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Natural History of Comorbid Orofacial Pain Among Women with Vestibulodynia

Eric Bair, MS, PhD[1,2], **Elizabeth Simmons, BS**[3,4], **Jessica Hartung, BS**[3,4], **Kinnari Desia, MD, MPH**[3], **William Maixner, DDS, PhD**[2], and **Denniz Zolnoun, MD, MPH**[2,3,4]

[1]Departments of Endodontics and Biostatistics, University of North Carolina, Chapel Hill, North Carolina, 27599-7450

[2]Regional Center for Neurosensory Disorders, School of Dentistry, University of North Carolina, Chapel Hill, North Carolina 27599-7435

[3]Pelvic Pain Research Unit, Department of Obstetrics & Gynecology, University of North Carolina, Chapel Hill, North Carolina 27599-7570

[4]University of North Carolina School of Medicine, Department of Obstetrics and Gynecology, Division of Advanced Laparoscopy and Pelvic Pain, Chapel Hill, North Carolina 27599-7570, Phone number: (919) 966-8202, Fax number: (919) 966-5833, Denniz_Zolnoun@med.unc.edu

Abstract

Objectives—We evaluated the stability of the comorbidity between vulvodynia and orofacial pain (OFP) and its associated clinical characteristics over a two-year follow up period.

Methods—In an earlier study of vestibulodynia patients, we administered questionnaires assessing demographic data, self-reported pain, anxiety, somatic awareness, and presence of signs and symptoms suggestive of clinical and subclinical OFP. The present study readministered the same surveys to a subset of the original cohort after a two-year follow up period.

Results—Of the 138 women in the previous study, 71 (51%) agreed to participate in the present study. We confirmed our earlier findings that 1) orofacial pain is a highly prevalent (66%) condition among women with vestibulodynia, and 2) compared to women with no OFP symptoms, those with OFP symptoms experience higher levels of anxiety (P=0.005), and somatic awareness (P<0.001). While OFP symptoms showed improvement in many of the vestibulodynia patients (33%) with OFP symptoms at baseline, 13% had either developed new symptoms or transitioned from subclinical to clinical OFP classification. Intercourse-related pain decreased in 69% of patients and increased in 24% of patients. Consistent with our earlier report, we did not observe significant differences with respect to demographics or severity of pain during intercourse among the subgroups.

Discussion—Orofacial pain is a common comorbidity among women with vestibulodynia, although the presence of OFP can vary over time. The comborbidity between vestibulodynia and OFP suggests that common underlying mechanisms may mediate both conditions.

CORRESPONDING AUTHOR AND REQUEST FOR REPRINTS: Denniz Zolnoun, MD, MPH, Department of Obstetrics and Gynecology, CB 7570, MacNider Building, University of North Carolina, Chapel Hill, NC 27599-7570, Phone: (919) 966-8202, Home: (919) 960-7624, Fax: (919) 966-5833, zolnound@med.unc.edu Reprints will not be available for this manuscript.

Keywords

vulvodynia; orofacial pain; vestibulodynia; somatization; temporomandibular disorder

Introduction

Vestibulodynia is the most common from of chronic vulvovaginal pain, which affects nearly 1 in 10 women at some point in their lifetime.[1] Vestibulodynia is also known as vulvar vestibulitis syndrome, localized vulvodynia, and, in 2004, was renamed as “provoked localized vulvodynia” by the International Society for the Study of Vulvovaginal Disease (ISSVD).[2] However, the clinical diagnosis of vestibulodynia has not changed since its original inception by Friedrich in 1987.[3] The diagnosis of vestibulodynia is a diagnosis of “exclusion” in that it is rendered only after excluding other “known causes” of persistent pain upon genital contact (i.e., tampon use) and tenderness to pressure localized within the vulvar mucosa (vestibule).[3] To date, the etiology and natural history of vestibulodynia remain poorly understood.

