

## NVA Research Update E-Newsletter

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### Feature Article

#### **Multi-parameter autonomic-based pain assessment: More is more?**

Loggia ML, Napadow V

Pain. 2012 May 24. [Epub ahead of print]

The ability to accurately measure pain represents the foundation for successful clinical management of this vexing symptom. As of today, pain assessment still relies primarily on self-report (e.g., ratings on a visual analogue scale), both in the clinical and experimental settings. Self-reports of pain, however, are subjective by nature, and can be influenced by a variety of psychosocial factors. An alternate option for objective markers of pain, with possible bedside applications, may be found through investigations of pain-related autonomic reactivity. In this issue of PAIN, Treister and colleagues [see abstract in 'Chronic Pain' section below] asked whether the linear combination of multiple autonomic parameters allows better estimation of the magnitude of pain perceived in response to stimuli of various intensities, compared to the use of each parameter independently. In their current study, Treister and colleagues observed that all ANS parameters differentiated 'no pain' from 'pain': as expected, HR, SCL and NSCF were significantly higher during painful compared to innocuous stimulation, while HRV-HF and PPGA were significantly lower. However, no parameter was able to independently distinguish between the three different pain levels. In contrast, when the authors linearly combined the signal from all five autonomic parameters, by fitting an ordinal cumulative logit model to the data, they observed that the integrated signal was not only able to distinguish 'no pain' from 'pain' stimuli, but also differentiated across the pain levels (high pain > medium pain > low pain > no pain). The results from this study are promising and suggest that autonomic-based pain assessment can benefit from the integration of multiple parameters. Although reactivity to evoked experimental pain may also differentiate chronic pain patients from healthy volunteers, future research needs to explore how the results of Treister et al. can be applied to characterize clinical pain in a patient population. In broader terms, this study suggests that integrating data from a variety of sources (e.g. multiple autonomic outflow metrics, or even combined ANS, functional imaging, behavioral metrics) should allow us to achieve a more accurate estimation of the pain experience. Successful chronic pain management is only as good as the tools used for accurate pain assessment. Future development of objective measures of pain that can complement or, in some cases, even serve as alternatives to patient self-report, promise to improve significantly how pain is managed in the clinical setting.

## **Vulvodynia / Vulvovaginal Pain**

### **Sexual medicine: When good isn't good enough-treatment for vulvodynia.**

Nguyen RH

Nat Rev Urol. 2012 Jul 17. doi: 10.1038/nrurol.2012.145. [Epub ahead of print]

Finding effective treatment for chronic vulvar pain—vulvodynia—is a challenge. Although two new studies answer critical questions regarding treatment effectiveness for two interventions, both studies found that approximately 40 percent of women still experience pain during sex (dyspareunia) despite treatment. Is this as good as it gets for these women?

### **Relationship between vulvodynia and chronic comorbid pain conditions.**

Reed BD, Harlow SD, Sen A, Rayna E, Chen D, Haefner HK

Obst and Gyn. July 2012. doi: 10.1097/AOG.0b013e31825957cf

**OBJECTIVE:** To estimate the relationship among the presence of vulvodynia, fibromyalgia, interstitial cystitis, and irritable bowel syndrome. **METHODS:** Validated questionnaire-based screening tests for the four pain conditions were completed by women with and without vulvodynia who were participating in the Michigan Woman to Woman Health Study, a longitudinal population-based survey in southeastern Michigan. Weighted population-based estimates of the prevalence and characteristics of participants with these chronic comorbid pain conditions were calculated using regression analyses. **RESULTS:** Of 1,940 women who completed the survey containing all four screening tests, 1,890 (97.4%) answered all screening questions and were included. The prevalences of the screening-based diagnoses ranged from 7.5% (95% confidence interval [CI] 6.2–9.0) for interstitial cystitis, 8.7% (95% CI 7.3–10.4) for vulvodynia, 9.4% (95% CI 8.1–11.0) for irritable bowel syndrome, to 11.8% (95% CI 10.1–13.7) for fibromyalgia with 27.1% screening positive for multiple conditions. The presence of vulvodynia was associated with the presence of each of the other comorbid pain conditions ( $P<.001$ , odds ratio 2.3–3.3). Demographic risk factors for each condition varied. Increasing age was not associated with greater numbers of comorbid conditions, and only low socioeconomic status was associated with having multiple comorbid conditions concurrently. **CONCLUSION:** Chronic pain conditions are common, and a subgroup of women with vulvodynia is more likely than those without vulvodynia to have one or more of the three other chronic pain conditions evaluated.

### **Assessing sensory perception on the vulva and on extragenital sites.**

Farage M, Miller KW, Zolnoun D, Ledger WJ

Op Wom Heal J. 2012.

Quantitative sensory testing (QST) measures perception thresholds of defined intensities of physical stimuli (e.g. temperature, touch, pressure, vibration). The frequency and severity of subjective sensory effects (itch, burn), though less quantifiable, can be characterized under defined conditions such as product testing. This article reviews two sources of published research on sensory perception on the vulva relative to extragenital sites: (1) systematic, quantitative sensory testing with defined stimuli and (2) vulvar sensory effects reported in clinical trials of external feminine hygiene products. In healthy women, the vulva is less sensitive to punctate touch and vibration than other body sites. Vulvar sensitivity to mechanical stimuli declines after menopause, but is restored by estrogen supplementation. Product trials of feminine wet wipes suggest that vulvar perception of stinging and of skin wetness also are attenuated after menopause, although perceptions of burning or itching appeared to be unaffected. More systematic, standardized conditions are needed to validate the continued use of QST on the vulva and to better define the characteristics and intensity of subjective vulvar sensations.

### **The effects of hormonal contraceptives on female sexuality: A review.**

Burrows LJ, Basha M, Goldstein AT

J Sex Med. 2012 Jul 12. doi: 10.1111/j.1743-6109.2012.02848.x. [Epub ahead of print]

**INTRODUCTION:** Hormonal contraceptives can influence female sexual function. **AIM:** The goal of this article was to provide a comprehensive review of the effects that various hormonal contraceptives may have on female sexual function. **METHODS:** A Medline search was conducted using several terms related to and including the terms contraception, oral contraceptive, female sexual function, dyspareunia, libido, and sexual desire. **RESULTS:** A thorough review of the effects of hormonal contraceptives on female sexual function. **CONCLUSIONS:** The sexual side effects of hormonal contraceptives are not well studied, particularly with regard to impact on libido. There appears to be mixed effects on libido, with a small percentage of women experiencing an increase or a decrease, and the majority being unaffected. Healthcare providers must be aware that hormonal contraceptive can have negative effects on female sexuality so they can counsel and care for their patients appropriately.

