



NVA Research Update E- Newsletter

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Vulvodynia

Web-based education about vulvodynia and its care among student healthcare staff: A quasi-experimental study.

Törnävä M, Koivula M, Helminen M, Suominen T.

Nurse Educ Pract. 2018 Jun 20;31:194-199. doi: 10.1016/j.nepr.2018.06.008.

<https://www.ncbi.nlm.nih.gov/pubmed/29986313>

Student healthcare providers are the type of primary healthcare professionals who usually have first contact with young women who have problems with intimacy, such as vulvar pain - known as vulvodynia. However, a need to increase healthcare professionals' level of knowledge of vulvodynia and its care has been identified. This study aimed to assess the awareness and knowledge of vulvodynia and its care among student healthcare providers, before and after Web-based education. The study design was national, descriptive and quasi-experimental, and was conducted across Finland. A total of 79 participants completed baseline measurements, 58 completed web-based education and 30 took part in a follow-up survey. A survey instrument called 'Awareness and knowledge of vulvodynia and its care' was developed for this study, and the data were collected using a web-based questionnaire. Descriptive statistical methods were used to evaluate the participants' awareness and knowledge of vulvodynia and its care before and after web-based education. The primary results indicated that the participants' awareness and knowledge of vulvodynia and its care was statistically significantly improved following web-based education.

Systematic Review of Treatment Outcome Measures for Vulvodynia.

Sadownik LA, Yong PJ, Smith KB.

J Low Genit Tract Dis. 2018 Jul;22(3):251-259. doi: 10.1097/LGT.0000000000000406.

<https://www.ncbi.nlm.nih.gov/pubmed/29933290>

OBJECTIVES OF THE STUDY: To systematically evaluate the literature regarding vulvodynia treatment outcome measures. **METHODS:** A systematic literature search on OVID, PubMed, and PsycINFO databases was conducted from inception until May 2016. Studies were included/excluded based on prespecified criteria. Reported outcome measures were organized into 6 core outcome domains recommended by the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT): pain; physical functioning, emotional functioning, participant ratings of global improvement and satisfaction with treatment, symptoms and adverse events, and participant disposition. **RESULTS:** Of the 206 articles identified for full-text screening, 33 met our criteria. One study adhered to all IMMPACT recommendations. The number of outcomes measured per study ranged from 1 to greater than 20. Patient-reported pain outcomes were found in the majority (27/33; 82%) of studies. Pain severity with intercourse was reported by 24 (73%) of 33 studies-9 different scales were used to measure this outcome. Clinician-reported outcomes were present in 14 (42%) of 33 studies. Methods of measuring vestibular sensitivity by "cotton swab" test were different in 8 of 10 studies. Other domains reported included; physical function (8/33 studies; 24%), sexual function (23/33 studies; 70%), and emotional function (13/33 studies; 39%). Symptoms and adverse events were reported by 15 (45%) of 33 studies. One study formally reported participant disposition using all the information recommended by CONSORT. **CONCLUSIONS:** Comparison of clinical trial results in vulvodynia is not possible because of a lack of standard treatment outcome measures. Vulvodynia researchers should apply the IMMPACT criteria to guide the development of a minimum core set of standard outcome measures that measure holistic health.

Provoked Vestibulodynia

Gabapentin for the Treatment of Vulvodynia: A Randomized Controlled Trial.

Brown CS, Bachmann GA, Wan J, Foster DC; Gabapentin (GABA) Study Group.

Obstet Gynecol. 2018 Jun;131(6):1000-1007. doi: 10.1097/AOG.0000000000002617.

<https://www.ncbi.nlm.nih.gov/pubmed/29742655>

OBJECTIVE: To evaluate whether extended-release gabapentin is more effective than placebo among women with vulvodynia. **METHODS:** In a multicenter double-blind, placebo-controlled randomized crossover trial, gabapentin (1,200-3,000 mg/d) was compared with a placebo. The primary outcome was mean pain intensity (0, no pain at all to 10, worst pain ever) on the tampon test (a standardized tampon insertion and removal test used as a surrogate marker for dyspareunia) during the last 7 days of the maintenance phase. Secondary outcomes included sexual intercourse pain and daily pain. A sample size of 53 provided 90% power to detect a 1-point reduction on the tampon test (.05 level, two-sided) between the two treatment phases. **RESULTS:** From August 2012 to January 2016, 230 women were screened at three academic institutions and 89 (mean age 37 years; 65% black) were randomized: 45 to gabapentin first and then placebo and 44 to placebo first and then gabapentin. Tampon test pain with gabapentin was not different compared with the placebo (adjusted mean 4.0, 95% CI 3.0-4.9 vs 4.3, 95% CI 3.4-5.2, difference -0.3, 95% CI -0.7 to 0.0; P=.07). Gabapentin also did not improve pain over placebo for sexual intercourse pain (adjusted mean 3.9, 95% CI 2.4-5.3 vs 4.0, 95% CI 2.5-5.4, difference -0.1, 95% CI -0.9 to 0.6; P=.76) and daily pain (adjusted mean 2.7, 95% CI 1.8-3.6 vs 2.9, 95% CI 2.0-3.8, difference -0.2, 95% CI -0.5 to -0.2; P=.36). Subset analyses found that longer pain duration and oral contraceptive nonuse were associated with minimal improvement in tampon test pain with gabapentin. **CONCLUSION:** In this cohort, extended-release gabapentin, as compared with a placebo, did not reduce