Although the clinical definition of vestibulodynia is based on a peripheral conceptualization of the painful process, an emerging body of evidence supports the idea that vestibulodynia is a complex pain disorder of the urogenital region.[4–6] In addition to higher pain sensitivity on mucosal contact, women with vestibulodynia show increased pain sensitivity in non-genital sites.[6] A higher prevalence of psychological traits, such as somatic awareness and anxiety, are similarly documented in this population.[7, 8] Collectively, these observations suggest that women with vestibulodynia may have an alteration in pain processing pathways similar to that seen in other pain disorders whereby certain psychosocial characteristics may facilitate the development and maintenance of a persistent pain state.[8, 9]

Granot and colleagues were the first to quantify the clinical implication of non-gynecological characteristics of patients with vestibulodynia. [10–12]They made an important observation that subgroups of women with vestibulodynia differed with respect to self-reported anxiety, somatic awareness, and non-genital pain sensitivity.[10–12] Women with higher non-genital pain sensitivity and anxiety tended to respond poorly to conventional treatments for vestibulodynia. [4] This work, as well as that of others,[13–15] has led to a gradual shift away from the traditional conceptualization of vestibulodynia as primarily a local mucosal inflammatory process.

We hypothesize that vestibulodynia is a group of disorders characterized by peripheral nociceptive stimuli in the vestibular mucosa (e.g., heightened inflammatory response) and central pain processing pathways. However, the extent to which these dysfunctions contribute to the overall clinical picture varies among individuals. In our earlier work, we postulated that comorbidity with orofacial pain (OFP) might be a clinical marker for a state of pain amplification among women with vestibulodynia.[8] We subsequently explored the prevalence and clinical characteristics of patients with vestibulodynia with or without comorbid OFP. Comorbid OFP was highly prevalent in our cohort of vestibulodynia patients.[8] The objective of this study is to examine the stability of OFP symptoms two years after the initial examination and evaluate the association between our baseline observations

and the clinical correlates of comorbid OFP. We also evaluated the validity of our OFP diagnosis by having a sample of seven subjects undergo evaluation by an orofacial pain specialist.

Materials and Methods

This retrospective cohort questionnaire study was conducted in 2007, approximately two years following the initial evaluation. It was approved by the institutional review board at the University of North Carolina at Chapel Hill. Of the previously described cohort of 138 women,[8] seventy-five percent (n=103) had given permission to be contacted for future research. A package containing consent forms, study materials, and a pre-stamped envelope was mailed to potential participants. We received 13 packages marked “Return to Sender” from women who could not be contacted and did not receive anything from the remaining 19 potential participants. Thus, our study sample consists of 71 women, representing 51% of the original cohort.

The battery of questionnaires included assessments for psychological characteristics and self-reported pain. Additionally, participants completed a 9-item, validated questionnaire in order to assess signs and symptoms suggestive of temporomandibular disorder (TMD).[16] Characteristics of these questionnaires are described below.

Pain Questionnaire

Self-reported pain with intercourse was assessed by administering the Gracely Pain Scale, which asks women to rate the lowest, average and maximal pain with intercourse on a scale of 0–100.[17] Modified versions of this questionnaire are commonly used for assessing pain among patients with idiopathic pain disorders (e.g., TMD and fibromyalgia).

Psychological Questionnaires

We administered questionnaires to assess anxiety (*Speilberger State-Trait Anxiety Inventory*), somatic awareness (*Pennebaker Inventory of Limbic Languidness*), and global psychological distress (*Brief Symptom Inventory-Global Severity Index*). The following is a brief description of these questionnaires.

The *State-Trait Anxiety Inventory (STAI)* consists of two 20-item questionnaires, which assess an individual’s current anxiety level and general propensity towards anxiety. This instrument has good reliability (retest reliability: r=.73 to .86, Cronbach’s α=0.83 to 0.92) and is widely utilized in clinical research.[18] The norm for a female population of comparable demographics is 36 on both scales. As a comparison, the average score of an inpatient neuropsychiatric population is 47.7 and 46.6, respectively for the state and trait anxiety scales.

