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The Genito-Pelvic Pain/Penetration Disorder Paradigm and Beyond

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CHAPTER

4

**Transcutaneous Electrical
Nerve Stimulation as an
Additional Treatment for
Women Suffering from
Therapy-Resistant Provoked
Vestibulodynia;
a Feasibility Study**

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ABSTRACT

Introduction. The current approach to women with provoked vestibulodynia (PVD) comprises a multidimensional, multidisciplinary therapeutic protocol. As PVD is considered to be a chronic pain disorder, transcutaneous electrical nerve stimulation (TENS) can be used as an additional therapy for women with otherwise therapy-resistant PVD.

Aims. The aims of this study were to evaluate whether TENS has a beneficial effect on vulvar pain, sexual functioning, and sexually-related personal distress in women with therapy-resistant PVD and to assess the effect of TENS on the need for vestibulectomy.

Methods. A longitudinal prospective follow-up study was performed on women with therapy-resistant PVD who received additional domiciliary TENS. Self-report questionnaires and visual analog scales (VASs) were completed at baseline (T1), post-TENS (T2), and follow-up (T3).

Main Outcome Measures. Vulvar pain, sexual functioning, and sexually-related personal distress were the main outcome measures.

Results. Thirty-nine women with therapy-resistant PVD were included. Mean age was 27 ± 5.6 years (range: 19 to 41); mean duration between TENS and T3 follow-up was 10.1 ± 10.7 months (range: 2 to 32). Vulvar pain VAS scores directly post-TENS (median 3.4) and at follow-up (median 3.2) were significantly ($P < 0.01$) lower than at baseline (median 8.0). Post-TENS, sexual functioning scores on the Female Sexual Functioning Index questionnaire had improved significantly ($P = 0.2$); these scores remained stable at follow-up. Sexually-related personal distress scores had improved significantly post-TENS ($P = 0.01$). Only 4% of the women who received TENS needed to undergo vestibulectomy vs. 23% in our previous patient population.

Conclusion. The addition of self-administered TENS to multidimensional treatment significantly reduced the level of vulvar pain and the need for vestibulectomy. The long-term effect was stable. These results not only support our hypothesis that TENS constitutes a feasible and beneficial addition to multidimensional treatment for therapy-resistant PVD, but also the notion that PVD can be considered as a chronic pain syndrome.

INTRODUCTION

Provoked vestibulodynia (PVD) is a subtype of vulvodynia characterized by pain in a certain area of the vulva [1,2]. The main complaint of woman with PVD is vulvar pain during sexual intercourse, although the pain can also be triggered by other forms of pressure, such as wearing tight clothes or inserting a finger or tampon [3]. PVD is the most common cause of dyspareunia before menopause [4]; it affects 16% of women in the general population [5].

Friedrich defined PVD as vestibular pain at attempted vaginal penetration, vulvar vestibular pain on touching with a wet cotton tip (positive touch test), and varying degrees of vestibular erythema [6]. However, erythema does not appear to be a useful diagnostic criterion, because the clinical judgment of its presence and severity is subjective [7]. In daily clinical practice, two other criteria are considered relevant: symptoms should be of at least three to six consecutive months' duration and other causes of acquired superficial dyspareunia must be ruled out [8]. Besides its influence on sexual functioning, PVD can strongly affect other quality of life aspects, e.g., psychological and relational functioning [9,10].

The etiology of PVD is still not fully understood. Traditionally, it was classified as a sexual dysfunction, but in the light of prevailing theories, which lean toward neurogenic inflammation and changes in local innervation and central pain processing [11], PVD is more likely to be a chronic pain disorder [4,12,13]. Owing to the lack of any clear etiology, PVD is considered to be a heterogeneous, multisystemic, and multifactorial disorder that should be treated with an individualized, multidimensional, and multidisciplinary approach [3,14]. The multidimensional treatment protocol encompasses six main areas [15]: the mucous membrane, the pelvic floor, the experience of pain, sexual and relational functioning, psychosocial adjustment and, if applicable, genital/sexual abuse. If none of these lines of action provide the desired result, the final treatment option at our clinic is vestibulectomy. Spoelstra et al. found that after multidimensional treatment, vestibulectomy had been necessary as a last resort in 23% of the women [16]. From a medical perspective, this high-impact surgery is an ultimum refugium, because it is irreversible and invasive. The purpose of vestibulectomy is to remove the painful tissue from the vulvar vestibule, presumably including pain receptors or pro-inflammatory molecules [3]. Some studies reported success rates of 61–94% for vestibulectomy [17]. Bergeron et al. encountered in their patient population (n = 29) a deterioration in vulvar pain at long-term follow-up in 9% of cases [7].