tampon test pain. These data do not support the recommendation of gabapentin alone as treatment for vulvodynia.

Vaginal diazepam plus transcutaneous electrical nerve stimulation to treat vestibulodynia: A randomized controlled trial.

Murina F, Felice R, Di Francesco S, Oneda S.

Eur J Obstet Gynecol Reprod Biol. 2018 Jun 26;228:148-153. doi: 10.1016/j.ejogrb.2018.06.026.

<https://www.ncbi.nlm.nih.gov/pubmed/29960200>

OBJECTIVE:To assess the effectiveness of vaginal diazepam in addition to transcutaneous electrical nerve stimulation (TENS) in the treatment of vestibulodynia (VBD). **STUDY DESIGN:** This study was a randomized, double-blind, placebo-controlled trial. Forty-two patients with VBD were randomized, 21 underwent diazepam and TENS (diazepam group) and 21 received placebo and TENS (placebo group). Vulvar pain was assessed on a 10-cm visual analogue scale (VAS) and dyspareunia according to the Marinoff dyspareunia scale. Vaginal surface electromyography (EMG) and vestibular current perception threshold (CPT) testing were performed at baseline and 60 days after treatment. The primary endpoints included the change in pain and dyspareunia from baseline to 60 days of pain and dyspareunia. The secondary endpoints was the variation in objectivity of pelvic floor muscle (PFM) function and vestibular nerve fiber current perception threshold (CPT). **RESULTS:** The VAS scores for pain from basal values of 7.5 and 7.2 for the diazepam and placebo, respectively, showed significant ($p < 0.01$) decreases from 4.7 to 4.3, but this difference was not statistically significant. The Marinoff dyspareunia scores in the diazepam group showed a significant difference ($p < 0.05$) from values measured in the placebo group. The ability to relax the PFM after contraction (difference between maximal contraction and rest tone) was significantly greater for the diazepam group versus the placebo group ($3.8 \mu\text{v}$ and $2.4 \mu\text{v}$, respectively, $p < 0.01$). The CPT values for all of the nerve fibers increased after the treatment, but this increase was significant in the diazepam group only for the values at a 5-Hz stimulation (C fibers) with a change of 47.8% vs 26.9% ($p < 0.05$). Only two patients reported a mild drowsiness in the diazepam group. **CONCLUSIONS:** The present study provided indications that vaginal diazepam plus TENS is useful to improve pain and PFM instability in women with VBD.

Abnormal vaginal microbioma is associated with severity of localized provoked vulvodynia. Role of aerobic vaginitis and Candida in the pathogenesis of vulvodynia.

Donders GGG, Bellen G, Ruban KS.

Eur J Clin Microbiol Infect Dis. 2018 Jun 22. doi: 10.1007/s10096-018-3299-2.

<https://www.ncbi.nlm.nih.gov/pubmed/29934834>

Localized provoked vulvodynia (LPV) causes introital dyspareunia in up to 14% of premenopausal women. Vaginal infections like candidosis may play a initiating role. The aim of this study was to test a possible association of vaginal microbiota alternations such as Candida vaginitis (CV), aerobic vaginitis (AV) and bacterial vaginosis (BV) with severity of vulvodynia and painful intercourse. In an observational study, Q-tip touch test (score 1 (no pain) to 10 (worst possible pain)) was performed on seven vestibular locations in 231 LPV patients presenting in the Vulvovaginal Disease Clinics in Tienen, Leuven and Antwerp, Belgium. Severity of pain upon attempting sexual intercourse was recorded in a similar scale. Both scales were compared to results from fresh wet mount phase contrast microscopy on vaginal fluid smears tested for abnormal vaginal flora (AVF), BV, AV and CV according the standardized microscopy method (Femicare). Fisher's exact test was used. Average age was 31.3 ± 11.6 years, and 58.8% ($n = 132$)

had secondary vestibulodynia. There was an inverse relation between the presence of Candida in the vaginal smears and pain score ($p = 0.03$). There was no relation of pain score, nor Q-tip score with BV. LPV patients with Q-tip score above 7 at 5 and/or 7 o'clock or at 1 and/or 11 o'clock had more often AV than women with lower pain scores (30 vs 14.5%, $p = 0.01$, and 39 vs 14.7%, $p < 0.005$, respectively). Detailed study of the vaginal microflora in patients demonstrates that the most severe patients suffer more from AV and less from Candida. These abnormalities need to be actively looked for and corrected before considering surgery or other therapies.