The *Pennebaker Inventory of Limbic Languidness (PILL)*[19] assesses somatization by capturing the frequency of occurrence of 54 common physical symptoms and sensations. It has high internal consistency (α=0.88) and adequate test-retest reliability (0.70 for a two-month period); the norm for the female population is 98–104. [8, 19] A high PILL score is an independent risk factor for the development of a chronic pain state and is shown to correlate

well with the number of tender muscle sites, pain sensitivity and progression to chronicity. [20, 21]

The *Brief Symptom Inventory (BSI)* consists of 53 items that evaluate psychological distress in nine areas: somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism. A global severity index (GSI) is obtained by combining the number and intensity of reported symptoms. Internal consistency using Cronbach's α ranges from a low of 0.75 (psychoticism) to a high of 0.85 (depression). Test-retest validity for the global severity index score is 0.90.[22]

To examine the prevalence of signs and symptoms suggestive of idiopathic pain disorders in the orofacial region, we readministered a 9-item, validated screening questionnaire that queried the participants on the frequency and duration of symptoms such as headache, facial and jaw pain, grinding, and clenching. The same survey was previously administered at baseline and has been shown to have high sensitivity (100%) and specificity (81%) when used to screen for patients with TMD.[8]

Women were classified into one of three categories (OFP, subclinical OFP, or no OFP) by an independent reviewer who did not observe the subjects' identification and responses to psychometric questionnaires.[8] Participants were classified as having OFP if they had previously been diagnosed with TMD by a health care provider or reported experiencing both provoked and spontaneous orofacial pain and endorsed greater than three episodes of headache or "sinus pain" per week. Alternatively, they were classified as having subclinical OFP if they reported provoked orofacial pain and greater than three episodes of headache or "sinus pain" per week but no spontaneous orofacial pain. Subjects also had to report using a night guard, teeth grinding, or teeth clenching to be classified as having subclinical OFP. Three women were excluded from this analysis due to missing data.

Note: Although the questionnaire was designed to screen for TMD, we used the terms "OFP" and "subclinical OFP" rather than "TMD" and "subclinical TMD." We used this terminology partly for consistency with the terminology in our earlier paper[8] and partly out of concern that the term "TMD" usually implies that the diagnosis was based on a clinical exam rather than a questionnaire. Since no clinical exam was performed for the majority of the patients in the present study, we were concerned that using the term "TMD" could mislead readers. However, the expectation is that women in the OFP group will have TMD pain rather than other types of orofacial pain.

Finally, a random sample of 7 women from the original cohort agreed to undergo an independent assessment by an orofacial pain expert at our Regional Center for Neurosensory Disorders. Diagnoses were made by trained examiners using the Research Diagnostic Criteria for TMD classification.[23] The examiners were trained and calibrated as part of the Orofacial Pain: Prospective Evaluation and Risk Assessment (OPPERA) study. Calibration was repeated over 12–15 month intervals, and inter-examiner reliability was excellent. See Slade et al. (2011) [24] for details of the training and calibration procedure. The examiners were blinded to the participants' questionnaire responses.

Data Analysis

Statistical analysis was performed using SAS version 9.1. The three OFP groups (OFP, subclinical OFP, no OFP) were compared with respect to each variable of interest. These characteristics include age, race, education, parity, marital status, duration of pain, and number of prior physicians seen for similar symptoms. Vestibulodynia-related pain and the psychological measures were also compared between the three groups. Also, the women who were retained in the cohort were compared with the women who were lost to follow up with respect to the demographic variables. The null hypothesis of no difference between the three groups was tested using Fisher's exact test for categorical variables and one-way analysis of variance (ANOVA) for continuous variables. All tests comparing the three groups were conducted at $\alpha=0.05$. If overall differences were detected ($p<0.05$), differences between the groups were evaluated using Bonferroni-adjusted t-tests.

The association between the psychological measures and changes in pain severity over time was also evaluated. First the women were dichotomized into two groups: those whose facial pain decreased from baseline to follow up (e.g., subclinical OFP became pain-free or OFP became subclinical OFP or pain-free) and those whose facial pain increased (e.g., subclinical OFP became OFP or pain-free became OFP or subclinical OFP). The null hypothesis of no difference between these two groups with respect to each psychological measure (measured both at baseline and at follow up) was evaluated using t-tests. Then the women were dichotomized into two groups again based on whether or not their average intercourse-related pain rating decreased or increased from baseline to follow up and the analysis was repeated. Finally, the Pearson correlation between each psychological measure (measured both at baseline and follow up) and each rating of intercourse-related pain (measured at follow up) was calculated, and the null hypothesis that each correlation is equal to 0 was tested using linear regression.