We therefore searched for a less intrusive treatment for PVD than vestibulectomy to enhance the therapeutic power of the multidimensional approach. One option is (domiciliary) transcutaneous electrical nerve stimulation (TENS) because of its positive effects in other chronic pain conditions [18] and its low impact. Possible complications of TENS are known to be skin irritation, electrode adherence problems and difficulty attaching the electrodes, skin rash, and a burning sensation at the electrode site [18]. TENS is believed to have two mechanisms for relieving pain. The first is the gate-control theory, which postulates presynaptic inhibition of pain signals by stimulation of non-nociceptive afferent neurons [19]. Activation of A β -nerve fibers might attenuate pain signals from nociceptor C-fibers on interneuronal and spinal levels. The second mechanism is believed to use the descending pain suppression pathway, which originates in the cortex and is therefore called supraspinal inhibition [20–22].

The first to study electrical stimulation (ES) in the management of sexual pain disorders were Nappi et al. [23]. They found that after weekly intravaginal ES with a probe in their patient population of 29 women with vestibular pain, dyspareunia, or vaginismus, the vestibular pain significantly declined. At present, only three short-term studies have been published on the use of TENS for PVD [24–26]. The effect of treating PVD with TENS was first studied by Murina et al. [24]. Placebo TENS was compared with functional TENS in a randomized controlled trial (RCT) on women with vestibulodynia with 3 months follow-up. They used a vaginal probe to administer functional or sham TENS in a clinical setting, twice a week. A significant difference in vulvar pain reduction was found between placebo and functional TENS [24]. In an evaluative study, Dionisi et al. [26] found that weekly biofeedback in combination with TENS and functional ES led to improvements in vulvar pain in 76% of the subjects. They also used an endo-vaginal probe to administer TENS. The visual analog scale (VAS) was used to measure vulvar pain directly post-TENS treatment. In 75.8% (110/145) of the women in this study, vulvar pain lowered after TENS treatment.

Recently, Murina et al. performed an RCT in which all the subjects received domiciliary TENS treatment and either a combination of palmitoylethanolamide (PEA) + transpolydatin or a placebo. In contrast with the University Medical Center Groningen (UMCG) protocol, which recommends TENS treatment three times daily, these subjects were advised to use TENS three times weekly. Vulvar pain and dyspareunia scores were significantly lower posttreatment than at baseline. Additional treatment with PEA and transpolydatin was only effective in the subjects with recent onset PVD or relapse. It was concluded that TENS (self-administered in a home setting) can be of benefit in the management of vestibulodynia [25]. However, in the existing studies on TENS for PVD, it is not clear

whether the women had completed multidimensional treatment before receiving TENS. Owing to the multisystemic and multifactorial nature of PVD, the effectiveness of treatment should not only depend on vulvar pain and dyspareunia reduction but also on the ability to resume and experience satisfactory sexual intercourse and to reduce sexually-related distress. Until now, knowledge about the long-term feasibility of domiciliary TENS is lacking.

The present study aims to determine whether domiciliary TENS is a feasible additional treatment in the multidimensional approach to women with therapy-resistant PVD.

MATERIALS AND METHODS

STUDY DESIGN

A longitudinal non-placebo controlled cohort study was performed to test the feasibility of TENS as an additional treatment for an end-of-the-line population with therapy-resistant PVD.

PARTICIPANTS

The study was comprised of 39 women between the ages of 19 and 41, who were diagnosed with PVD by an experienced gynecologist annex sexologist at the UMCG. They received supplementary domiciliary TENS treatment between July 2009 and August 2013. A certified pelvic floor physiotherapist instructed the women on the proper use of TENS. Eligible candidates were required to be able to read and speak the Dutch language and be willing to give signed informed consent. Exclusion criteria were a cardiac pacemaker and/or pregnancy.