Facilitators and barriers in the diagnostic process of vulvovaginal complaints (vulvodynia) in general practice: a qualitative study.

Leusink P, Teunissen D, Lucassen PL, Laan ET, Lagro-Janssen AL.

Eur J Gen Pract. 2018 Dec;24(1):92-98. doi: 10.1080/13814788.2017.1420774.

<https://www.ncbi.nlm.nih.gov/pubmed/29359605>

BACKGROUND: The gap between the relatively high prevalence of provoked vulvodynia (PVD) in the general population and the low incidence in primary care can partly be explained by physicians' lack of knowledge about the assessment and management of PVD. **OBJECTIVES:** To recognize barriers and facilitators of GPs in the diagnostic process of women presenting with recurrent vulvovaginal complaints. **METHODS:** A qualitative focus group study in 17 Dutch GPs, five men and 12 women. An interview guide, based on the scientific literature and the expertise of the researchers, including a vignette of a patient, was used to direct the discussion between the GPs. The interviews were audiotaped and transcribed verbatim. A systematic text analysis of the transcripts was performed after data saturation was reached. **RESULTS:** Analysis of the interviews generated three major themes: Identifying and discussing sexual complaints, importance of gender in professional experience, and coping with professional uncertainty. Within these themes, the reluctance regarding sexual complaints, male gender, negative emotional responses when faced with professional uncertainty, as well as lack of education were barriers to the diagnostic process and management of PVD. Female gender and understanding that patients can profit from enquiring about sexual health issues were found to be facilitating factors. **CONCLUSIONS:** To improve the care for women with PVD, attitude and skills of GPs regarding taking a sexual history and performing a vulvovaginal examination should be addressed, as well as GPs' coping strategies regarding their professional uncertainty.

When Self-Worth Is Tied to One's Sexual and Romantic Relationship: Associations with Well-Being in Couples Coping with Genito-Pelvic Pain.

Glowacka M, Bergeron S, Dubé J, Rosen NO.

Arch Sex Behav. 2018 Aug;47(6):1649-1661. doi: 10.1007/s10508-017-1126-y. Epub 2018 Jan 5.

<https://www.ncbi.nlm.nih.gov/pubmed/29305775>

Contingent self-worth (CSW; the pursuit of self-esteem via a particular domain in one's life) impacts well-being based on one's perceived success or failure in the contingent domain. In a community sample, individuals with sexual problems reported greater sexual CSW-self-worth dependent on maintaining a sexual relationship-than those without problems. Couples coping with provoked vestibulodynia (PVD), a genito-pelvic pain condition, perceive failures in their sexual relationship, which could be associated with more pain and poorer well-being. In contrast, relationship CSW-self-worth dependent on the overall romantic relationship-may act as a buffer against adverse outcomes. Eighty-two women with PVD and their partners completed online standardized measures of

sexual and relationship CSW, sexual distress and satisfaction, relationship satisfaction, and depressive symptoms, and women reported their pain intensity. Analyses were based on the actor-partner interdependence model. Women with PVD who reported greater sexual CSW experienced more sexual distress and pain. Additionally, when partners reported greater sexual CSW, they were less sexually and relationally satisfied and more sexually distressed, and women had greater depressive symptoms and lower relationship satisfaction. In contrast, when partners reported higher relationship CSW, they were more sexually and relationally satisfied and less sexually distressed, and women reported lower depressive symptoms and greater relationship satisfaction. Results suggest that couples' (particularly partners') greater sexual CSW is linked to poorer sexual, relational, and psychological well-being in couples affected by PVD, whereas partners' greater relationship CSW is associated with better well-being. Thus, sexual and relationship CSW may be important treatment targets for interventions aimed at improving how couples adjust to PVD.

Co-morbid Disorders

Female Sexual Dysfunction and the Placebo Effect: A Meta-analysis.

Weinberger JM, Houman J, Caron AT, Patel DN, Baskin AS, Ackerman AL, Eilber KS, Anger JT.

Obstet Gynecol. 2018 Jul 10. doi: 10.1097/AOG.0000000000002733.

<https://www.ncbi.nlm.nih.gov/pubmed/29995725>

OBJECTIVE:To quantify the placebo effect of various pharmacologic modalities including neuromodulators, hormonal agents, and onabotulinum toxin A for female sexual dysfunction.