Results

Among the 7 women who underwent an independent examination by an orofacial pain specialist, 5 were diagnosed with TMD. One of these five women was also diagnosed with fibromyalgia. The remaining two women did not meet the diagnostic criteria for TMD.

In general, participants were highly educated, Caucasian women in their early-to-mid-thirties (Table 1). OFP symptoms were present in 66% (n=47) of the participants. Of those, 49% (n=23) were classified as having subclinical OFP and 51% (n=24) were classified as having OFP. No significant demographic differences were observed among the subgroups, which was consistent with our earlier results. Only 7 women reported no intercourse-related pain. However, the average intercourse-related pain rating was significantly lower than it was in the original cohort (mean difference=18.0, $p<0.0001$). Also, no significant differences were observed between women retained in the cohort and women who were lost to follow up with respect to any of the demographic measures (Supplementary Table 1).

Similar to our earlier report, we observed significant differences in psychological characteristics among the three subgroups (Table 2). Compared to OFP-free patients with vestibulodynia, those with comorbid OFP had significantly higher levels of anxiety (STAI-

state 36.6 vs. 44.8, p=0.025) and somatic awareness (PILL, 102.9 vs. 128.9, p=0.0007). Women with subclinical OFP scored somewhere in the middle of the range delineated between OFP and OFP-free. (Table 2) Also, self-reported severity of pain during intercourse did not differ among subgroups of women with OFP (average pain, 36.1 vs. 39.2, p=0.807).

Seventy-three percent (11/15) of OFP-free patients at baseline remained free of symptoms, whereas only 41% (9/22) and 53% (18/34) of vestibulodynia patients with subclinical and clinical OFP stayed within their respective category. (Table 3) Forty-three percent (24/56) of vestibulodynia patients with OFP symptoms at baseline showed reduced OFP symptoms at two-year follow-up. However, 27% (4/15) of OFP-free vestibulodynia patients developed new symptoms, and 23% (5/22) of patients with subclinical OFP transitioned to clinical OFP (n=5; 7%) classification by the time of the follow-up study.

No significant associations were observed between any of the psychological measures and improvement in either OFP or intercourse-related pain (Supplementary Table 2). In general no significant correlations were observed between the psychological measures at baseline and the intercourse-related pain levels at follow up (Supplementary Table 3). The psychological measures collected at follow up were generally positively correlated with intercourse-related pain, but (with a few exceptions) these correlations were not statistically significant.

Discussion

In our cohort 89% (61/68) of women with vestibulodynia reported at least some intercourse-related pain at the time of follow up, and 65% (44/68) of these women had symptoms of orofacial pain. Similar to our earlier report, patients with comorbid OFP had higher levels of psychological distress. However, intercourse-related pain and demographic characteristics did not differ among the subgroups.

TMD is the most common form of chronic orofacial pain affecting upward of 10% of the adult population, and approximately 80% of the treated cases are women in their early-to-mid-adulthood.[24, 25] A previous study found that 49% of TMD patients showed complete remission after a five-year follow up period, and 23% reported a reduction in pain. [26] Similarly, 43% of our cohort with OFP at baseline showed either improvement in symptoms (20%) or were OFP-free (23%) after two years. Thus, the trajectory of improvement in our cohort at 5 years is likely to be consistent with what has been reported in the literature. On the other hand, it is interesting to note that 16% (6/37) of women without OFP at baseline developed OFP during the two-year follow up period, which is much higher than the reported TMD incidence rate in the literature.[27–29] The sample size in our cohort is relatively small, so this result should be interpreted cautiously. However, this suggests that not only is vestibulodynia comorbid with TMD but TMD-free women with vestibulodynia may be at higher risk of developing TMD.