All the women diagnosed with PVD underwent multidimensional treatment according to the UMCG protocol, which was based on the results of two studies at the UMCG in 1996 and 2011 [15,16]. The treatment was also in accordance with the recommendations of the 3rd International Consultation on Sexual Medicine (2009). Patients who did not experience sufficient pain reduction on completion of the multimodal approach received additional (domiciliary) TENS treatment. They answered questionnaires directly before starting TENS (T1 = baseline) and at the end of TENS (T2 = post-TENS) to measure vulvar pain, sexual functioning, and sexually related personal distress. At long-term follow-up between January and August 2013 (T3), the women were asked to complete the same questionnaires and a separate general questionnaire on demographic and clinical characteristics (see Figure 1). All the questionnaires were coded and upon receipt, transferred to an anonymous database. The key to the codes was held by the data manager.

Approval for the study was requested from the institutional review board, but as there were no interventions besides questionnaires, the institutional review board considered this study to be an evaluation of standard health care. Consequently, this study did not fall under the legislation of the Dutch law on medical research into humans.

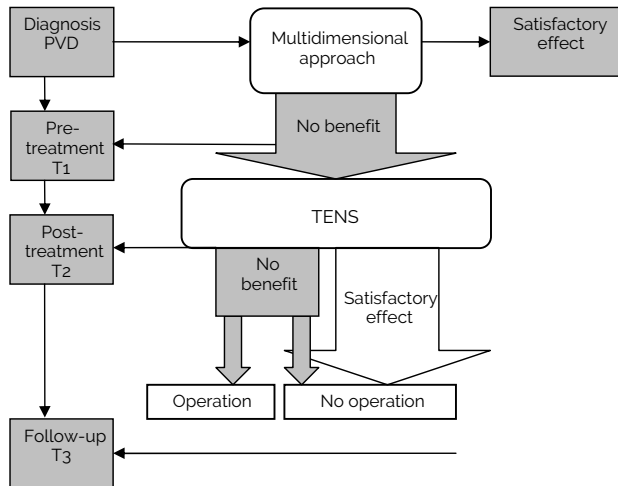


Figure 1 | Flowchart of the study design. Women diagnosed with PVD underwent multidimensional treatment. TENS was offered when this approach did not achieve sufficient pain reduction. Questionnaires were completed pre-TENS (T1), post-TENS (T2), and at follow-up (T3) to measure vulvar pain, sexual functioning, and sexually-related personal distress. PVD = provoked vestibulodynia; TENS = transcutaneous electrical nerve stimulation.

TENS PROCEDURE

PRIMO PRO equipment from CEFAR Medical AB (Malmö, Sweden) was used. This device had a dual channel setup. Adhesive electrodes were applied to the labia majora (on intact, clean, and non-greasy skin) in a V-shape (caudally on both sides of the introitus; cranially angled toward the groin). The electrodes used were oval and are 4.0 by 6.5 centimeters. If women had trouble with these electrodes, i.e., they did not adhere to the skin or caused mild skin irritation, then alternative electrodes were used that were square and 5.0 by 5.0 centimeters. There was no known difference in efficacy between electrodes, only size and adhesive substance. But difference in size was not considered to be relevant as long as the electrodes are placed over the nerves that innervate the introitus of the vagina. TENS frequency was 80 Hz with a pulse duration of 50 or 180 microseconds. Women started with 180 microseconds pulse duration; if this duration proved too sensitive for women, setting was changed by the physiotherapist to 50 microseconds for the remaining treatment. Pulse intensity was increased to the maximal

level that was still comfortable. To ensure good adherence of the electrodes and prevent irritation by "waxing" the skin, women were advised to shave the labia majora once a week and not to use the TENS device on the day of shaving to prevent irritation. After initial administration of the TENS by a pelvic floor physiotherapist, the women received one or two instruction sessions. The number of sessions depended on how swiftly each individual learned the procedure. They then applied the TENS treatment themselves two to three times a day at home at their own convenience, for a total duration of 90 minutes per day. Patients were instructed to continue the treatment for at least 12–16 weeks. The women returned to the physiotherapist after 6–8 weeks to evaluate the TENS treatment. If a patient no longer required TENS (i.e., the complaints had diminished to her satisfaction), the treatment was stopped.