### **Biopsychosocial predictors of postmenopausal dyspareunia: The role of steroid hormones, vulvovaginal atrophy, cognitive-emotional factors, and dyadic adjustment.**

Kao A, Binik YM, Amsel R, Funaro D, Leroux N, Khalifé S

J Sex Med. 2012 May 23. doi: 10.1111/j.1743-6109.2012.02771.x. [Epub ahead of print]

**INTRODUCTION:** Although dyspareunia experienced after menopause is widely attributed to declining estrogen levels and vulvovaginal atrophy, critical reviews of the literature have suggested that these factors are incomplete as explanatory mechanisms. Little is known about psychosocial factors that may also be implicated in postmenopausal dyspareunic pain. **AIM:** To determine the extent to which levels of estrogens and progesterone, vulvovaginal atrophy, cognitive-emotional factors, and dyadic adjustment are predictive of postmenopausal dyspareunic pain intensity. **METHODS:** A total of 182 postmenopausal dyspareunia sufferers underwent a structured interview concerning sociodemographic status as well as medical and pain histories, gynecological examination, cytological evaluation, a blood draw, and answered a series of self-report questionnaires. Given the large number of genital and pelvic pain variables measured, a principal components analysis was undertaken to identify a smaller number of components representing meaningful dimensions of genital and pelvic pain. **MAIN OUTCOME MEASURE:** Pain severity ratings during intercourse were obtained using the McGill Pain Questionnaire. Pain ratings were also obtained during gynecological assessment. Serum estrone, estradiol, and progesterone levels were measured via immunoassay. The Vaginal Atrophy Index and maturation value were used to determine vulvovaginal atrophy severity. Participants completed the Pain Catastrophizing Scale, State-Trait Anxiety Inventory, The Beck Depression Inventory-II, and Dyadic Adjustment Scale. **RESULTS:** Hormone levels were not found to be consistent predictors of pain severity. Maturation value and cognitive-emotional variables (e.g., catastrophization, depression, anxiety) were significant predictors of vestibular pain, which affected over 90% of our sample. Relationship adjustment variables were inversely associated with pain severity within several genital locations. **CONCLUSION:** Results suggest that the traditional hypoestrogen and vulvovaginal atrophy conceptualization of postmenopausal dyspareunia is an insufficient explanatory model, and that pain is also influenced by cognitive, affective, and dyadic factors.

### **A population-based study of pregnancy and delivery characteristics among women with vulvodinia.**

Nguyen RHN, Stewart EG, Harlow BL

Pain and Ther. 2012 July 21.

Full article can be accessed publicly at: <http://www.springerlink.com/content/2193-651X>

**INTRODUCTION:** To examine pregnancy and delivery characteristics of women with and without vulvodinia. **METHODS:** The authors analyzed 227 vulvodinia cases that were less than 45 years old at pain onset; controls were age matched 1:1 to cases and had no history of vulvar pain. Pregnancy and delivery events were assessed after age at first vulvar pain onset (the reference age) in cases and a matched age in controls. **RESULTS:** The authors observed no significant

difference between cases and controls in achieving pregnancy after reference age. Also, no difference in pregnancy outcome was observed between cases and controls ( $P = 0.87$ ). There was an indication that cases were more likely to receive a Cesarean section delivery ( $P = 0.07$ ). In addition, 37.1% of cases who had vaginal delivery versus 11.3% of controls ( $P < 0.01$ ) reported pain at 2 months postpartum. Comparing only women with vulvodynia, women who had intermittent pain versus constant pain were more than twice as likely to have a pregnancy (adjusted odds ratio 2.26, 95% CI 1.10–4.60). **CONCLUSIONS:** Women with vulvodynia may be as likely as other women to carry their pregnancy to birth; however, they may experience higher rates of Cesarean section delivery and could reflect a selection towards those women with vulvodynia who have inconsistent pain.

### **Managing pregnancy and delivery in women with sexual pain disorders.**

Rosenbaum TY, Padoa A

J Sex Med. 2012.

**INTRODUCTION:** Vaginismus and dyspareunia most commonly affect women in their childbearing years, yet sexual function, and not childbirth, has been the focus of most research. **AIM:** The aim of this study is to discuss pregnancy and birth outcomes in women with sexual pain disorders (SPDs) and address practical concerns of patients and practitioners regarding management during pregnancy, pelvic examination, labor, and delivery. **METHODS:** Review of the relevant literature and recommendations based on clinical expertise of the authors. **RESULTS:** A review of SPD, conception, and birth outcomes is provided as well as clinical recommendations for prenatal, labor, and delivery management of women with SPD. **CONCLUSIONS:** Practitioners involved in obstetrical care should be knowledgeable about SPD and provide appropriate modifications and interventions.

### **Three-dimensional ultrasound of the pelvic floor 18-24 months after the first delivery: is there a correlation to delivery mode and persisting pelvic floor disorders?**

Falkert A, Willmann A, Endreß E, Meint P, Seelbach-Göbel B

Ultrasound Obstet Gynecol. 2012 Jun 29. doi: 10.1002/uog.11214. [Epub ahead of print]

**OBJECTIVES:** Three-dimensional ultrasound has shown to be a reliable and reproducible method for visualization of morphologic changes to the female levator ani muscle. Aim of this study was to evaluate the relationship of persisting pelvic floor disorders 18-24 months after the first delivery, biometrical measurements of the pelvic floor and mode of delivery. **METHODS:** In this prospective observational study, 130 primiparae were recruited (all of them Caucasians with singleton pregnancy and cephalic presentation). A three-dimensional perineal ultrasound was performed on the second day and 18-24 months after their first delivery with standardized settings. Volumes were obtained at rest and on valsalva maneuver, biometric measurements of the levator hiatus were determined in axial and sagittal planes. Different obstetric and constitutional parameters were obtained from our clinical files, a standardized questionnaire was used to evaluate persisting pelvic floor disorders 18-24 months after the first delivery. **RESULTS:** Follow-up rate was 59 % ( $n = 77$ ). The biometric measurements showed a significantly larger hiatal area in the vaginal delivery group even two years after the first delivery ( $p < 0.01$ ), whereas subgroup analysis of the vaginal (spontaneous vs. operative vaginal) and cesarean (primary= elective vs. secondary= after onset of labor) delivery groups did not reach significance. Although there was no statistic correlation to delivery mode, women with a persisting stress urinary incontinence two years after first delivery had a larger hiatal area than women without any problems ( $p < 0.01$ ). No significant differences were found in women with bladder urgency or dyspareunia. **CONCLUSIONS:** Three-dimensional transperineal ultrasound is easily accessible and can provide useful information on morphologic changes of the female pelvic floor. In our study, women with vaginal or vaginal operative delivery had a significant larger hiatal area and axial distension than women who delivered by cesarean section even two years after their first delivery. Performing three-dimensional ultrasound after the first delivery may help to identify women at high-risk for persisting pelvic floor disorders.