The exact mechanism responsible for the association between musckeloskeletal pain of the orofacial region and provoked pain of the urogenital region is unknown.[8] However, it is possible that a common underlying biological vulnerability may be a predisposing factor for

the genesis of pain in both conditions.[8, 9, 30] Alternatively, a persistent pain state in women with vestibulodynia may predispose them to development of other idiopathic pain conditions such as fibromyalgia and/or TMD via central sensitization.[6]

Research in idiopathic pain disorders (e.g., TMD) requires conceptual models of the interplay between biological, psychological, and environmental factors and how these factors may ultimately affect the clinical phenotype of individuals with pain.[9] Such a model is presently lacking in vestibulodynia. In the absence of such a multi-dimensional model, individual symptoms and characteristics are more likely to be misconstrued as "causal." This follow up study provides confirmatory evidence of our baseline results suggesting that vestibulodynia is an idiopathic pain disorder that is comorbid with TMD.

A conceptual model for the development of TMD has been proposed wherein TMD (and other chronic pain conditions) are caused by a variety of genetic and environmental factors resulting in dysregulation in the central nervous system (CNS), which is manifested in the form of heightened pain sensitivity and psychological distress (Supplementary Figure 1).[9, 25] Note that this model implies a common set of risk factors for all idiopathic pain conditions. Thus, not only does the model predict that TMD will be comorbid with vestibulodynia but also that both TMD and vestibulodynia are comorbid with other common idiopathic pain conditions. Moreover, the model predicts that these common risk factors for idiopathic pain (namely heightened pain sensitivity and psychological distress) will be present in patients with TMD and vulvodynia (and other chronic pain conditions).

Consistent with our baseline results, we observed that a significant proportion of vestibulodynia patients had comorbid OFP and that patients with comorbid OFP have higher levels of psychological distress. Consistent with what has been observed elsewhere,[31] the largest differences between OFP patients and patients without OFP were observed with respect to measures of somatic awareness (i.e., PILL and the somatization subscale of the BSI), with small differences apparent in measures of anxiety and depression. This is particularly noteworthy because psychological distress is associated with nearly all idiopathic pain disorders, and it may be caused by specific genetic variants that mediate the activities of central pain regulatory pathways.[32] This study provides additional evidence in support of our earlier hypothesis that "… subgroups of women with vestibulodynia may share the same vulnerability as women with temporomandibular disorder. Thus, the associations between certain psychological traits and signs/symptoms of OFP among women with vestibulodynia suggest that an inherent susceptibility may permit or even precede the development of vestibulodynia in certain women." [8]

It is interesting to note that several earlier studies have shown that vestibulodynia patients with high levels of psychological distress are more likely to report pain after a vestibulectomy.[13, 14] This is consistent with the hypothesis that many forms of vestibulodynia are idiopathic pain conditions mediated by dysregulation in the CNS. If vestibulodynia is centrally mediated, patients will experience symptoms common to other idiopathic pain conditions (e.g., psychological distress). Moreover, treatments targeted at the vaginal region (e.g., vestibulectomy) are unlikely to be effective since they will not treat the CNS dysregulation that is truly responsible for the pain.

While our results are interesting, it is important to note that our population primarily consists of patients with severe vestibulodynia that were recruited in a tertiary referral setting. Therefore, the findings from our patient population may not be generalizable. Furthermore, the 71 (out of the original cohort of 138) women who completed the 2-year follow up questionnaires may differ from those we were unable to reach. Nevertheless, it is unlikely that women who could not be reached would significantly change our findings because the associations between vulvodynia and OFP and between OFP and psychological distress remained nearly identical to our initial observation. Moreover, there were no significant demographic differences between the women who were retained in the cohort and the women who were lost to follow up.

Also, the sample size is relatively small, which limits the power to detect associations between variables of interest. In particular, the fact that no significant difference was observed between OFP and non-OFP women with respect to the anxiety and depression subscales of the BSI is most likely the result of insufficient power, since similar measures have been shown to be associated with TMD in larger studies.[31] Similarly, the lack of a significant correlation between the psychological variables and intercourse-related pain and the lack of an association between the psychological measures and improvement in pain severity may also be the result of insufficient power. A similar study would need to be conducted with a larger sample to definitely answer the question of whether psychological distress is predictive of poorer treatment outcomes.

