SEXUAL MEDICINE REVIEWS

Systematic Review of the Effectiveness of Physical Therapy Modalities in Women With Provoked Vestibulodynia

Mélanie Morin, PT, PhD,[1] Marie-Soleil Carroll, MA,[2] and Sophie Bergeron, PhD[3]

ABSTRACT

Introduction: Pelvic floor muscle physical therapy is recommended in clinical guidelines for women with provoked vestibulodynia (PVD). Including isolated or combined treatment modalities, physical therapy is viewed as an effective first-line intervention, yet no systematic review concerning the effectiveness of physical therapy has been conducted.

Aim: To systematically appraise the current literature on the effectiveness of physical therapy modalities for decreasing pain during intercourse and improving sexual function in women with PVD.

Methods: A systematic literature search using PubMed, Scopus, CINHAL, and PEDro was conducted until October 2016. Moreover, a manual search from reference lists of included articles was performed. Ongoing trials also were reviewed using clinicaltrial.gov and ISRCTNregistry. Randomized controlled trials, prospective and retrospective cohorts, and case reports evaluating the effect of isolated or combined physical therapy modalities in women with PVD were included in the review.

Main Outcome Measures: Main outcome measures were pain during intercourse, sexual function, and patient's perceived improvement.

Results: The literature search resulted in 43 eligible studies including 7 randomized controlled trials, 20 prospective studies, 5 retrospective studies, 6 case reports, and 6 study protocols. Most studies had a high risk of bias mainly associated with the lack of a comparison group. Another common bias was related to insufficient sample size, non-validated outcomes, non-standardized intervention, and use of other ongoing treatment. The vast majority of studies showed that physical therapy modalities such as biofeedback, dilators, electrical stimulation, education, multimodal physical therapy, and multidisciplinary approaches were effective for decreasing pain during intercourse and improving sexual function.

Conclusion: The positive findings for the effectiveness of physical therapy modalities in women with PVD should be investigated further in robust and well-designed randomized controlled trials. **Morin M, Carroll M-S, Bergeron S. Systematic Review of the Effectiveness of Physical Therapy Modalities in Women With Provoked Vestibulodynia. Sex Med Rev 2017;X:XXX–XXX.**

Key Words: Vulvodynia; Dyspareunia; Provoked Vestibulodynia; Genito-Pelvic Pain; Physical Therapy Modalities; Rehabilitation; Pelvic Floor

INTRODUCTION

Vulvodynia is a neglected chronic pain condition affecting up to 7% to 8% of women younger than 40 years.[1] According to a recent terminology consensus from leading international societies including the International Society for the Study of Women's Sexual Health,[2] vulvodynia can be categorized as provoked (eg, insertional, contact) or spontaneous or mixed (provoked and spontaneous). Provoked localized vulvodynia, more specifically provoked vestibulodynia (PVD), is recognized as the leading cause of premenopausal vulvodynia.[3] Women with PVD describe a sharp pain or burning sensation at the entry of the vagina during application of pressure or attempted vaginal

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penetration.[3] Not only is PVD related to relationship difficulties and psychological distress,[4] it also is reported to disrupt personal lives, severely affect sexual function, and negatively affect quality of life.[5,6]

The etiology of PVD is hypothesized to be multifactorial and several pathophysiologic pathways have been suggested, including inflammatory, hormonal, congenital, genetic, neuroproliferative, and muscular factors.[7] Of these, involvement of the pelvic floor muscles (PFMs) has gained growing attention and has been demonstrated in several controlled studies.[8–12] Heightened PFM tone and decreased strength, speed of contraction, coordination, and endurance have been found in women with PVD.[8–11] Addressing these muscle alterations, PFM physical therapy is listed as first-line treatment by several clinical guidelines.[13–15] A survey conducted of vulvodynia experts also found that physical therapy is judged the most effective intervention.[16] Physical therapy treatment encompasses several modalities used in combination or isolation. According to Hartmann et al,[17] the most commonly used interventions include PFM exercises with or without biofeedback, manual therapy, education (removal of irritant, sexual function, and bowel and bladder retraining), electrotherapy, and dilators and insertion techniques. It should be emphasized that these modalities are not exclusively used by physical therapists and can be integrated in other health professionals' treatment approaches. Modalities were selected in this present review to represent the most accurate portrayal of current physical therapy practices. Physical therapy interventions aim at rehabilitating the PFMs by (i) increasing muscle awareness and proprioception; (ii) improving muscle relaxation and discrimination; (iii) normalizing muscle tone; (iv) increasing elasticity of the muscle and vaginal tissues and desensitizing the painful area, and (v) decreasing fear of vaginal penetration.[18] The goal of this review was to systematically appraise the current literature on the effectiveness of physical therapy modalities for decreasing pain during intercourse and improving sexual function in women with PVD.

