been forwarded to explain the causation of CPP:

- a) 'Failure of USLs to support' Frankenhäuser (Th11-L2) and sacral ganglia (S2-S4). The force of gravity stimulates the nerves and causes them to send afferent signals of pain to the cortex [13].
- b) 'Pain as a result of spastic contractions and colics of USL'

It has been previously hypothesized [11] that smooth muscle fibers inside the USL can induce painful spastic contractions. These colic pains are located especially on the left side of the pelvis and are said to be associated with spastic constipation.

- c) 'Pain induced by irritation of Frankenhäuser ganglion'. The Frankenhäuser ganglion, the cervico-uterine ganglion, or the so-called 'pelvic brain' is located bilaterally paracervical and paravaginal in the posterior fornix [15].
- d) 'Pelvic venous congestive syndrome' (PVCS) is characterized by chronic pain affecting 13–40% of women and is due to lower pelvic varicose veins. PVCS generates chronic pain, as well as the feeling of tension in the lower abdomen and/ or the pelvis [6]. From the point of view of Petros [13], pelvic congestion is secondary to ligament laxity and may occur even in nulliparous or independently of pregnancy, in the following conditions: normally, uterosacral ligaments support the uterus and the sacral and Frankenhäuser nerve plexuses. He hypothesized that due to ligament laxity, gravitational force can create a stretching force of the nerves, which in turn causes pain. The same laxity may cause the 'wrinkling' of the pelvic veins in these tissues, thus obstructing flow and generating congestion.
- e) 'Activation of unmyelinated C fibres emanating from urothelial stretch receptors' [36].

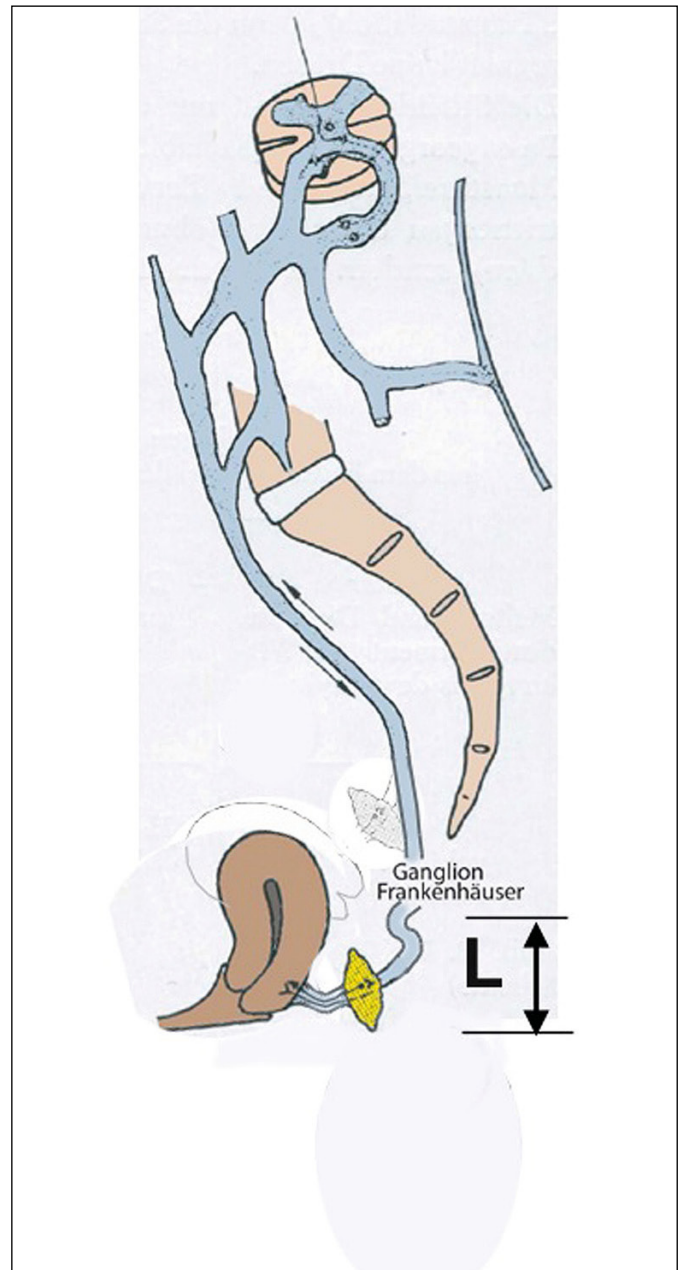


Figure 4. Pathogenesis of chronic pelvic pain. The ganglions of Frankenhäuser and the sacral plexuses are supported by uterosacral ligaments (USL) at their uterine end. 'L' indicates ligament laxity. The posterior directional forces are weakened and cannot stretch the USLs sufficiently for them to support the nerves. The nerves may be stimulated by gravity, by the prolapse, or by intercourse to fire off and be perceived as pain by the cortex. Published by permission from the *Pelvi-perineology Journal* [11].

CONCLUSIONS

Chronic pelvic pain syndrome (CPPUS) is a major problem seriously affecting the quality of life in up to 20% of women. Differentiation from other causes

of pelvic pain can be made by using the pictorial algorithm to identify one or more coexisting posterior fornix symptoms that almost invariably co-occur.

Chronic pelvic pain, bladder and bowel incontinence occur in predictable symptom groupings, which are associated with apical prolapse. USL repair, whether native tissue or (preferably) using a posterior sling has the potential to improve clinical practice, QoL for women and open new research directions.

Symptoms, especially pain, are the sentinels of pelvic floor dysfunction and they are almost invariably associated with uterine prolapse, often minimal. Symptoms cannot validly be ignored by any expert body issuing recommendations on prolapse man-

agement and results. Failure to cure pre-existing symptoms needs to be included as an index of failure of that type of surgery.

Mixed incontinence and pelvic pain improved significantly in patients after RALUSLS or RALSC. In RALUSLS patients, urgency, frequency, and urge incontinence also improved, whereas additional improvement in nocturia and dyspareunia was evident only in RALSC patients. De novo LUTS developing after the procedures, need careful patient consultation prior to surgery [39].

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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