Patients were free to choose their own application protocol, for instance, twice a day for 45 minutes. The total duration of treatment and the amount of time spent per week depended on how the women experienced the TENS treatment. Recommended use of TENS was three times daily for a total duration of 90 minutes. Time until benefit varied per woman and was not recorded objectively. After their last appointment with the physiotherapist, the patients kept the TENS equipment. They were then free to use it according to their needs and wishes. Some patients told the physiotherapist that they still used TENS occasionally when their symptoms required. Thus, the patients became independent and were given the means to direct their own treatment. No data were gathered on the use of TENS after long-term follow-up (T3).

QUESTIONNAIRES

Demographic and Clinical Variables

A single investigator collected all the data. General demographic and clinical data were obtained at prospective follow-up using a general questionnaire. These data included inter alia, age, marital status, and the use of medication and/or contraception. Additional data were obtained on pregnancy, childbirth and complications during and/or afterward, the presence of dyspareunia at the first (attempt at) sexual intercourse, current pain level during sexual activity and/or intercourse, and whether the women were able to have satisfactory intercourse at follow-up (T3). The women were also asked posttreatment at follow-up (T3) if they would recommend TENS treatment to other women with PVD.

Vulvar Pain

The McGill Pain Questionnaire–Dutch language version (MPQ-DLV) was used to evaluate the severity of pain and pain perception. The MPQ-DLV contains a VAS and 20 groups of

three to four pain-descriptive words arranged in progressive intensity. Overall intensity of vulvar pain was assessed on a 10-cm VAS on which the subject had to place a mark to indicate her pain level. Zero centimeter means no pain while 10 cm means the worst possible pain imaginable. The minimum VAS score was defined as the lowest level of vulvar pain experienced during the last (attempt at) sexual intercourse. Maximum VAS score was defined as the highest level of vulvar pain experienced during (attempts at) sexual intercourse. The VAS is a wellknown and widely used quantitative method to measure pain [27].

Domain scores on sensory, affective, and evaluative domains of pain were calculated using the number and order of intensity of the descriptive words. The MPQ-DLV is a reliable instrument to measure pain [28]. Total scores can range from 0 to 78. A higher score indicates increased pain and more severe pain perception.

Sexual Functioning

Sexual functioning was evaluated using the Female Sexual Functioning Index (FSFI). This is a brief self-report index, which consists of six domains: sexual desire, arousal, lubrication, orgasm, satisfaction, and genital pain. The Dutch version of the FSFI questionnaire is a reliable and valid measurement tool [29]. The total score can vary from 2 to 36. Lower scores indicate poorer sexual functioning. The cutoff score for differentiating between women with and without sexual dysfunction is 26.55 [30].

Sexually-Related Personal Distress

The Dutch version of the Female Sexual Distress Score (FSDS) was used to assess personal distress associated with sexual problems. It is known to be a reliable and valid instrument [29]. The total score can range between 0 and 48. Higher scores indicate more personal distress; 15 is the cutoff score of the FSDS [31].

STATISTICAL ANALYSIS

IBM SPSS statistics for Windows version 20.0 (Released 2011 IBM Corp, Armonk, NY, USA) was used to analyze the anonymized data from the women with PVD who received additional TENS between July 2009 and August 2013 after standard multidimensional treatment and completed one or more questionnaires at two or more of the data collection times. Quantitative comparisons of the baseline (T1), post-TENS (T2), and follow-up (T3) values on the MPQ-VAS, FSFI, and FSDS were made using nonparametric tests for repeated measures. The scores obtained at the three data collection times mostly had

an abnormal distribution. This was tested using q-q plots and histograms. To prevent difficulty with interpretation, all the values were compared using a nonparametric test: Wilcoxon signed-rank test. All the tests were two tailed; significance level was $P < 0.05$.

RESULTS

A total of 39 women with therapy-resistant PVD were included in this prospective follow-up study.

Patient characteristics (at T3) are shown in Table 1. Mean age was 26.7 ± 5.6 years (range: 19 to 41). In 35% of the women, the total duration of symptoms was 3–5 years; in 19%, the duration was shorter, while in 46% the symptoms had been present for more than 6 years. Mean duration of TENS was 6.2 ± 4.0 months (range: 1 to 12).