### **The effects of uterine fundal pressure (Kristeller maneuver) on pelvic floor function after vaginal delivery.**

Sartore A, De Seta F, Maso G, Ricci G, Alberico S, Borelli M, Guaschino S  
Arch Gynecol Obstet. 2012 Jun 30. [Epub ahead of print]

**PURPOSE:** To evaluate the role of uterine fundal pressure during the second stage of labor (Kristeller maneuver) on pelvic floor dysfunction (urinary and anal incontinence, genital prolapse, pelvic floor strength). **METHODS:** 522 primiparous women, enrolled 3 months after vaginal delivery, were divided in two groups: group A (297 women) identifies the women who received Kristeller maneuvers with different indications (e.g. fetal distress, failure to progress, mother exhaustion), group B (225 women) the women without maneuver. Participants were questioned about urogynecological symptoms and examined by Q-tip test, digital test, vaginal perineometry and uroflowmetric stop test score. **RESULTS:** Mediolateral episiotomies, dyspareunia and perineal pain were significantly higher in Kristeller group, whereas urinary and anal incontinence, genital prolapse and pelvic floor strength were not significantly different between the groups. **CONCLUSIONS:** Kristeller maneuver does not modify puerperal pelvic floor function but increases the rate of episiotomies.

### **Sexual arousal in women with provoked vestibulodynia: The application of laser doppler imaging to sexual pain.**

Boyer SC, Pukall CF, Chamberlain SM  
J Sex Med. 2012 Jul 30. DOI: 10.1111/j.1743-6109.2012.02855.x

**INTRODUCTION:** Women with provoked vestibulodynia (PVD) report lower sexual arousal than nonaffected women, however, laboratory studies of arousal have reported contradictory results about whether group differences exist in genital and subjective arousal. **AIM:** To examine genital and subjective sexual arousal in women with and without PVD. **METHODS:** Eligible women with and without PVD (N = 42) attended a laboratory session that included an interview, questionnaire completion, and genital imaging. A direct measure of superficial blood flow—laser Doppler imaging—was used to assess vulvar blood flow levels while participants watched three films, including an erotic film. Participants answered questions about their level of sexual arousal before, during, and after the erotic film. **MAIN OUTCOME MEASURES:** Average vulvar blood flow levels during the baseline and erotic films, numerical ratings of subjective sexual arousal and anxiety, as well as questionnaire measures of arousal. **RESULTS:** There was a significant group difference in genital arousal, whereby the PVD group showed a lower genital response to the erotic film, as well as a significant interaction between baseline blood flow and group membership. Separate group regression analyses demonstrated that baseline blood flow explained a substantial amount of the variance in erotic film blood flow in the control group (70%), while only 27% was explained by this variable in the PVD group. There were no differences in subjective sexual arousal or anxiety between the groups. Across questionnaire measures, women with PVD reported lower sexual arousal than the control group. **CONCLUSIONS:** The results suggest that women with PVD show lower genital responsiveness than nonaffected women to sexual stimuli in a laboratory setting and that their genital arousal is likely impacted by a number of biopsychosocial factors.

### **Harmful or helpful: perceived solicitous and facilitative partner responses are differentially associated with pain and sexual satisfaction in women with provoked vestibulodynia.**

Rosen NO, Bergeron S, Glowacka M, Delisle I, Baxter ML  
J Sex Med. 2012 Jul 19. doi: 10.1111/j.1743-6109.2012.02851.x. [Epub ahead of print]

**INTRODUCTION:** Provoked vestibulodynia (PVD) is a highly prevalent vulvovaginal pain condition that negatively affects women's emotional, sexual, and relationship well-being. Recent studies have investigated the role of interpersonal variables, including partner responses. **AIM:** We examined whether solicitous and facilitative partner responses were differentially associated with vulvovaginal pain and sexual satisfaction in women with PVD by examining each predictor while controlling for the other. **METHODS:** One hundred twenty-one women (M age = 30.60, SD = 10.53) with PVD or self-reported symptoms of PVD completed the solicitous subscale of the spouse response scale of the Multidimensional Pain Inventory, and the facilitative subscale of the Spouse Response Inventory. Participants also completed measures of

pain, sexual function, sexual satisfaction, trait anxiety, and avoidance of pain and sexual behaviors (referred to as "avoidance"). MAIN OUTCOME MEASURES: Dependent measures were the (i) Pain Rating Index of the McGill Pain Questionnaire with reference to pain during vaginal intercourse and (ii) Global Measure of Sexual Satisfaction Scale. RESULTS: Controlling for trait anxiety and avoidance, higher solicitous partner responses were associated with higher vulvovaginal pain intensity ( $\beta = 0.20$ ,  $P = 0.03$ ), and higher facilitative partner responses were associated with lower pain intensity ( $\beta = -0.20$ ,  $P = 0.04$ ). Controlling for sexual function, trait anxiety, and avoidance, higher facilitative partner responses were associated with higher sexual satisfaction ( $\beta = 0.15$ ,  $P = 0.05$ ). CONCLUSIONS: Findings suggest that facilitative partner responses may aid in alleviating vulvovaginal pain and improving sexual satisfaction, whereas solicitous partner responses may contribute to greater pain.

### **The medicalization of women's sexual pain.**

Farrell J, Cacchioni T  
J Sex Res. 2012 Jul;49(4):328-36.

The medicalization of women's sexual problems under the overall rubric of female sexual dysfunction (FSD) has been thoroughly critiqued by feminist scholars, health practitioners, and sex therapists. However, there has been much less commentary on the medicalization of women's sexual pain—currently, a subset of an official FSD diagnosis. This article critically examines interdisciplinary understandings and ways of addressing sexual pain. It analyzes these frameworks in relation to feminist theories on medicalization, heteronormativity, and the reciprocal relationship between these two processes. We argue that many women who experience sexual pain have been eager for medicalization as a path to minimizing pain during sexual activity and reinstating normative heterosexual practices and identities. These goals have been lobbied for by patient advocacy groups and noted by professionals in the field. Although there are some clear benefits to this case for medicalization, there are also theoretical, personal, and political costs. Guided by a growing body of feminist theoretical and qualitative, empirical research on this topic, as well as the first author's personal experience of sexual pain, this article highlights some alternatives to medicalization and makes suggestions for change.

### **Neuralgia of the pudendal nerve following violent trauma: Analgesia by pudendal neuromodulation.** [Article in German]

Heinze K, Nehiban M, von Ophoven A  
Urologe A. 2012 Jul 4. [Epub ahead of print]

Pudendal neuralgia is a neuropathic disease which is predominantly caused by pelvic trauma with pressure or stretching strain of the pudendal nerve. The Nantes criteria are used for the differential diagnostics of this disease and therapy includes pressure-relieving and analgesic measures using laparoscopic or open decompression procedures. This article reports the case of a female patient who developed pudendal neuralgia following violent trauma to the pelvic and urogenital regions. Due to the complexity of the symptoms combined sacral and pudendal neuromodulation (PNM) was carried out. A direct comparison of neuromodulative techniques revealed that PNM was superior resulting in almost complete freedom from pain. The PNM procedure could represent a therapeutic option for treatment of pudendal neuralgia.