Another reason for caution when interpreting the results in Supplementary Table 3 is the fact that our cohort only includes women with vestibulodynia and thus is not representative of the general population. If pain-free women were included in our cohort, it is likely that these women would also have low levels of psychological distress, which might cause the correlation between psychological distress and intercourse-related pain to be significantly greater than 0. Thus, the lack of an association between psychological distress and intercourse-related pain in our cohort may imply that psychological distress is not associated with the severity of intercourse-related among women with vestibulodynia. However, if does not imply that psychological distress is not associated with the presence of intercourse-related pain, because pain-free women were not included in our cohort.

Finally, it is worth noting that OFP was evaluated by questionnaire rather than a “gold standard” clinical exam. Although the questionnaire that was used has been shown to have excellent specificity and sensitivity for predicting examiner-verified TMD[8] (and performed well in our small validation sample of 7 women), it is possible that some women were misdiagnosed.

Further confirmation of our hypothesis that vestibulodynia is a chronic condition mediated by dysregulation in the CNS would require recruiting additional women with vestibulodynia and evaluating them for the presence of TMD and other comorbid pain conditions. We are currently recruiting women for such a study and evaluating them both for the presence of TMD (and other idiopathic pain conditions) and for other measures known to be associated with idiopathic pain (such as measures of experimental pain sensitivity and psychological distress).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Harlow BL, Stewart EG. A population-based assessment of chronic unexplained vulvar pain: have we underestimated the prevalence of vulvodynia? Journal of the American Medical Women's Association (1972). 2003; 58:82–88.
2. Bachmann GA, Rosen R, Pinn VW, Utian WH, Ayers C, Basson R, et al. Vulvodynia: a state-of-the-art consensus on definitions, diagnosis and management. J Reprod Med. 2006; 51:447–456. [PubMed: 16846081]
3. Zolnoun D, Hartmann K, Lamvu G, As-Sanie S, Maixner W, Steege J. A conceptual model for the pathophysiology of vulvar vestibulitis syndrome. Obstet Gynecol Surv. 2006; 61:395–401. quiz 23. [PubMed: 16719941]
4. Granot M, Zimmer EZ, Friedman M, Lowenstein L, Yarnitsky D. Association between quantitative sensory testing, treatment choice, and subsequent pain reduction in vulvar vestibulitis syndrome. J Pain. 2004; 5:226–232. [PubMed: 15162345]
5. Foster DC, Dworkin RH, Wood RW. Effects of intradermal foot and forearm capsaicin injections in normal and vulvodynia-afflicted women. Pain. 2005; 117:128–136. [PubMed: 16087295]
6. Giesecke J, Reed BD, Haefner HK, Giesecke T, Clauw DJ, Gracely RH. Quantitative sensory testing in vulvodynia patients and increased peripheral pressure pain sensitivity. Obstet Gynecol. 2004; 104:126–133. [PubMed: 15229011]
7. Zolnoun D, Park EM, Moore CG, Liebert CA, Tu FF, As-Sanie S. Somatization and psychological distress among women with vulvar vestibulitis syndrome. International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics. 2008; 103:38–43.
8. Zolnoun DA, Rohl J, Moore CG, Perinetti-Liebert C, Lamvu GM, Maixner W. Overlap between orofacial pain and vulvar vestibulitis syndrome. Clin J Pain. 2008; 24:187–191. [PubMed: 18287822]
9. Diatchenko L, Nackley AG, Slade GD, Fillingim RB, Maixner W. Idiopathic pain disorders--pathways of vulnerability. Pain. 2006; 123:226–230. [PubMed: 16777329]
10. Granot M, Friedman M, Yarnitsky D, Tamir A, Zimmer EZ. Primary and secondary vulvar vestibulitis syndrome: systemic pain perception and psychophysical characteristics. Am J Obstet Gynecol. 2004; 191:138–142. [PubMed: 15295354]
11. Granot M, Friedman M, Yarnitsky D, Zimmer EZ. Enhancement of the perception of systemic pain in women with vulvar vestibulitis. Bjog. 2002; 109:863–866. [PubMed: 12197364]
12. Granot M, Lavee Y. Psychological factors associated with perception of experimental pain in vulvar vestibulitis syndrome. J Sex Marital Ther. 2005; 31:285–302. [PubMed: 16020147]
13. Eanes A, Bair E, Martin C, Iyer P, Zolnoun D. Psychosexual correlates of persistent postsurgical pain in patients with vulvodynia. International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics. 2011; 113:225–228.
14. Bohm-Starke N, Rylander E. Surgery for localized, provoked vestibulodynia: a long-term follow-up study. J Reprod Med. 2008; 53:83–89. [PubMed: 18357798]
15. Heddini U, Bohm-Starke N, Nilsson KW, Johannesson U. Provoked vestibulodynia-medical factors and comorbidity associated with treatment outcome. J Sex Med. 2012; 9:1400–1406. [PubMed: 22376009]