METHODS

Search Strategy

This systematic review adhered to guidelines detailed in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[19] A literature search of peer-reviewed journals was undertaken using PubMed, SCOPUS, which includes EMBASE, CINAHL, PEDRO, and EBMreview, from the earliest date to October 2016. Protocol registries (ie, clinicaltrials.gov and ISRCTN) also were screened for upcoming trials. Search terms were *provoked vestibulodynia, vulvodynia, dyspareunia, vestibulitis, genito-pelvic pain/penetration disorder, physical therapy, physiotherapy, biofeedback, pelvic floor exercises, pelvic floor muscle training, manual therapy, electromyography, vaginal dilator, perineal massage, transcutaneous electrical nerve stimulation, electrical stimulation,* and *electrotherapy* (further details on search strategy are provided in the Appendix). The reference lists of eligible studies and relevant systematic reviews also were searched for additional articles that had not been found in the main search.

Eligibility Criteria

Randomized controlled trials (RCTs), prospective and retrospective cohorts, case reports, and study protocols involving women with PVD or superficial dyspareunia were included in the review. Studies selected had to report on the effectiveness of a physical therapy intervention, which could include any of the following modalities: education, PFM exercises with or without biofeedback, manual therapy, electrotherapy, and dilators or insertion techniques. The studies were considered eligible when including outcomes evaluating pain during intercourse, sexual function, and patient's perceived improvement. Studies were excluded if they were published in languages other than English and involved women with other pelvic pain conditions, such as chronic pelvic pain, endometriosis, sexually transmitted infections, other vulvovaginal infections, cancer, dermatologic conditions, atrophy, or deep dyspareunia.

Data Collection and Analysis

Two authors (M.M. and M.S.C.) independently sorted all studies from the searches using titles and abstracts; disagreements were discussed until consensus. For each study, level of bias was evaluated using the Cochrane Risk of Bias criteria.[20] The following potential biases were evaluated as having a low, high, or unclear risk: selection bias (randomization method, allocation concealment), performance bias (blinding and equivalent care), detection bias (blinding of outcome assessment), attrition bias (dropout), reporting bias (selective reporting), and other bias (ie, lack of information on sample characteristics, outcome measurement not sensible to change, inappropriate statistic).

RESULTS

Study Characteristics and Study Quality Assessment

In total, 2,004 studies were retrieved from the search after removal of duplicates (Figure 1 shows the flow of studies). Of these, 1,951 studies were excluded because they failed to meet the eligibility criteria. Fifty-three studies were read in full and 10 were excluded, resulting in 43 relevant studies included in this systematic review. The search yielded 7 RCTs, 19 prospective studies, 5 retrospective studies, 6 case reports, and 6 study protocols.

A summary of study designs, patient characteristics, sample sizes, interventions, outcome assessments, duration of follow-up, and findings is listed in Table 1. The quality assessment undertaken indicated that most studies reviewed had a high risk of bias related to selection bias (no randomization in 31 of 38, no allocation concealment in 31 of 38, and unclear concealment in

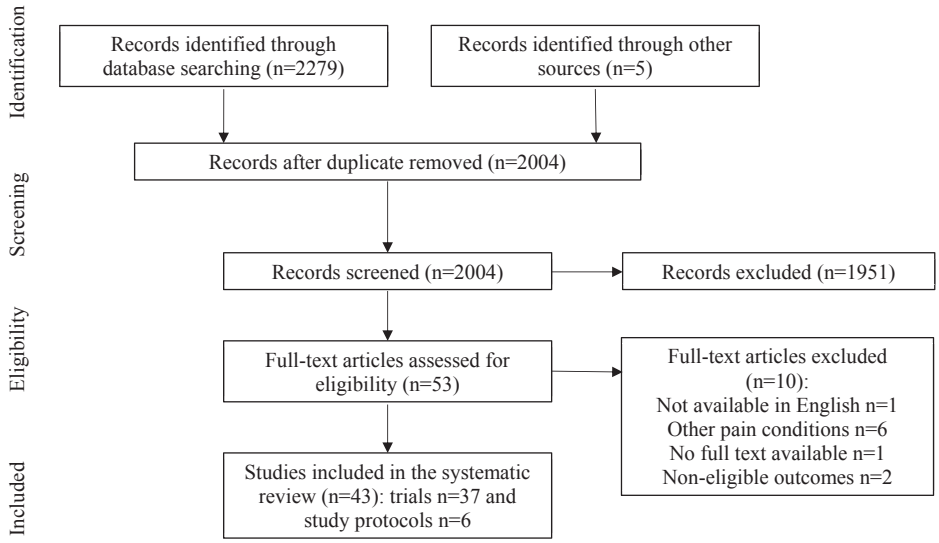

Figure 1. Flowchart of study selection.