## Chronic Pain

### **The efficacy of acupuncture in human pain models: A randomized, controlled, double-blinded study.**

Rebhorn C, Breimhorst M, Buniatyan D, Vogel C, Birklein F, Eberle T  
Pain. 2012 Jun 25. [Epub ahead of print]

Acupuncture is frequently used to treat pain, although data supporting the analgesic efficacy from placebo-controlled studies is sparse. In order to get evidence for acupuncture analgesia we performed a study with 2 well-recognized experimental human pain models - the cold-pressor (CP) test and intradermal capsaicin injection. Fifty healthy men were included. Our study compared Traditional Chinese Medicine-based acupuncture to sham acupuncture with Streitberger placebo needles in a randomized, controlled, double-blinded trial. The primary endpoint was the reduction of mean pain intensity during 3minutes of CP test or of mean pain intensity within 10minutes after capsaicin injection. Secondary parameters were defined to substantiate the findings. To ensure comparability, somatosensory (measured by quantitative sensory testing) and psychological parameters were investigated and found to be the same in both groups. Analyses (repeated-measures analyses of variance) showed a significant ( $P=0.009$ ) but clinically questionable pain reduction in the verum group for capsaicin-induced pain, which was mainly driven by an effect of Traditional Chinese Medicine acupuncture on small pain ratings (max. reduction from 7/100 rating at baseline to 2.5/100 at intervention). Neither pin-prick hyperalgesia, nor allodynia, nor neurogenic flare associated with capsaicin injection, nor pain ratings during the CP test, were significantly different between groups. In addition, there was no placebo response. Attitude towards acupuncture and partial unblinding did not affect the results. We conclude that acupuncture on predefined points has a minor effect on experimental pain in healthy subjects.

### **A snapshot and scorecard for analgesic clinical trials for chronic pain: The RReACT database.**

Greene K, Dworkin RH, Rowbotham MC  
Pain. 2012 Jul 15. [Epub ahead of print]

No Abstract available.

### **Predicting response to pregabalin from pretreatment pain quality: Clinical applications of the pain quality assessment scale.**

Gammaitoni AR, Smugar SS, Jensen MP, Galer BS, Bolognese JA, Alon A, Hewitt DJ  
Pain Med. 2012 Jul 3. doi: 10.1111/j.1526-4637.2012.01423.x. [Epub ahead of print]

**OBJECTIVE:** The aim of this study is to assess the Pain Quality Assessment Scale (PQAS) in predicting pregabalin in peripheral neuropathic pain (NP). **STUDY DESIGN:** Post hoc analysis of a double-blind, placebo-controlled, enriched enrollment, randomized withdrawal trial evaluating pregabalin in 99 patients with NP who completed the PQAS, which comprises 20 questions regarding individual pain domains and qualities that are scored into three scales: paroxysmal, deep, and surface. **METHOD:** Patients rated the average pain intensity and pain quality using the PQAS at baseline; average pain intensity was assessed again after 40 days of treatment with pregabalin. Associations between pretreatment PQAS scores and treatment response were estimated using Pearson's  $r$ . Logistic regression was used to identify pretreatment PQAS scores contributing unique variance to predicting treatment response. **RESULTS:** Fifty participants provided baseline PQAS scores and received pregabalin for the entire length of the study. Nine of 23 PQAS baseline scales and items were significantly associated with treatment response to pregabalin: the paroxysmal and deep scales, and the items assessing the following pain domains and qualities: intensity, electric, tingling, cramping, radiating, throbbing, and deep ( $P$  values range, 0.002-0.045;  $r$ s range, 0.28-0.43). The PQAS items assessing sharp, hot, and unpleasant pain items demonstrated nonsignificant trends ( $P<0.10$ ) to be associated with treatment response. In the logistic regression analysis, pretreatment PQAS scores had 77% sensitivity and 83% specificity to correctly identify pregabalin responders. Significantly correlated PQAS items had a sensitivity of 85% and specificity of 76%. **CONCLUSION:**

Pretitration PQAS scores reliably predicted pregabalin responders in patients with NP.

### **Randomized control trial of topical clonidine for treatment of painful diabetic neuropathy.**

Campbell CM, Kipnes MS, Stouch BC, Brady KL, Kelly M, Schmidt WK, Petersen KL, Rowbotham MC, Campbell JN  
Pain. 2012 Jun 8. [Epub ahead of print]

A length-dependent neuropathy with pain in the feet is a common complication of diabetes (painful diabetic neuropathy). It was hypothesized that pain may arise from sensitized-hyperactive cutaneous nociceptors, and that this abnormal signaling may be reduced by topical administration of the  $\alpha(2)$ -adrenergic agonist, clonidine, to the painful area. This was a randomized, double-blind, placebo-controlled, parallel-group, multicenter trial. Nociceptor function was measured by determining the painfulness of 0.1% topical capsaicin applied to the pretibial area of each subject for 30 minutes during screening. Subjects were then randomized to receive 0.1% topical clonidine gel (n=89) or placebo gel (n=90) applied 3 times a day to their feet for 12 weeks. The difference in foot pain at week 12 in relation to baseline, rated on a 0-10 numerical pain rating scale (NPRS), was compared between groups. Baseline NPRS was imputed for missing data for subjects who terminated the study early. The subjects treated with clonidine showed a trend toward decreased foot pain compared to the placebo-treated group (the primary endpoint;  $P=0.07$ ). In subjects who felt any level of pain to capsaicin, clonidine was superior to placebo ( $P<0.05$ ). In subjects with a capsaicin pain rating  $\geq 2$  (0-10, NPRS), the mean decrease in foot pain was 2.6 for active compared to 1.4 for placebo ( $P=0.01$ ). Topical clonidine gel significantly reduces the level of foot pain in painful diabetic neuropathy subjects with functional (and possibly sensitized) nociceptors in the affected skin as revealed by testing with topical capsaicin. Screening for cutaneous nociceptor function may help distinguish candidates for topical therapy for neuropathic pain.

### **Off-label uses of trazodone: a review.**

Bossini L, Casolaro I, Koukouna D, Cecchini F, Fagiolini A  
Expert Opin Pharmacother. 2012 Aug;13(12):1707-17. Epub 2012 Jun 20.