16. Gonzalez YM, Schiffman E, Gordon SM, Seago B, Truelove EL, Slade G, et al. Development of a brief and effective temporomandibular disorder pain screening questionnaire: reliability and validity. J Am Dent Assoc. 2011; 142:1183–1191. [PubMed: 21965492]
17. Gracely RH. Evaluation of multi-dimensional pain scales. Pain. 1992; 48:297–300. [PubMed: 1594252]
18. Speilberger, CDGR.; Lushene, R.; Vagg, PR.; Jacobs, GA. Manual for the state-trait anxiety inventory (form Y1). Palo Alto: Consulting Psychology Press; 1983.
19. Pennebaker JW, Gonder-Frederick L, Stewart H, Elfman L, Skelton JA. Physical symptoms associated with blood pressure. Psychophysiology. 1982; 19:201–210. [PubMed: 7071299]
20. Huang GJ, LeResche L, Critchlow CW, Martin MD, Drangsholt MT. Risk factors for diagnostic subgroups of painful temporomandibular disorders (TMD). J Dent Res. 2002; 81:284–288. [PubMed: 12097315]
21. Rammelsberg P, LeResche L, Dworkin S, Mancl L. Longitudinal outcome of temporomandibular disorders: a 5-year epidemiologic study of muscle disorders defined by research diagnostic criteria for temporomandibular disorders. J Orofac Pain. 2003; 17:9–20. [PubMed: 12756926]
22. Derogatis LR, Melisaratos N. The Brief Symptom Inventory: an introductory report. Psychological medicine. 1983; 13:595–605. [PubMed: 6622612]
23. Schiffman EL, Ohrbach R, Truelove EL, Tai F, Anderson GC, Pan W, et al. The Research Diagnostic Criteria for Temporomandibular Disorders. V: methods used to establish and validate revised Axis I diagnostic algorithms. J Orofac Pain. 2010; 24:63–78. [PubMed: 20213032]
24. Slade GD, Bair E, By K, Mulkey F, Baraian C, Rothwell R, et al. Study methods, recruitment, sociodemographic findings, and demographic representativeness in the OPPERA study. J Pain. 2011; 12:T12–T26. [PubMed: 22074749]
25. Maixner W, Diatchenko L, Dubner R, Fillingim RB, Greenspan JD, Knott C, et al. Orofacial pain prospective evaluation and risk assessment study--the OPPERA study. J Pain. 2011; 12:T4–T11. e1–e2. [PubMed: 22074751]
26. Ohrbach R, Dworkin SF. Five-year outcomes in TMD: relationship of changes in pain to changes in physical and psychological variables. Pain. 1998; 74:315–326. [PubMed: 9520246]
27. Aggarwal VR, Macfarlane GJ, Farragher TM, McBeth J. Risk factors for onset of chronic oro-facial pain--results of the North Cheshire oro-facial pain prospective population study. Pain. 2010; 149:354–359. [PubMed: 20304556]
28. Kindler S, Samietz S, Houshmand M, Grabe HJ, Bernhardt O, Biffar R, et al. Depressive and anxiety symptoms as risk factors for temporomandibular joint pain: a prospective cohort study in the general population. J Pain. 2012; 13:1188–1197. [PubMed: 23141187]
29. Slade D, Bair E, Greenspan JD, Dubner R, Fillingim LA, Maixner W, et al. Signs and symptoms of first-onset TMD and socio-demographic predictors of its development: the OPPERA prospective cohort study. J Pain. In press.
30. Diatchenko L, Nackley AG, Tchivileva IE, Shabalina SA, Maixner W. Genetic architecture of human pain perception. Trends Genet. 2007; 23:605–613. [PubMed: 18023497]
31. Fillingim RB, Ohrbach R, Greenspan JD, Knott C, Dubner R, Bair E, et al. Potential psychosocial risk factors for chronic TMD: descriptive data and empirically identified domains from the OPPERA case-control study. J Pain. 2011; 12:T46–T60. [PubMed: 22074752]
32. Gunter WD, Shepard JD, Foreman RD, Myers DA, Greenwood-Van Meerveld B. Evidence for visceral hypersensitivity in high-anxiety rats. Physiol Behav. 2000; 69:379–382. [PubMed: 10869605]