the remaining studies) introduced by the absence of randomization or comparison group (Table 2 presents a summary of the risks of bias). The high risk for performance bias should be cautiously interpreted, considering the nature of the treatments in which blinding of participants for the intervention was not feasible. Only one study avoided this bias by investigating electrical stimulation compared with a sham current.[48] The Consolidated Standards of Reporting Trials (CONSORT) group[57] discussed this issue for non-pharmacologic interventions in which placebo physical modalities are not likely to be credible for the participants. For detection bias, only four studies could be considered as presenting low risk; in three studies, the assessors were unaware of group allocation[24,48,49] and in one study, the assessor was an independent clinical associate and patient self-reported outcomes were used.[22] Attrition bias was avoided in most studies (34 studies). Across studies, the risk of reporting bias often remained unclear because of insufficient information. Only two studies registered their protocols[36,42] and one was a follow-up to a previous trial,[24] decreasing the risk to a low level. Concerning the other risks of bias, non-validated outcomes were used in eight studies.[18,21,30,44,46,52,56] Moreover, in 16 studies, the treatment was administered in a non-standardized manner; therefore, there was variation in modalities used or duration of treatment for each participant.[18,21,30,31,34,37,38,40,43,44,46,52–56] Eleven studies even reported that other treatments were used during the study, which likely contributed to the treatment efficacy.[21,24-26,33,40,47,49,50,54,55] Most importantly, sample size calculation was reported in only four studies,[22,27,42,48] making it difficult to interpret whether non-significant findings in the remaining studies were due to insufficient study power. Overall, considering the marked heterogeneity of the studies and that most lacked a control or comparison group, all studies were narratively reviewed.

The treatments were divided into the following categories: biofeedback, dilators, electrical stimulation, manual therapy, education, multimodal physical therapy, and multidisciplinary and multimodal approaches.

Biofeedback

Women with PVD have been shown to present heightened PFM tone, which encompasses an active (contractile) component and a passive (viscoelastic) component.[11] The active component pertains to normal and pathologic muscle activation. Pathologic activation has been found in women with PVD in addition to difficulties in muscle relaxation and decreased strength, control, and endurance.[9,11,12] Biofeedback treatment has been proposed to train the PFMs to gain better control of the pelvic floor musculature, to promote muscle relaxation, and to improve contractile properties. The assistance of visual feedback of muscle activity is particularly relevant in women with pain because more than 50% of women without symptoms have difficulty achieving an adequate PFM contraction with only verbal instructions.[58,59] The effectiveness of biofeedback in women with PVD was investigated in three prospective studies, one case report, and two RCTs, with an additional 2.5-year follow-up. Glazer et al[33] first developed an electromyographic (EMG) biofeedback protocol for women with vulvar pain and showed that 52% of the entire sample reported pain-free sexual intercourse after 16 weeks of treatment in a prospective study.[33] Similar results were found in another study with a more homogeneous sample of women with PVD.[44] This treatment protocol also was validated in a single case report using a web platform for real-time and remote treatment (telemedicine).[32] A prospective non-randomized study also was undertaken by Granot et al[37] to compare vestibulectomy, no treatment, and one of three non-surgical treatments (ie, biofeedback, cognitive-behavioral therapy [CBT], or use of hypoallergenic agents). They found that 79% of participants who underwent vestibulectomy had a significant decrease of pain, whereas the success rates were 48% for those who received non-surgical treatments and 12% for the no-treatment group. It is