DATA SOURCES: Using Meta-analyses Of Observational Studies in Epidemiology guidelines, we conducted a systematic review of PubMed, EMBASE, ClinicalTrials.gov, and the Cochrane Review databases. **METHODS OF STUDY SELECTION:** Eleven search terms, "female sexual dysfunction" "treatment" in combination with "hypoactive sexual desire," "arousal disorder," "sexual pain disorder," "genitourinary syndrome of menopause," "orgasmic disorder," "vulvovaginal atrophy," "vaginismus," "vaginal atrophy," "vulvodinia," and "vestibulitis," were used. Studies were included if their design was randomized, included a placebo arm, and used the Female Sexual Function Index as an outcome measure. **TABULATION, INTEGRATION, AND RESULTS:** The placebo effect on the Female Sexual Function Index was compared with each respective study's treatment effect using inverse-variance weighting in a random-effects analysis model. Six hundred five relevant articles were retrieved. Twenty-four randomized controlled trials included a placebo arm. Of these, eight studies used the Female Sexual Function Index. Across these studies, 1,723 women with clinical pretreatment female sexual dysfunction received placebo. Two thousand two hundred thirty-six women were in the treatment arm of the respective studies and received various pharmacologic interventions including flibanserin, bupropion, onabotulinum toxin A, intravaginal prasterone, intranasal oxytocin, ospemifene, and bremelanotide. Women receiving placebo improved 3.62 (95% CI 3.29-3.94) on the Female Sexual Function Index. The treatment arm had a corresponding increase of 5.35 (95% CI 4.13-6.57).

CONCLUSION: This meta-analysis of Level I evidence demonstrates that 67.7% of the treatment effect for female sexual dysfunction is accounted for by placebo. Our findings suggest that the current treatments for female sexual dysfunction are, overall, minimally superior to placebo, which emphasizes the ongoing need for more efficacious treatment for female sexual dysfunction.

Research Design Characteristics of Published Pharmacologic Randomized Clinical Trials for Irritable Bowel Syndrome and Chronic Pelvic Pain Conditions: An ACTION Systematic Review.

Gewandter JS, Chaudari J, Iwan KB, Kitt R, As-Sanie S, Bachmann G, Clemens Q, Lai HH, Tu F, Verne GN, Vincent K, Wesselmann U, Zhou Q, Turk DC, Dworkin RH, Smith SM

J Pain. 2018 Jul;19(7):717-726. doi: 10.1016/j.jpain.2018.01.007. Epub 2018 Feb 2.

<https://www.ncbi.nlm.nih.gov/pubmed/29412183>

Chronic pain conditions occurring in the lower abdomen and pelvis are common, often challenging to manage, and can negatively affect health-related quality of life. Methodological challenges in designing randomized clinical trials (RCTs) for these conditions likely contributes to the limited number of available treatments. The goal of this systematic review of RCTs of pharmacologic treatments for irritable bowel syndrome and 3 common chronic pelvic pain conditions are to: 1) summarize the primary end points and entry criteria, and 2) evaluate the clarity of reporting of important methodological details. In total, 127 RCTs were included in the analysis. The most common inclusion criteria were a minimum pain duration (81%), fulfilling an established diagnostic criteria (61%), and reporting a minimum pain intensity (42%). Primary end points were identified for only 57% of trials. These end points, summarized in this article, were highly variable. The results of this systematic review can be used to inform future research to optimize the entry criteria and outcome measures for pain conditions occurring in the lower abdomen and pelvis, to increase transparency in reporting to allow for proper interpretation of RCT results for clinical and policy applications, and to facilitate the aggregation of data in meta-analyses.

PERSPECTIVE: This article summarizes entry criteria and outcome measures and the clarity of reporting of these important design features in RCTs of irritable bowel syndrome and 3 common chronic pelvic pain conditions. These results can be used to improve design of future trials of these largely unaddressed pain conditions.

Vulvar vestibular effects of ospemifene: a pilot study.

Murina F, Di Francesco S, Oneda S.

Gynecol Endocrinol. 2018 Jul;34(7):631-635. doi: 10.1080/09513590.2018.1427717. Epub 2018 Jan 15.

<https://www.ncbi.nlm.nih.gov/pubmed/29334798>

The study aimed to assess the effects of ospemifene on vulvar vestibule in postmenopausal women with vulvar pain and dyspareunia. Fifty-five postmenopausal women used oral ospemifene 60 mg/d for 60 d. Symptoms of dryness, burning, and dyspareunia were evaluated on a 10 cm visual analog scale. Visual examination of the vulvar vestibule was also conducted. Patients also underwent current perception threshold (CPT) testing obtained from the vulvar vestibule. Fifty-five patients (94.6%) completed the treatment. Hot flashes were the most frequent adverse effects, but this led to a discontinuation of therapy in three patients (5.4%). After therapy, there was a statistically significant decrease from the baseline in the mean scores for dryness, burning, and dyspareunia and reduction of vestibular trophic score (baseline value of 11.2-4.2 after the therapy, $p \leq 0.02$) and cotton swab test scores (2.81 compared with 1.25, $p = .001$). There was a difference in CPT values for all nerve fibers and more consistent for C fibers (-38% of sensitivity). These results confirm the efficacy of ospemifene on postmenopausal vestibular symptoms and signs; moreover, the drug was effective in normalizing vestibular innervation sensitivity.