Table 1

Characteristics of the Study Participants

Patient Characteristics	No OFP n	No OFP Mean ± SD or Freq (%)	Sub-clinical OPF n	Sub-clinical OPF Mean ± SD or Freq (%)	Clinical OFP n	Clinical OFP Mean ± SD or Freq (%)	P*
Age	24	32.8 ± 7.3	23	32 ± 5.7	24	34.6 ± 9	0.494
White	24	22 (92%)	23	21 (91%)	24	21 (86%)	1.000
College education or beyond	24	20 (83%)	23	21 (91%)	24	22 (92%)	0.733
Nulliparous	24	17 (71%)	23	15 (65%)	24	14 (58%)	0.694
Married	24	18 (75%)	23	18 (75%)	24	21 (88%)	0.564
Intercourse related pain (GPS)	24		23		24		
Low		20 ± 25.4		12.8 ± 16.7		21.3 ± 27.7	0.430
Average		36.1 ± 29.4		33 ± 22.8		39.2 ± 35.5	0.807
High		51 ± 32.1		60 ± 29.7		54.1 ± 35.2	0.628

OFP, orofacial pain syndrome. GPS, Gracely Pain Scale.

*Significance testing based upon ANOVA test for continuous variables and Fisher's Exact Tests for categorical.

Table 2

Psychological Characteristics of Subgroups of Women with Vestibulodynia.

Psychological Scores	N0 OFP n=24 MEAN (SD)	Sub-clinical OFP n=23 MEAN (SD)	Clinical OFP n=24 MEAN (SD)	P*	Multiple Comparisons Bonferroni Adjusted Results
STAI- state	36.6 (2.0)	41.1 (2.3)	44.8 (1.9)	0.0250	Clinical > No OFP
STAI – trait	39.1 (2.4)	42.2 (1.9)	46.7 (2.2)	0.0540	Clinical > No OFP
PILL – somatization	102.9 (4.0)	111.3 (4.5)	128.9 (5.5)	0.0007	Clinical > Sub-clinical and No OFP
BSI-GSI	0.7 (0.1)	0.7 (0.1)	1.0 (0.1)	0.0601	----
Anxiety	0.7 (0.1)	0.9 (0.2)	1.1 (0.1)	0.0936	----
Somatization	0.5 (0.1)	0.6 (0.1)	1.0 (0.1)	0.0041	Clinical > Sub-clinical and No OFP
Depression	0.8 (0.2)	0.7 (0.2)	1.1 (0.2)	0.1830	----

*Significance testing based upon ANOVA test.

†STAI-S, Spielberger State Anxiety Inventory describing situational or state related anxiety

‡STAI-T, Spielberger Trait Anxiety Inventory describing general propensity (trait) toward anxiety

§PILL, Pennebaker Inventory of Limbic Languidness

‖BSI-GSI, Brief Symptom Inventory -Global Severity Index, composite score for psychological distress with individual subscale scores

Table 3

Diagnostic category of OFP*: baseline vs. 2 year follow-up (row %)

	2 year follow-up		
Diagnostic Category	**No OFP**	**Subclinical OFP**	**Clinical OFP**
No OFP	11 (78.6%)	2 (14.3%)	1 (7.1%)
Subclinical OFP	8 (36.4%)	9 (40.9%)	5 (22.7%)
Clinical OFP	5 (14.7%)	11 (32.4%)	18 (52.9%)

* OFP: Orofacial Pain