**INTRODUCTION:** Trazodone is an antidepressant belonging to the class of serotonin receptor antagonists and reuptake inhibitors. It is approved by the FDA for the treatment of depression. Insomnia is the most frequent reason for prescription of trazodone. It has also been proven useful in the treatment of anxiety disorders. Other off-label uses include the treatment of bulimia, benzodiazepine/alcohol dependence, fibromyalgia, central nervous system degenerative diseases (behavioral disorders in dementia and other organic disorders), schizophrenia, chronic pain disease and diabetic neuropathy, sexual dysfunction. **AREAS COVERED:** This paper evaluates trazodone's efficacy and safety in its off-label uses. It also discusses the possibility that a combination of trazodone with SSRIs may prevent or treat some of the SSRI side effects, such as anxiety, insomnia and sexual dysfunction, in addition to synergistically increasing SSRIs' antidepressant activity. **EXPERT OPINION:** Few clinical trials have been conducted to evaluate trazodone's efficacy in the treatment of the diseases and symptoms for which it is often used in clinical practice. More studies are necessary to investigate possible new therapeutic indications, and to scientifically demonstrate the risk/benefit ratio for the many conditions for which trazodone is used, but not approved by the FDA.

### **Opioids and neuropathic pain.**

Smith HS  
Pain Physician. 2012 Jul;15(3 Suppl):ES93-ES110.

Opioids are broad spectrum analgesics that may be beneficial to alleviate the intense perception of algesia in patients suffering with pain. They have been one of the most controversial analgesics, in part because of their potential for addiction. Opioids or any currently available analgesic will not provide effective analgesia for every patient with chronic neuropathic pain (NP), but overall opioids are considered to be a second or third line class of analgesics that may provide reasonable analgesia to some patients with chronic NP. Although opioids may alleviate chronic NP, overall, NP



tends to be less opioid responsive than nociceptive pain. The mechanisms that may contribute to neuropathic pain may simultaneously also contribute to diminishing the antinociceptive properties of opioids for neuropathic pain. Some of these mechanisms may also contribute to analgesic tolerance and/or opioid-induced hyperalgesia. Hyperalgesia consequently to nerve insult and opioid-induced analgesic tolerance, may both involve the N-methyl-D-aspartate (NMDA) receptor and share part of intracellular events producing a state of neural hyperexcitation. Conversely, opioid therapy may contribute to nociceptive processes that may be involved in neuropathic pain such as opioid-induced cholecystokinin release. Furthermore, within NP, peripheral NP appears to be the most opioid responsive, followed by spinal NP while supraspinal NP tends to be the least responsive to opioids. Although, there is no robust evidence that any specific opioid agent is better than any other opioid at effectively treating NP, it is conceivable that some opioids/opioid-like analgesic agents may be particularly well suited to alleviate NP in certain patients suffering from neuropathic pain.

### **Differentiating between heat pain intensities: The combined effect of multiple autonomic parameters.**

Treister R, Klinger M, Zuckerman G, Aryeh IG, Eisenberg E  
Pain. 2012 Sep;153(9):1807-14. Epub 2012 May 29.

Although it is well known that pain induces changes in autonomic parameters, the extent to which these changes correlate with the experience of pain is under debate. The aim of the present study was to compare a combination of multiple autonomic parameters and each parameter alone in their ability to differentiate among 4 categories of pain intensity. Tonic heat stimuli (1minute) were individually adjusted to induce no pain, low, medium, and high pain in 45 healthy volunteers. Electrocardiogram, photoplethysmogram, and galvanic skin response were recorded, and the following parameters were calculated: heart rate; heart rate variability-high frequency (0.15 to 0.4Hz) spectral power; skin conductance level; number of skin conduction fluctuations; and photoplethysmographic pulse wave amplitude. A combination of parameters was created by fitting an ordinal cumulative logit model to the data and using linear coefficients of the model. Friedman test with post-hoc Wilcoxon test were used to compare between pain intensity categories for every parameter alone and for their linear combination. All of the parameters successfully differentiated between no pain and all other pain categories. However, none of the parameters differentiated between all 3 pain categories (i.e., low and medium; medium and high; low and high). In contrast, the linear combination of parameters significantly differentiated not only between pain and no pain, but also between all pain categories ( $P < .001$  to  $.02$ ). These results suggest that multiparameter approaches should be further investigated to make progress toward reliable autonomic-based pain assessment.

### **Experimental spinal cord stimulation and neuropathic pain: Mechanism of action, technical aspects, and effectiveness.**

Smits H, van Kleef M, Holsheimer J, Joosten EA  
Pain Pract. 2012 Jul 11. doi: 10.1111/j.1533-2500.2012.00579.x. [Epub ahead of print]

Spinal cord stimulation (SCS) is a valuable treatment for chronic intractable neuropathic pain. Although SCS has gone through a technological revolution over the last four decades, the neurophysiologic and biochemical mechanisms of action have only been partly elucidated. Animal experimental work has provided some evidence for spinal as well as supraspinal mechanisms of neuropathic pain relief of SCS. A SCS computer model of the electrical properties of the human spinal cord revealed many basic neurophysiologic principles that were clinically validated later on. The main question in clinical SCS is how to further improve the effectiveness of SCS as there is still a significant failure rate of 30%. In this context, experimental studies are needed to elucidate which target pain neuron(s) are involved, as well as with what exact electrical stimulation this target neuron can be influenced to produce an optimal suppression of neuropathic pain. This article reviews the basic clinical and experimental technical aspects in relation to the effectiveness of SCS in view of recent understanding of the dorsal horn pain circuit involved. These data may then result in experiments needed for an improved understanding of the mechanisms underlying SCS and consequently lead to improvement and increased effectiveness of SCS in neuropathic pain as a clinical therapy.

### **The role of the immune system in the generation of neuropathic pain.**

Calvo M, Dawes JM, Bennett DL

Lancet Neurol. 2012 Jul;11(7):629-42.

Persistent pain is a sequela of several neurological conditions with a primary immune basis, such as Guillain-Barré syndrome and multiple sclerosis. Additionally, diverse forms of injury to the peripheral or the central nervous systems—whether traumatic, metabolic, or toxic—result in substantial recruitment and activation of immune cells. This response involves the innate immune system, but evidence also exists of T-lymphocyte recruitment, and in some patient cohorts antibodies to neuronal antigens have been reported. Mediators released by immune cells, such as cytokines, sensitise nociceptive signaling in the peripheral and central nervous systems. Preclinical data suggest an immune pathogenesis of neuropathic pain, but clinical evidence of a central role of the immune system is less clear. An important challenge for the future is to establish to what extent this immune response initiates or maintains neuropathic pain in patients and thus whether it is amenable to therapy.

### **Depressed pain patients differ from other depressed groups: Examination of cognitive content in a sentence completion task.**

Rusu AC, Pincus T, Morley S

Pain. 2012 Jul 4. [Epub ahead of print]

Depression is a common feature of chronic pain, but there is limited research into the content and frequency of depressed cognitions in pain patients. A limitation of previous research is the failure to include nonpain depressed comparison groups. The present study used a sentence completion task to investigate the content of cognition in 4 groups of participants: with pain and concurrent depression, pain without depression, depression without pain, and with neither pain nor depression. One hundred seventy-two participants generated sentences to a set of predefined stems. Complete responses were coded by affective valence (negative, positive, and neutral) and health-related content. As predicted, participants with depression (with and without pain) produced more negative responses than nondepressed participants (with and without pain); participants with pain (depressed and nondepressed) produced more health responses than those without pain (depressed and controls); participants with depression and pain produced more negative health responses than any other group. The strengths of the current study are the inclusion of the depressed nonpain group, the use of a comprehensive coding scheme applied by 2 independent raters, and the presence of depression validated through a diagnostic interview. In contrast to depressed groups without pain, participants with pain and depression exhibit a cognitive bias specific to negative aspect of health. This focus facilitates understanding of the relationship between depression and pain processing: The implications for therapeutic interventions are discussed.