Correlation between Anatomical Segments of the Pudendal Nerve and Clinical Findings of the Patient with Pudendal Neuralgia.

Pereira A, Pérez-Medina T, Rodríguez-Tapia A, Chiverto Y, Lizarraga S.

Gynecol Obstet Invest. 2018 Jul 13:1-7. doi: 10.1159/000489497.

<https://www.ncbi.nlm.nih.gov/pubmed/30007962>

BACKGROUND: The objective was to describe clinical findings and outcomes of patients with pudendal neuralgia in relation with the anatomical segment affected. **METHODS:** Fifty-one consecutive patients with chronic perineal pain (CPP) located in the areas supplied by the pudendal nerve (PN), from January 2011 to June 2012, were analyzed. **RESULTS:** The distribution of pain at perineal, dorsal clitoris and inferior anal nerves was 92.2, 31.4 and 25.5% respectively. The duration of pain was longer when the dorsal clitoris nerve (DCN) was affected ($p < 0,003$). The pain in the pudendal canal was frequently associated with the radiation of pain to the inferior members ($p < 0.043$). **CONCLUSION:** CPP and radiation of pain to lower limbs suggest a disorder at the second segment of PN. A positive Tinel sign in the third segment indicates a nerve entrapment. In terminal branches, pain was more frequent at the perineal nerve and more persistent at the DCN.

Endoscopic transperineal pudendal nerve decompression: operative pudendoscopy.

Beco J, Seidel L, Albert A.

Surg Endosc. 2018 Aug;32(8):3720-3731. doi: 10.1007/s00464-018-6239-4. Epub 2018 May 23.

<https://www.ncbi.nlm.nih.gov/pubmed/29796819>

BACKGROUND: Pudendal nerve entrapment can produce a pudendal syndrome comprising perineodynia together with urinary, sexual, and anorectal symptoms. This syndrome can be treated surgically by the transperineal approach. By using an endoscope during the procedure ("operative pudendoscopy"), the surgeon has close-up visual control of each decompression steps, demonstrates the different levels of entrapment, and cuts the sacrospinous ligament under visual control. The aim of this study was to describe the technical details of this new technique and its outcome in the treatment of the pudendal syndrome. **METHODS:** A series of 113 patients with severe pudendal syndrome underwent operative pudendoscopy. A complete history, pain visual analog scale (VAS) for perineodynia, and four scores evaluating the main symptoms (ICIQ-SF, NHI-CPSI, St Mark's, and Wexner) were obtained before and at least 24 months after surgery. The three clinical signs of pudendal syndrome (abnormal pinprick sensitivity, painful skin rolling test, and painful pudendal nerve) and perineal descent were analyzed before and after surgery in 91 patients. **RESULTS:** The mean operating time per side was 50.3 ± 15.2 min and the average hospital stay was 2.1 ± 0.4 days. Perineodynia VAS dropped from 7.2 ± 1.4 to 4.5 ± 2.9 after surgery ($p < 0.0001$) and the symptoms scores significantly improved. Frequency of sexual arousal syndrome, dyspareunia, and cystalgia was also significantly reduced. Pathological perineal descent (≥ 1.5 cm measured with a Perineocaliper®) observed in 13 patients was reduced from 1.81 to 0.77 cm after surgery ($p < 0.0001$). The only significant complication was severe hemorrhage in one patient induced by an inferior gluteal vessel laceration and successfully treated by arterial embolization. **CONCLUSIONS:** A complete pudendal nerve decompression, from the distal branches to the sacral foramina, safely performed under visual

control by using operative pudendoscopy markedly improves clinical signs and symptoms of the pudendal syndrome.

Dermatological Conditions

Association of Retinoic Acid Receptor β Gene With Onset and Progression of Lichen Sclerosus-Associated Vulvar Squamous Cell Carcinoma.

Rotondo JC, Borghi A, Selvatici R, Mazzoni E, Bononi I, Corazza M, Kussini J, Montinari E, Gafà R, Tognon M, Martini F.

JAMA Dermatol. 2018 Jul 1;154(7):819-823. doi: 10.1001/jamadermatol.2018.1373.