Table 1 Characteristics of the study population at T3

		Study population Mean or N	%
Age (years)	19-41	26.7	-
Duration of symptoms (years)	<2	6	19
	3-5	11	35
	6-9	7	23
	9>	7	23
Duration of treatment (months)	1.0-12.0	6.2	-
Primary/ lifelong PVD		11	35
Nulliparous		28	90
Medical history	Recurrent vaginal candidiasis	7	23
	Irritable bowel syndrome	2	6
	Depression	4	13
	Vestibulectomy	3	10
Civil status	Married	4	13
	Relationship, living apart	6	19
	Living together	9	29
	Divorced	1	3
	Single	11	35
Highest education level	University	5	16
	Community college	15	48
	Secondary education	8	26
	High school	3	10
Negative sexual experiences		10	33
Use of oral contraceptives		13	42
Medication use	Tricyclic antidepressants	1	3
	Selective serotonin re-uptake inhibitors	3	10

PVD = provoked vestibulodynia; T3 = follow-up

In 65% of the women, the complaints had started after initially pain-free intercourse (secondary PVD). In our study population, 23% (7/31) had a history of recurrent vaginal candidiasis; three women (10%) had undergone vestibulectomy prior to TENS; 13% (4/31) were suffering from depression; and all but one of the women were using a selective serotonin reuptake inhibitor. None of the patients in this study reported pain or local irritation from the electrodes. Mean follow-up (T3) after completion of TENS (T2) was 10.1 ± 10.7 months (range: 2 to 32).

MPQ-DLV: VAS

Table 2 shows the vulvar pain VAS scores at the most recent (attempt at) sexual intercourse. VAS, minimum VAS, and maximum VAS scores were significantly lower post-TENS (T2) than at baseline (T1) (median VAS from 8 at T1 to 3.4 at T2, $P < 0.001$; minimum VAS 5.3 to 2.1, $P = 0.01$; maximum VAS 8.3 to 6.1, $P < 0.001$). At follow-up (T3), the scores were not significantly different from those at post-TENS (T2) ($P = 0.74$). Figure 2 shows a box plot of the VAS scores. There was a significant decrease in the VAS score after TENS and no significant increase at follow-up.

MPQ-DLV: PAIN DESCRIPTIVE WORDS

At baseline (T1), the women who completed the MPQ-DLV to assess the intensity and characteristics of vulvar pain mostly described the pain as strained (44%), burning, ripping, and scorching (38%). Post-TENS (T2), the words chosen most often were stinging (33%), scorching, and burning (56%). At long-term follow-up (T3), burning (50%), strained (43%), and sharp (32%) were the most common.

The scores per domain of the MPQ-DLV are shown in Table 2. Scores were given for the total number of words chosen (NWC-t) and for the sum of the ranks of the words (PRI-t). At post-TENS (T2), NWC-t and PRI-t were significantly lower than at baseline (T1) ($P = 0.01$ and $P < 0.001$, respectively). The scores remained at this post-TENS level at follow-up (T3) and were still significantly lower than at baseline (NWC-t, $P = 0.02$; PRI-t, $P = 0.01$).

Table 2 Scores on the three questionnaires at baseline (T1), post-TENS (T2), and follow-up (T3)