### **Telomeres and epigenetics: Potential relevance to chronic pain.**

Sibille KT, Witek-Janusek L, Mathews HL, Fillingim RB

Pain. 2012 Jul 4. [Epub ahead of print]

No Abstract Available.

## **Intercellular communication in sensory ganglia by purinergic receptors and gap junctions: Implications for chronic pain.**

Hanani M

Brain Res. 2012 Jul 4. [Epub ahead of print]

Peripheral injury can cause abnormal activity in sensory neurons, which is a major factor in chronic pain. Recent work has shown that injury induces major changes not only in sensory neurons but also in the main type of glial cells in sensory ganglia satellite glial cells (SGCs), and that interactions between sensory neurons and SGCs contribute to neuronal activity in pain models. The main functional changes observed in SGCs after injury are an increased gap junction-mediated coupling among these cells, and augmented sensitivity to ATP. There is evidence that the augmented gap junctions contribute to neuronal hyperexcitability in pain models, but the mechanism underlying this effect is not known. The changes in SGCs described above have been found following a wide range of injuries (both axotomy and inflammation) in somatic, orofacial and visceral regions, and therefore appear to be a general feature in chronic pain. We have found that in cultures of sensory ganglia calcium signals can spread from an SGC to neighboring cells by calcium waves, which are mediated by gap junctions and ATP acting on purinergic P2 receptors. A model is proposed to explain how augmented gap junctions and greater sensitivity to ATP can combine to produce enhanced calcium waves, which can lead to neuronal excitation. Thus this simple scheme can account for several major changes in sensory ganglia that are common to a great variety of pain models.

## **Vulvovaginal Disorders**

### **Clinical scoring system for vulvar lichen sclerosus.**

Günther AR, Duclos K, Jahns BG, Krause E, Amann E, Limacher A, Mueller MD, Jüni P  
J Sex Med. 2012 Jul 3. doi: 10.1111/j.1743-6109.2012.02814.x. [Epub ahead of print]

**INTRODUCTION:** Vulvar lichen sclerosus (LS) is a chronic inflammatory and mutilating disease, which goes often undetected for years. Advanced disease severely affects quality of life like sexual disorders and is also associated with an increased risk of vulvar cancer. **AIM:** To develop and validate a patient-administered symptom score and a physician-administered clinical score for the diagnosis and evaluation of vulvar LS. **METHODS:** We included 24 patients with established LS diagnosis and 49 with other vulvar disease. The physician-administered score was based on six clinical features and the patient-administered score was a symptom-based four-item composite score. We determined inter-item correlations and internal consistency of both scores, and estimated sensitivities, specificities, likelihood ratios, and posttest probabilities for different cutoffs of the physician-administered score. **MAIN OUTCOME MEASURES:** Characteristics of patients with and without LS were compared using  $\chi^2$  and unpaired t-test as required. We then determined Cronbach's alpha as a measure of the overall consistency of scores and calculated positive and negative likelihoods. **RESULTS:** Lack of redundancy of items (correlation coefficients  $< 0.90$ ) and internal consistency (Cronbach's  $\alpha \geq 0.70$ ) suggested that final composite scores were valid and yielded excellent power to rule in LS. **CONCLUSION:** Scores may be useful for assessing symptoms of vulvar disorders, to ease diagnosis of LS and to evaluate treatment response over time.

### **Prevalence of sacral spinal (Tarlov) cysts in persistent genital arousal disorder.**

Komisaruk BR, Lee HJ

J Sex Med. 2012 May 17. doi: 10.1111/j.1743-6109.2012.02765.x. [Epub ahead of print]

**INTRODUCTION:** Neither consistent etiology nor treatment have been established for Persistent Genital Arousal Disorder (PGAD), which is characterized by uninvited, unwelcome, and distressing genital sensation. Sacral (Tarlov) cysts, which form on dorsal (sensory) roots, most commonly of S2 and S3 in the sacral spine, are reported to produce genital

symptoms that bear similarities to those described for PGAD. AIMS: The present study ascertained the incidence of Tarlov cysts in the sacral spine of women with PGAD symptoms. METHODS: Women in a PGAD internet support group were asked to submit MRIs of their sacral region to the investigators, who evaluated the MRIs for the presence or absence of Tarlov cysts. MAIN OUTCOME MEASURES: The presence or absence of Tarlov cysts at the level of the sacral spine. RESULTS: Tarlov cysts were present in 12 of the first 18 (66.7%) MRIs submitted to the investigators by women who suffer from PGAD symptoms. By contrast to this incidence, that of Tarlov cysts reported in the literature for large samples of the population observed for various disorders (e.g., lumbosacral pain) is 1.2-9.0%. CONCLUSION: Tarlov cysts have been described in the literature as producing paresthesias and genital sensory disturbances. Hence, at least some cases of PGAD might be considered to be a Tarlov cyst-induced paresthesia. Based on the relatively high occurrence of Tarlov cysts currently observed in women who suffer from PGAD symptoms, it would seem advisable to suspect Tarlov cysts as a possible organic etiological factor underlying PGAD.

#### **Identification of Candida species associated with vulvovaginal candidiasis by multiplex PCR.**

Mahmoudi Rad M, Zafarhandi ASH, Amel Zabihi M, Tavallaee M, Mirdamadi Y  
Infect Dis Obstet Gynecol. 2012;2012:872169. Epub 2012 Jun 26.

BACKGROUND: Vulvovaginal candidiasis is a common infection. The aim of this study was to identify the species of vaginal Candida isolates by using multiplex PCR technique. METHODS: 191 isolates from patients admitted to Mahdiah hospital were identified. The vaginal swab specimens were cultured on Sabouraud Dextrose Agar. The ITS1 region between the 18S and 5.8S rRNA genes and a specific DNA fragment within the ITS2 region were amplified. The multiplex PCR products were separated by electrophoresis in 2% agarose gel, visualized by staining with ethidium bromide, and photographed. Descriptive statistics, Chi-square test, and Spearman correlation were used to summarize the findings. RESULTS: *C. albicans* and *C. glabrata* were the most common species isolated from the specimens. A mix of *C. glabrata* and *C. albicans* was the most common mixed infection isolated from the samples. The analysis revealed a significant positive association between older age and infection with *C. glabrata* isolates (Spearman's rho = 0.89, P = 0.015). CONCLUSION: Multiplex PCR is a fast, yet reliable method to identify Candida species. *C. albicans* and then *C. glabrata* are the two most common causes of vulvovaginal candidiasis. The number of mixed fungal infections is higher among Iranian population compared to international reports.