<https://www.ncbi.nlm.nih.gov/pubmed/29898214>

Importance: Molecular alterations in lichen sclerosus-associated vulvar squamous cell carcinoma (LS-VSCC) are largely unknown. **Objective:** To determine whether the retinoic acid receptor β (RAR β) tumor-suppressor gene is involved in the onset and/or progression of LS-VSCC. **Design, Setting, and Participants:** The case-control study, conducted at University-Hospital of Ferrara, Italy, included 20 LS-VSCC (mean [SD] age, 75 [3] years) and 20 cancer-associated vulvar LS (caVLS; mean [SD] age, 62 [11] years) formalin-fixed embedded tissue specimens, 20 cancer-free vulvar LS (cfVLS), and 20 normal skin fresh specimens from diagnostic biopsies and women surgically treated for nonmalignant skin lesions, respectively. RAR β gene expression and promoter methylation were investigated in LS-VSCC and caVLS adjacent to VSCC specimens, and in cfVLS and normal skin specimens, as controls, by RT-Q real-time polymerase chain reaction (PCR) analysis, and sequencing of PCR-amplified bisulfite-treated DNA. c-Jun expression, an RAR β pathway-related gene, was also investigated. **Main Outcomes and Measures:** RAR β expression, correlation with its promoter methylation and c-Jun expression, and association with onset or progression of LS-VSCC. **Results:** In LS-VSCC, RAR β messenger RNA was 3.4-, 3.6-, and 4.8-fold lower than in caVLS ($P = .001$), cfVLS ($P = .005$), and normal skin ($P < .001$), respectively. The RAR β mRNA levels were similar in caVLS, cfVLS, and normal skin. The RAR β promoter was hypermethylated in 18 (90%) of 20 LS-VSCC, 11 (55%) of 20 cfVLS, 10 (50%) of 20 caVLS, and 5 (25%) of 20 in the normal skin group. The degree of methylation of RAR β promoter was higher in LS-VSCC, ranging from 5 to 9 (full promoter methylation) CpGs methylated, than in caVLS ($P = .02$), cfVLS ($P = .03$), or normal skin ($P < .001$), which was up to 5 CpGs methylated. Importantly, 0 of 8 LS-VSCC with 5 to 6 CpGs methylated and 5 (63%) of 8 LS-VSCC with 7 to 8 CpGs methylated were from patients with lymph node metastasis at diagnosis, respectively, whereas there were 2 of 2 (100%) LS-VSCC samples with 9 CpG methylated from patients with lymph node metastasis at diagnosis and subsequent recurrence. In LS-VSCC c-Jun mRNA was 4.3-, 1.4-, and 2.6-fold higher than in caVLS ($P < .001$), cfVLS ($P = .001$), and normal skin ($P < .001$), respectively. The expression of c-Jun was similar in caVLS, cfVLS, and normal skin. **Conclusions and Relevance:** Hypermethylation-induced RAR β down-expression was associated with LS-VSCC and correlates with the upregulation of c-Jun. The degree of methylation of RAR β promoter increased with the malignancy of LS-VSCC. Therefore, RAR β gene dysregulation may play a role in progression of LS-VSCC, and RAR β promoter methylation status may be used as a prognostic marker in clinical treatment of patients with LS-VSCC.

The use of PRP (platelet-rich plasma) in patients affected by genital lichen sclerosis: clinical analysis and results.

Tedesco M, Pranteda G, Chichierchia G, Paolino G, Latini A, Orsini D, Cristaudo A, Foddai ML, Migliano E, Morrone A.

J Eur Acad Dermatol Venereol. 2018 Jul 27. doi: 10.1111/jdv.15190.

<https://www.ncbi.nlm.nih.gov/pubmed/30051614>

An original exploration of genital lichen sclerosis: the semantic connectivity map.

Cazzaniga S, Naldi L, Virgili A, Di Landro A, Simon D, Corazza M, Borghi A; other members of the GLS Italian Study Group.

J Eur Acad Dermatol Venereol. 2018 Jul 27. doi: 10.1111/jdv.15191.

<https://www.ncbi.nlm.nih.gov/pubmed/30051519>

Expression of galectin-7 in vulvar lichen sclerosis and its effect on dermal fibroblasts.

Zhao Y, Zhao S, Li H, Qin X, Wu X.

Oncol Lett. 2018 Aug;16(2):2559-2564. doi: 10.3892/ol.2018.8897. Epub 2018 Jun 4.