	Descriptive						Statistics					
	Baseline T1			Post-TENS T2			Follow-up T3		T1 - T2	T1 - T3	T2 - T3	
	Median	Quartiles	n	Median	Quartiles	n	Median	Quartiles	n	P (n [*])	P (n [*])	P (n [*])
MPQ-DLV												
VAS Score	8	6.6, 8.8	39	3.4	1.9, 7.0	31	3.2	2.1, 6.7	28	.00 (31)	.00 (28)	.74 (20)
Min VAS	5.3	2.1, 6.2	31	2.1	1.0, 4.3	26	2.4	0.6, 4.0	27	.01 (25)	.01 (22)	.65 (18)
Max VAS	8.3	7.3, 9.3	31	6.1	3.0, 8.2	26	5.9	3.6, 7.7	27	.00 (25)	.00 (22)	.68 (18)
NWC-t	11.0	9.0, 15.0	34	10.0	3.0, 13.0	27	9.5	6.0, 12.0	28	.01 (27)	.02 (25)	.94 (18)
PRI-t	24.0	17.8, 32.0	34	16.0	6.0, 23.0	27	18.0	8.3, 24.3	28	.00 (27)	.01 (25)	.81 (18)
FSFI												
Desire	3.0	2.4, 4.2	30	3.6	3.0, 4.4	22	3.6	3.0, 4.2	28	.02 (20)	.08 (22)	.52 (16)
Arousal	3.6	2.4, 4.9	30	4.8	3.8, 5.4	22	4.8	3.7, 5.3	28	.03 (20)	.06 (22)	.73 (16)
Lubrication	4.1	2.7, 5.4	30	4.8	3.6, 5.5	22	4.8	3.9, 5.4	28	.12 (20)	.49 (22)	1.0 (16)
Orgasm	4.8	3.1, 5.6	30	5.2	4.4, 5.7	22	5.2	4.4, 5.9	28	.10 (20)	.07 (22)	.63 (16)
Satisfaction	2.6	1.6, 4.4	30	4.0	1.6, 5.2	22	4.6	2.1, 5.6	28	.15 (20)	.01 (22)	.50 (16)
Pain	0	0, 1.2	30	0	0, 4.4	22	2.0	0, 3.9	28	.14 (20)	.01 (22)	.72 (16)
Total FSFI	19.1	14.9, 22.9	30	25.0	18.0, 27.5	22	23.4	21.0, 28.4	28	.02 (20)	.01 (22)	.80 (16)
FSDS												
Total FSDS	32.0	27.0, 23.0	15	20.5	11.5, 31.8	20	21.0	13.5, 33.5	25	.01 (14)	.07 (8)	.42 (12)

*Number of paired observations included in the statistical analysis

Descriptive values are given as medians (50th percentile) and quartiles (25th and 75th percentiles) of the scores; difference between paired values was calculated with Wilcoxon signed-rank test between two related measures; n = number of subjects or pairs used in the analysis; P value = significance level; two tailed FSDS = Female Sexual Distress Score; FSFI = Female Sexual Functioning Index; MPQ-DLV = McGill Pain Questionnaire–Dutch language version; NWC-t = total number of words that the women chose; PRI-t = sum of the ranks of the words the women chose; TENS = transcutaneous electrical nerve stimulation; VAS = visual analog scale

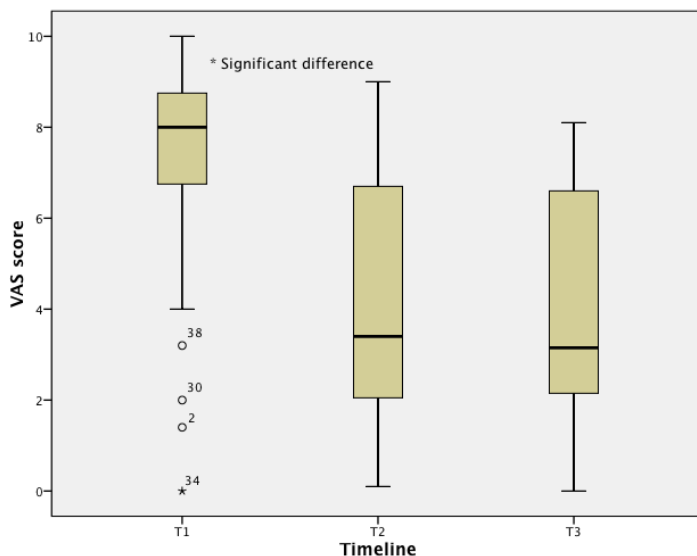


Figure 2 | Box plot of the VAS vulvar pain scores at baseline (T1), post-TENS (T2), and follow-up (T3). Box plot of the median, upper, and lower quartiles (box) and the minimum and maximum values within 1.5 times the interquartile range (whisker) and outliers (circles). TENS = transcutaneous electrical nerve stimulation; VAS = visual analog scale.