#### **Lactobacillus helveticus HY7801 ameliorates vulvovaginal candidiasis in mice by inhibiting fungal growth and NF- $\kappa$ B activation.**

Joo HM, Kim KA, Myoung KS, Ahn YT, Lee JH, Huh CS, Han MJ, Kim DH  
Int Immunopharmacol. 2012 Sep;14(1):39-46. Epub 2012 Jun 23.

The anti-inflammatory effects of hydrogen peroxide-producing lactic acid bacteria (LAB) against *Candida albicans*-induced vulvovaginal candidiasis in  $\beta$ -estradiol-immunosuppressed mice were examined. Oral and intravaginal treatment with these LABs significantly decreased the level of viable *C. albicans* within the vaginal cavity as well as the quantitated myeloperoxidase activity in the vaginal tissues when compared with control untreated mice. Out of all of the LABs tested, *Lactobacillus helveticus* HY7801 (LH) most potently inhibited vulvovaginal candidiasis. LH also inhibited the expression of the pro-inflammatory cytokines including TNF- $\alpha$ , IL-1 $\beta$  and IL-6, and inflammatory enzymes, COX-2 and iNOS, as well as the activation of NF- $\kappa$ B. However, the addition of LH led to an increase in IL-10 cytokine expression in the vaginal tissues. In addition, the decrease of Lactobacillaceae and the increase of Pasteurellaceae caused by treatment with *C. albicans* were reversed with oral and intravaginal administration of LH, suggesting a potential shift in the vaginal microflora present. Addition of LH was toxic to *C. albicans* in vitro when cultured with HeLa cells. Oral administration of LH inhibited lipopolysaccharide (LPS)-induced TNF- $\alpha$  and IL-1 $\beta$  expressions in  $\beta$ -estradiol-immunosuppressed mice but reversed the expression of anti-inflammatory cytokine IL-10 in comparison to levels observed in the normal control group. LH also inhibited the expression of the pro-inflammatory cytokines, TNF- $\alpha$  and IL-1 $\beta$ , and the activation of NF- $\kappa$ B in LPS-stimulated peritoneal macrophages. Based on these findings, LH may ameliorate vulvovaginal candidiasis by suppressing the NF- $\kappa$ B pathway, as well as through inhibition of the growth of *C. albicans*.

## **Probiotic lactobacillus and estrogen effects on vaginal epithelial gene expression responses to *Candida albicans*.**

Wagner RD, Johnson SJ

J Biomed Sci. 2012 Jun 20;19(1):58. [Epub ahead of print]

**BACKGROUND:** Vaginal epithelial cells have receptors, signal transduction mechanisms, and cytokine secretion capabilities to recruit host defenses against *Candida albicans* infections. This research evaluates how probiotic lactobacilli affect the defensive epithelial response. **METHODS:** This study used quantitative reverse transcription-polymerase chain reaction assay (qRT-PCR), flow cytometry, and a multiplex immunoassay to observe changes in the regulation of gene expression related to cytokine responses in the VK2 (E6/E7) vaginal epithelial cell line treated with 17 $\beta$ -estradiol, exposed to probiotic *Lactobacillus rhamnosus* GR-1<sup>®</sup> and *Lactobacillus reuteri* RC-14<sup>®</sup> and challenged with *C. albicans*. Data were statistically evaluated by repeated measures analysis of variance and paired t-tests where appropriate. **RESULTS:** *C. albicans* induced mRNA expression of genes related to inflammatory cytokine responses associated with nuclear factor-kappa B (NF- $\kappa$ B) and mitogen-activated protein kinase (MAPK) signal transduction pathways. 17 $\beta$ -estradiol suppressed expression of interleukin-1 $\alpha$  (IL-1 $\alpha$ ), IL-6, IL-8, and tumor necrosis factor alpha (TNF $\alpha$ ) mRNA. Probiotic lactobacilli suppressed *C. albicans*-induced nuclear factor-kappa B inhibitor kinase kinase alpha (I $\kappa$ k $\alpha$ ), Toll-like receptor-2 (TLR2), TLR6, IL-8, and TNF $\alpha$ , also suggesting inhibition of NF- $\kappa$ B signaling. The lactobacilli induced expression of IL-1 $\alpha$ , and IL-1 $\beta$  mRNA, which was not inhibited by curcumin, suggesting that they induce an alternate inflammatory signal transduction pathway to NF- $\kappa$ B, such as the mitogen activated protein kinase and activator protein-1 (MAPK/AP-1) signal transduction pathway. Curcumin inhibited IL-13 secretion, suggesting that expression of this cytokine is mainly regulated by NF- $\kappa$ B signaling in VK2 cells. **CONCLUSIONS:** The results suggest that *C. albicans* infection induces pro-inflammatory responses in vaginal epithelial cells, and estrogen and lactobacilli suppress expression of NF- $\kappa$ B-related inflammatory genes. Probiotic lactobacilli may induce IL-1 $\alpha$  and IL-1 $\beta$  expression by an alternate signal transduction pathway, such as MAPK/AP-1. Activation of alternate signaling mechanisms by lactobacilli to modify epithelial cell cytokine production may be a mechanism for probiotic modulation of morbidity in vulvovaginal candidiasis.

## **Probiotic interference of *Lactobacillus rhamnosus* GR-1 and *Lactobacillus reuteri* RC-14 with the opportunistic fungal pathogen *Candida albicans*.**

Köhler GA, Assefa S, Reid G

Infect Dis Obstet Gynecol. 2012;2012:636474. Epub 2012 Jul 1.

*Candida albicans* is the most important *Candida* species causing vulvovaginal candidiasis (VVC). VVC has significant medical and economical impact on women's health and wellbeing. While current antifungal treatment is reasonably effective, supportive and preventive measures such as application of probiotics are required to reduce the incidence of VVC. We investigated the potential of the probiotics *Lactobacillus rhamnosus* GR-1 and *Lactobacillus reuteri* RC-14 towards control of *C. albicans*. In vitro experiments demonstrated that lactic acid at low pH plays a major role in suppressing fungal growth. Viability staining following cocultures with lactobacilli revealed that *C. albicans* cells lost metabolic activity and eventually were killed. Transcriptome analyses showed increased expression of stress-related genes and lower expression of genes involved in fluconazole resistance, which might explain the increased eradication of *Candida* in a previous clinical study on conjoint probiotic therapy. Our results provide insights on the impact of probiotics on *C. albicans* survival.