<https://www.ncbi.nlm.nih.gov/pubmed/30013650>

Lichen sclerosis is a chronic and inflammatory disease. Extensive studies have focused on the epidermis, with the dermis or epidermis-dermis receiving less attention. To investigate the role of galectin-7, a keratinocyte protein, in vulvar lichen sclerosis (VLS) and its potential effects on dermal fibroblasts, immunohistochemical staining was performed with VLS tissue samples and normal control samples. The expression of galectin-7 was determined by evaluating the galectin-7 integrated density analysis, and further assessed by western blot analysis. Dermal fibroblasts were isolated from the normal tissue of the female anogenital region following sexual plastic surgery. A cell viability assay was performed on isolated dermal fibroblast cells in the presence or absence of galectin-7. Reverse transcription-quantitative polymerase chain reaction (RT-qPCR) was performed to determine the transcriptional level of collagen I and collagen III in the response to different doses of galectin-7. In the immunohistochemical analysis, galectin-7 demonstrated a significantly elevated level in VLS, compared to control tissues, which was confirmed by western blot analysis. In the analysis of primary dermal fibroblast cells, galectin-7 significantly inhibited the viability rate of fibroblasts in a dose-dependent manner. RT-qPCR data revealed that the transcription level of collagen I and collagen III were positively associated with the galectin-7 treatment concentration. The overexpression of galectin-7 is associated with the progression of VLS in the epidermis, a high concentration of galectin-7 inhibits the viability of the primary vulvar dermal fibroblasts, and stimulates the accumulation of collagen I and collagen III in dermal fibroblast cultures, thus galectin-7 may serve as a drug target during VLS progression.

Urethral lichen sclerosis under the microscope: a survey of academic pathologists.

Erickson BA, Tesdahl BA, Voznesensky MA, Breyer BN, Voelzke BB, Alsikafi NF, Vanni AJ, Broghammer JA, Buckley JC, Myers JB, Brant WO, Zhao LC, Smith Iii TG, Swick BL, Dahmouh L.

Can J Urol. 2018 Jun;25(3):9328-9333.

<https://www.ncbi.nlm.nih.gov/pubmed/29900821>

INTRODUCTION: Given the poor understanding of the pathophysiology of genital lichen sclerosus (GLS) and a lack of accepted definitive diagnostic criteria, we proposed to survey pathologists regarding their understanding of GLS. We hypothesized that significant disagreement about GLS will exist.

MATERIALS AND METHODS: All urologists participating in the Trauma and Urologic Reconstruction Network of Surgeons identified genitourinary (GUP) and dermatopathologists (DP) at their respective institutions who were then invited to participate in an online survey regarding their experience with diagnosing GLS, GLS pathophysiology and its relationship to urethral stricture disease. **RESULTS:** There were 23 (12 DP, 11 GUP) pathologists that completed the survey. The most agreed upon criteria for diagnosis were dermal collagen homogenization (85.7%), loss of the normal rete pattern (33.3%) and atrophic epidermis (28.5%). No pathologists believed GLS had an infectious etiology (19% maybe, 42% unknown) and 19% believed GLS to be an autoimmune disorder (42% maybe, 38% unknown); 19% believed LS to be premalignant, but 52% believed it was associated with cancer; 80% believed that LS could involve the urethra (DP (92%) versus GUP (67%); $p = 0.272$). Of those diagnosing urethral GLS, 80% of DUP believed that GLS must first involve the glans/prepuce before involving the urethra, while all GUP believed that urethral disease could exist in isolation ($p = 0.007$). **CONCLUSIONS:** There was significant disagreement in this specialized cohort of pathologists when diagnosing GLS. A logical first step appears to be improving agreement on how to best describe and classify the disease. This may lead to improve treatments.

Diagnosis and Treatment of Vulvar Lichen Sclerosus: An Update for Dermatologists.

Lee A, Fischer G.

Am J Clin Dermatol. 2018 Jul 9. doi: 10.1007/s40257-018-0364-7.

<https://www.ncbi.nlm.nih.gov/pubmed/29987650>

Vulvar lichen sclerosus is an important skin disease that is common in women in their 50 s and beyond; however, it can also affect females of any age, including children. If not treated, it has the potential to cause significant and permanent scarring and deformity of the vulvar structure. In addition, if untreated, it is associated with a 2-6% lifetime risk of malignant squamous neoplasia of the vulva. Lichen sclerosus has been considered a difficult to manage condition; however, both serious complications can potentially be prevented with early intervention with topical corticosteroid, suggesting that the course of the disease can be treatment modified.

Incidence of vulval squamous cell carcinoma in women with vulval lichen sclerosus in an Australian tertiary referral centre.

Meani R, Howard A, Veysey E.

Australas J Dermatol. 2018 Jun 22. doi: 10.1111/ajd.12873.

<https://www.ncbi.nlm.nih.gov/pubmed/29932211>

Prospective evaluation of the frequency of genital lichen sclerosus in 79 patients with systemic sclerosis.

Goussot R, Francès C, Cury K, Bessis D, Martin T, Chatelus E, Mahé A, Messer L, Séverac F, Meyer N, Lipsker D.

Br J Dermatol. 2018 Jun 21. doi: 10.1111/bjd.16898.

<https://www.ncbi.nlm.nih.gov/pubmed/29928761>

Classic and Hypertrophic Vulvar Lichen Planus.

Day T, Weigner J, Scurry J.