FSFI AND FSDS

Table 2 shows the median scores and quartiles on the FSFI and FSDS questionnaires at baseline, post-TENS, and follow-up. FSFI domain scores, FSFI total scores, and FSDS total scores were compared. Results of the statistical analysis are shown on the right side of Table 2; T2 and T3 values were both compared with baseline values. FSFI total score was significantly higher post-TENS (T2) than at baseline (T1) ($P = 0.02$). At post-TENS, there were significant increases in desire and arousal. At follow-up, the changes in desire and arousal were no longer significant. Instead, domain scores on satisfaction and pain reduction were significantly higher than at baseline (T1). The FSDS scores for sexually-related personal distress had improved significantly at post-TENS (T2) ($P = 0.01$). At T3, the median score was not significantly different from that at post-TENS ($P = 0.42$). The percentages of women who had normal FSDS scores (i.e., below cutoff) increased from 13% at baseline to 35% post-TENS and to 36% at follow-up.

GENERAL QUESTIONNAIRE

Table 3 shows the results of the general demographic and clinical questionnaire completed by 31 women at follow-up (T3). Post-TENS, 19 (61%) of the women had resumed sexual intercourse.

Only 2 out of these 19 women (11%) reported completely pain-free sexual intercourse. However, 79% of these 19 women who completed the questionnaire reported that sexual intercourse was satisfactory. And 87% of the 31 women who completed the general questionnaire at follow-up (T3) would recommend the treatment to other women with PVD. Three of the 31 women underwent a vestibulectomy before TENS. Of the remaining 28 women, only 1 woman underwent additional vestibulectomy after TENS treatment.

Table 3 | Status quo post-TENS based on the general questionnaire and a medical file survey (n = 31)

	Study population	%
Pain during sexual activity	23 /30	77
Resumption of intercourse after TENS	19 /31	61
Intercourse completely pain-free	2/19	11
Able to enjoy intercourse	15/19	79
Subject would recommend TENS to other women with PVD	27 /31	87

PVD = provoked vestibulodynia; TENS = transcutaneous electrical nerve stimulation

DISCUSSION

The aim of this longitudinal non-placebo controlled cohort study was to demonstrate that domiciliary TENS is a feasible and beneficial additional treatment for women with therapy-resistant PVD, i.e., that it leads to pain reduction, less need for surgery, and better sexual functioning.

We found that compared with baseline (T1), vulvar pain had decreased significantly post-TENS (T2). At follow-up (T3) (mean duration: 10.1 months), vulvar pain scores were still significantly lower than at baseline (T1). Scores on the MPQ showed that pain intensity perception was significantly lower post-TENS (T2) and that it remained at the same low level at long-term follow-up (T3). Sexual functioning improved significantly after TENS and only deteriorated slightly in the long-term. At follow-up (T3), sexual functioning scores were also significantly higher than at baseline (T1). Before they started TENS, our population of women reported having a high level of personal distress as a result of their PVD related sexual problems. After TENS (T2), this distress level was significantly lower ($P = 0.01$). The addition of TENS to multidimensional treatment meant that ultimately, only 4% of our study population needed vestibulectomy, in contrast with 23% previously [16]. These results confirm our hypothesis that TENS forms a feasible addition to multidimensional treatment for women with therapy-resistant PVD. This low-impact treatment yielded very positive results.

Our results of TENS on sexual functioning and vulvar pain 10 months post-TENS were in agreement with those reported in the placebo controlled study by Murina et al. [24] after a mean follow-up of 3 months. In the two studies, median VAS scores for vulvar pain decreased significantly.

Whereas we used a domiciliary selfadministered TENS protocol with cutaneous electrodes for 90 minutes per day, Murina et al. [24] sent their patients to a physiotherapy clinic where TENS was performed twice a week with a vaginal probe.

Our population had a longer history of PVD symptoms (81% had been experiencing symptoms for more than 3 years vs. a mean of 16.8 months in the study by Murina et al. [24]) and the complaints had proved to be relatively more resistant to other (multidimensional) treatment options. In addition, our findings expand upon those of previous studies, as TENS was also beneficial and feasible when applied cutaneously and as a last resort.

We opted to apply TENS in a domiciliary protocol because this is patient friendly, cost-effective, and the women could be expected to be more relaxed in their home environment. The results of the present study confirmed the conclusion drawn by Murina et al. [25] that TENS is of significant benefit in the management of PVD, also when applied in a home setting. In addition, we evaluated several extra dimensions to examine the feasibility of domiciliary TENS: the ability to resume intercourse, experience satisfactory intercourse, and reduce sexually-related personal distress. Positive effects of TENS were found on all these dimensions. These are very promising findings, particularly for women with therapy-resistant PVD when taking into account the multisystemic and multifactorial nature of PVD.