### **Embolization to treat pelvic congestion syndrome and vulval varicose veins.**

van der Vleuten CJ, van Kempen JA, Schultze-Kool LJ  
Int J Gynaecol Obstet. 2012 Jun 22. [Epub ahead of print]

**OBJECTIVE:** To evaluate the efficacy of embolization for treating the symptoms of pelvic congestion syndrome (PCS). **METHODS:** Twenty-one women with PCS who were treated with embolization at Radboud University Nijmegen Medical Centre between 2003 and 2008 were sent a questionnaire about their symptoms before embolization, 2 months after the first embolization, and at the time the survey was conducted. **RESULTS:** All patients completed the questionnaire. Two months after the first embolization, 14 (66.7%) women had some degree of improvement of symptoms. Nine (42.9%) patients underwent a second embolization. At the time the survey was conducted, 16 (76.2%) patients had some degree of improvement of symptoms. In addition to improvements in varicose veins and pelvic pain, there was improvement of hemorrhoids. **CONCLUSION:** Embolization of pelvic varicosities may be an effective treatment in a well-selected group of patients with PCS. If there is no improvement of symptoms after initial embolization, a second procedure is unlikely to be effective.

### **Clinical presentation and epidemiology of female genital tuberculosis in eastern Sudan.**

Ali AA, Abdallah TM  
Int J Gynaecol Obstet. 2012 Jun 20. [Epub ahead of print]

**OBJECTIVE:** To describe the epidemiology and clinical presentation of female genital tuberculosis (FGTB) among women in eastern Sudan. **METHODS:** A cross-sectional survey was conducted at Kassala Maternity Hospital, Sudan, from January 1 to December 31, 2010. **RESULTS:** Of the 2778 women presenting with various gynecologic symptoms, 44 suspected cases of FGTB were identified. Granulomatous tissue reactions were observed in 25 of the suspected FGTB cases, yielding an incidence of 0.9%. The majority (20/25; 80%) of these patients presented with chronic pelvic and lower abdominal pain; however, 68.0% (17/25) presented with pelvic mass, cyst and/or abscess; 48.0% (12/25) had dyspareunia; 40.0% (10/25) were infertile; 28% (7/25) had menstrual dysfunction; 20.0% (5/25) had dysmenorrhea; and 4.0% (1/25) experienced postmenopausal bleeding. Body mass index, residence, and educational level were significantly different between women diagnosed with FGTB and those where FGTB was excluded (P values=0.02, 0.03, and 0.01, respectively). However, no significant differences were found in age and Bacillus Calmette-Guérin vaccination status. **CONCLUSION:** Clinical suspicion may facilitate and improve the detection of FGTB, with chronic pelvic pain identified as the predominant clinical presentation among women in eastern Sudan.

### **Quality of life in women with vulvar cancer submitted to surgical treatment: a comparative study.**

de Melo Ferreira AP, de Figueiredo EM, Lima RA, Cândido EB, de Castro Monteiro MV, de Figueiredo Franco TM, Traiman P, da Silva-Filho AL  
Eur J Obstet Gynecol Reprod Biol. 2012 Jul 13. [Epub ahead of print]

**OBJECTIVES:** To investigate the occurrence and severity of lymphoedema of the lower extremities (LLE), quality of life (QoL), and urinary and sexual dysfunction in women with vulvar cancer submitted to surgical treatment. **STUDY DESIGN:** Twenty-eight patients with vulvar cancer submitted to vulvectomy and inguinofemoral lymphadenectomy and 28 healthy, age-matched women (control group) were evaluated. The occurrence and severity of LLE were determined by Miller's Clinical Evaluation. QoL, urinary function and sexual function were assessed by the EORTC QLQ-C30, SF-ICIQ and FSFI questionnaires, respectively. The differences between groups and correlations were assessed using Student's t-test, Chi-squared test, Mann-Whitney U-test and Spearman's rho test. **RESULTS:** The groups were similar in terms of marital status, educational status, menopausal status, hormone therapy and height. The occurrence and severity of LLE were higher in women with vulvar cancer compared with the control group ( $p < 0.001$  and  $p = 0.003$ , respectively). A significant association was found between the severity of LLE and advanced age ( $p = 0.04$ ), and the severity of LLE and higher body mass index (BMI;  $p = 0.04$ ) in patients with vulvar cancer. In the patients with vulvar cancer, there was a significant correlation between the severity of LLE and worse QoL in the following domains: physical, cognitive,

emotional, social, fatigue, pain, sleep and financial questions ( $p < 0.05$ ). There was no difference in urinary function between the two groups ( $p = 0.113$ ). Age and number of deliveries were the only variables associated with the occurrence of urinary incontinence ( $p = 0.01$ ). Urinary incontinence was present in women with a mean age of  $74.9 \pm 4.6$  years and a mean of  $7.3 \pm 1.3$  normal deliveries. There was no difference between the groups in terms of the sexual function. Multivariate analysis showed an association between sexual function and age ( $p = 0.01$ ), and sexual function and being in a stable relationship ( $p = 0.02$ ). **CONCLUSION:** Patients submitted to vulvectomy or inguinofemoral lymphadenectomy for vulvar cancer are at higher risk of developing LLE compared with healthy, age-matched women. This has a negative effect on QoL, but does not interfere with urinary or sexual function.

### **A modified triple incision technique for women with locally advanced vulvar cancer: A description of the technique and outcomes.**

Li J, Zhou H, Wang LJ, Lu XM, Rao QX, Lu HW, Lin ZQ

Eur J Obstet Gynecol Reprod Biol. 2012 Jun 25. [Epub ahead of print]

**OBJECTIVE:** Women with locally advanced vulvar carcinoma have an excellent chance of a cure by undergoing a radical vulvectomy with an "en bloc" inguinofemoral lymphadenectomy, but the morbidity associated this surgical approach is substantial. To achieve an outcome comparable with the traditional radical method in terms of oncologic safety, and an improved post-operative quality of life, we modified the classic triple-incision technique and suggested it as an alternative for these patients. The aim of this study was to report this new technique. **STUDY DESIGN:** Between January 2004 and November 2009, 24 patients with clinical stage T2 ( $\geq 4$ cm) or T3 invasive vulvar cancer underwent surgical treatment with our modified triple incision technique. Their clinical and surgical complications and follow-up data were retrospectively reviewed. **RESULTS:** The post-surgical complications were as follows: lymphoedema in 45.8%, wound breakdown in 20.8% and cellulitis in 8.3%. After a median follow-up of 35.5 months, three (12.5%) patients developed a recurrence in the skin bridge (2/24, 8.3%) or lungs (1/24, 4.2%). All patients suffering from skin bridge recurrences were salvaged by local re-resection. Four (16.7%) cases of death were noted: three (12.5%) patients died of non-cancer-related diseases and one (4.2%) died from a multifocal pulmonary metastasis; no evidence of vulvar or groin disease was observed at these patients' last follow-up. **CONCLUSION:** The modified triple-incision technique described in this preliminary study appears to be safe, feasible and tolerable for patients with a locally advanced vulvar cancer, and offers an acceptable morbidity.