J Low Genit Tract Dis. 2018 Oct;22(4):387-395. doi: 10.1097/LGT.0000000000000419.

<https://www.ncbi.nlm.nih.gov/pubmed/29994816>

OBJECTIVES: Three types of lichen planus (LP) occur on the vulva: erosive, classic, and hypertrophic. The latter 2 occur on keratinized skin and little is known about their clinicopathologic appearance.

MATERIALS AND METHODS: Vulvar biopsies of keratinized skin reported as LP or "lichenoid" between 2011 and 2017 were reviewed. Inclusion required age of older than 18 years, a lichenoid tissue reaction, and insufficient abnormal dermal collagen to diagnose lichen sclerosus. Clinical and histopathologic data were collected and cases were categorized as hypertrophic, classic, or nonspecific lichenoid dermatosis. Descriptive statistics were performed and groups were compared with the Fisher exact test. **RESULTS:** Sixty-three cases met criteria for inclusion. Twenty-nine (46%) cases were categorized as hypertrophic LP, 21 (33%) as classic LP, and 13 (21%) as nonspecific lichenoid dermatosis. There were no significant differences in age, primary symptom, biopsy location, or duration of disease between the 3 groups.

When compared with classic and nonspecific disease, hypertrophic LP was less likely to have comorbid dermatoses and more likely to be red, diffuse, have scale crust, and contain plasma cells in the infiltrate. Nonspecific disease had similar clinical features to classic LP but was less likely than the other 2 categories to have a dense lymphocytic infiltrate and exocytosis. **CONCLUSIONS:** Vulvar LP on keratinized skin has a diversity of appearances and presents a clinicopathologic challenge. Further research is required to understand the natural history of hypertrophic LP and the underlying diagnosis of nonspecific lichenoid cases. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Lichen sclerosus associated with Nd:YAG laser therapy.

Bostanci S, Akay BN, Ertop P, Vural S, Okcu Heper A.

J Cosmet Laser Ther. 2018 Jun 1:1-2. doi: 10.1080/14764172.2018.1461231.

<https://www.ncbi.nlm.nih.gov/pubmed/29856231>

Laser is the most efficient and popular method in hair removal. The most common side effects of laser assisted hair removal are pain, erythema, edema, hypopigmentation, hyperpigmentation, blistering, crusting, erosions, purpura, folliculitis, and scar formation (1). Herein, for the first time we describe a case of lichen sclerosus (LS) following hair removal with long pulsed 1064 nm Nd:YAG laser therapy.

Vestibular Sclerosis: Is This a New, Distinct Clinicopathological Entity?

Croker BA, Scurry JP, Petry FM, Fischer G.

J Low Genit Tract Dis. 2018 Jul;22(3):260-263. doi: 10.1097/LGT.0000000000000404.

<https://www.ncbi.nlm.nih.gov/pubmed/29933291>

OBJECTIVES: The aims of this case series were to present a series of patients with clinical and histopathological findings consistent with a recently described condition vestibular sclerosis (VS) and to contribute to the current discussion of whether VS is a subset of lichen sclerosus (LS) or a distinct entity.

MATERIALS AND METHODS: This case series of 6 women for a 12-month period was initiated from an ongoing collaboration between a gynecological dermatologist and an anatomical pathologist specializing in gynecological dermatopathology. **RESULTS:** We describe 6 women with white, hyperkeratotic patches and plaques confined to the vulvar vestibule with stromal sclerosis and an absence of inflammation on histology. All our patients were either perimenopausal or postmenopausal. The condition was either asymptomatic or characterized by mild to moderate dyspareunia. No patient had LS elsewhere on the vulva. There was no response to estrogen or topical corticosteroid therapy in symptomatic patients. **CONCLUSIONS:** Vestibular sclerosis may be a new distinct clinicopathological entity, which is in the differential diagnosis of white plaques and patches in the vulvar vestibule. The characteristic siting in the anterior vestibule only, in the presence of an otherwise normal vulva and absence of inflammation on histology, is a reason to separate this condition from LS.

Lichen sclerosus in pregnancy: A review of 33 cases.

Nguyen Y, Bradford J, Fischer G.

Aust N Z J Obstet Gynaecol. 2018 Jun 19. doi: 10.1111/ajo.12812.

<https://www.ncbi.nlm.nih.gov/pubmed/29920642>

Vulval lichen sclerosus (VLS) is a chronic inflammatory skin condition affecting the anogenital area in women. Serious long-term consequences of VLS include the risk of developing squamous cell carcinoma of the vulva as well as of scarring and alteration of vulval architecture. The treatment of choice for genital lichen sclerosus in females is potent to very potent topical corticosteroids. There are few published data on the course of VLS in pregnancy. We present our experience of managing 33 pregnancies in 29 women with VLS.