In 2011, Spoelstra et al. used a comparable broad set of end points to evaluate the effects of multidimensional treatment without the addition of TENS in women with PVD. They observed decreased vulvar pain in 81%, but 23% still had to be referred for vestibulectomy [16]. In the present study, 87% of the women perceived a decrease in vulvar pain and only 4% ultimately needed to undergo surgery. There could be some overlap between the population in the present study and that of Spoelstra et al. in 2011 [16]. In theory, participants in the study by Spoelstra et al. who did not experience sufficient relief (19%) could have been included in the present study. Although some of the population characteristics were different (primary PVD: 59% vs. 35%, nulliparous: 33% vs. 90%), all the women had received multidimensional treatment according to the UMCG protocol. Therefore, comparison of the two studies provides valuable information. Probably the most important limitation of the present study was the lack of a placebo control. It is widely acknowledged that the blind administration of a placebo, which gives

patients the expectation of pain relief, often has a significant placebo analgesic effect [32]. In the literature, several placebo RCTs have been published on TENS treatment for various types of chronic pain. Oosterhof et al. did not observe any significant difference between TENS and sham TENS in patients with chronic pain. Remarkably enough, they did not find any evidence of long-term placebo effects of sham TENS [33]. In contrast, Murina et al. did find a significant difference in vulvar pain reduction between sham TENS and TENS in women with vestibulodynia [24]. Sluka and Walsh also found that TENS decreased hyperalgesia in animal research, which is less subject to placebo effects [20]. The strong placebo effect found in other PVD treatment studies suggests that women's realization of the availability of treatment constitutes a powerful psychological component. New sham TENS devices are currently being developed that will enable placebo RCTs on the effectiveness of domiciliary TENS in women with (therapy-resistant) PVD.

This study population comprised women with a relatively long duration of symptoms. A relatively high percentage of them had a medical history of depression or recurrent vaginal yeast infections. Compared with the 12-monthly rate of mood disorders in Dutch women aged between 18 and 44 years (7.1%) [34], our population had a relatively high rate (13%).

In the present study, nonspecific factors might also play a role - as is the case in all therapies - such as perceived control or attention from the therapist [35]. Additional therapeutic effects might have arisen from the personal attention of the pelvic floor physiotherapist who trained the women to perform the self-administered domiciliary TENS [3,15].

A limitation of this study is the fact that women were highly responsible for their own treatment. Owing to the domiciliary use of TENS, it was not possible to determine the compliance rate. However, the therapist had the impression that most women who underwent this treatment were very motivated to follow the treatment as was prescribed. In some cases, she did check proper use when she doubted compliance dedication to therapy. Also, the very act of placing the cutaneous electrodes could promote familiarity with the genital area and in itself be therapeutic. Another important aspect could be (perceived) control as one of the main nonspecific therapeutic factors [35]. The strong placebo effect found in studies on the treatment of PVD suggests that women's realization of the availability of treatment holds a powerful psychological component. Our hypothesis that TENS would be beneficial to women with therapy-resistant PVD was supported by the reductions in vulvar pain, (partial) recovery of sexual functioning, reduced sexually related personal distress, and the very high rate of positive

recommendations of TENS to fellow sufferers. This study showed that TENS treatment was a feasible addition to the multidimensional, multifaceted treatment approach. All patients with therapy-resistant PVD should be offered TENS before their gynecologist considers the last resort of vestibulectomy. Even if future research shows a large placebo effect, this does not undermine the benefit of TENS and the absence of irreversible complications for women with therapy-resistant PVD, many of whom have had debilitating symptoms for many years. In this group of women, any effect, however small, represents a giant leap forward in the challenge of treating PVD.

CONCLUSION

In women with therapy-resistant PVD, TENS was a feasible and beneficial additional treatment option. It led to significant decreases in vulvar pain and improvements in sexual functioning in the short and long-term. By adding TENS to the multidimensional treatment approach to PVD, it is possible to reduce the need for invasive and irreversible vestibulectomy.

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PART
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