Table 1. Methodologic characteristics of included studies

Study	Design	N	Population	Intervention	Outcomes	Duration of follow-up	Results	Comments
Backman et al[21]	Prospective cohort study	27	Women with PVD	Combined physical and psychosexual therapies, average treatment time 53 wk (19–92); PT, 30 min per session, average 15 sessions (9–26); desensitization and insertion technique showed by midwife; psychosexual therapy 60 min per session, average 12 sessions; included issues on psychosexual adjustment, sexual functioning, and stress elimination	Pain during intercourse (homemade questionnaire; 1 = never; 2 = mild or occasional, not preventing intercourse; 3 = moderate, sometimes preventing intercourse; 4 = moderate to severe, most times preventing intercourse); sexual functioning (homemade questionnaire); improvement (homemade questionnaire; 1 = complete recovery; 2 = major improvement; 3 = minor improvement; 4 = no difference; 5 = deterioration)	≥6 mo	16 of 24 (67%) reported occasional or mild pain not interfering with intercourse; 19 of 24 (79%) reported cure or great improvement; improvement of general sexual functioning was reported by 15 of 24 women (63%)	Dropout 3 of 27 (lack of motivation); no comparison group (not randomized, no concealment); not blinded; non-validated outcomes; variation in treatment and follow-up duration; other ongoing treatment for some women; no a priori sample size calculation
Bergeron et al[22]	RCT	87	Women with VVS (ie, PVD; diagnosis according to Bergeron et al[23])	Randomized to 1 of 3 treatments (12 wk): vestibulectomy (n = 29), BF (n = 29), Glazer protocol (8 45-min sessions of over 12 wk, home BF twice daily); GCBT (n = 29 including education and information about vulvar pain, sexual anatomy, progressive muscle relaxation, abdominal breathing, Kegel exercises, vaginal dilation	VPI (cotton-swab test); pain intensity (NRS = 0–10); MPQ; sexual function (Sexual History Form, Derogatis Sexual Functioning Inventory); adherence (frequency of home exercises); patients were considered adherent when complying with ≥70% of their home exercise; subjective improvement (scale: 0 = worse to 5 = complete cure)	After treatment and 6 mo	All treatment groups reported statistically significant decreases on pain measurements (VPI, NRS, MPQ sensory subscale) although vestibulectomy showed greatest decrease (in ITT analysis, only VPI remained significantly better for vestibulectomy group); improvement assessed with NRS: 35.0% in BF group vs 52.5% in vestibulectomy and	Dropout before receiving treatment: 7 of 29 in vestibulectomy group, 1 of 29 in BF group, 1 of 29 in GCBT group; dropout after treatment: 2 of 29 in BF group; dropout at 6-mo follow-up: 3 of 29 in vestibulectomy group, 8 of 29 in BF group; total dropout: 10 of 29 in vestibulectomy group, 11 of 29 in BF group, 1 of 29 in GCBT group; randomized; concealment not

(continued)

Table 1. Continued

Study	Design	N	Population	Intervention	Outcomes	Duration of follow-up	Results	Comments
							37.5% in GCBT groups; all 3 treatments were equally effective at improving sexual function and MPQ total score; adherence: 57% for BF and 65% for GCBT; subjective improvement (complete relief or great improvement of pain); analysis by treatment received; 15 of 22 in vestibulectomy group (2 reported worsening), 10 of 28 in BF group, 11 of 28 in GCBT group	specified; independent assessor (some data self-reported, others obtained in structured interview); Sample size calculation reported in[24]. The predetermined sample was partly obtained because of dropouts
Bergeron et al[18]	Retrospective study	35	Women with VVS (ie, PVD)	PT: average = 7 sessions (mean = 15.8 mo) including education, manual techniques, BF, electrical stimulation, and home exercises (vaginal dilatation)	Interview; pain during intercourse (7-point scale, from "a lot worse" to "complete relief of pain"); sexual functioning (no mention of which questionnaire was used)	Unclear	Significant decrease in pain during intercourse and pain during gynecologic examinations; increase in intercourse frequency and in levels of sexual desire and arousal; improvement in pain during intercourse: 3 of 35 (8.6%) reported complete relief, 15 of 35 (42.9%) reported great improvement, 7 of 35 (20.0%) reported moderate improvement, 6 of 35 (17.1%) reported little improvement, 3 of 35 (8.36%) reported no improvement, 1 of 35 (2.8%) reported deterioration	No comparison group (not randomized, no concealment, no blinding); non-validated outcomes; variation in treatment duration; duration of follow-up unclear; use of other treatment reported; however, none of these treatments were associated with outcomes; no a priori sample size calculation

(continued)

Table 1. Continued

Study	Design	N	Population	Intervention	Outcomes	Duration of follow-up	Results	Comments
Bergeron et al[24]	RCT, 2.5-y follow-up[22]	51 of 65 patients who completed main study	Women with VVS (ie, PVD; diagnosis according to Bergeron et al[23])	Vestibulectomy (n = 15), BF (n = 17), GCBT (n = 19)	VPI (cotton-swab test); pain intensity (NRS = 0–10); MPQ; sexual function (Sexual History Form, Derogatis Sexual Functioning Inventory)	2.5 y after previous 6-mo follow-up (Bergeron et al, 2001)[22]	Patients had less pain (VPI, NRS, MPQ) at 2.5-y follow-up than at previous 6-mo follow-up; GCBT and vestibulectomy groups had less pain than BF group; improvement in sexual function in all 3 groups was maintained and there were no group differences; 17 of 51 participants reported having used other means to alleviate their pain during follow-up period: 8 tried PT, 4 tried psychotherapy, 5 tried mild remedies; it is not specified in which group they were	Dropout 14 of 65 (last observation carried forward); randomized; concealment not specified; assessor blinded; other ongoing treatment for some women; sample size calculation provided for original study
Brotto et al[25]	Prospective cohort study	29	Women with PVD	Education seminars: 3 1-h sessions 3 wk apart by gynecologist; sessions focused on PVD and its diagnosis, general description of treatment, sexual function, pain pathophysiology and presentation of case examples that illustrated management options	Sexual function (fsfi), sexual distress (fsds), no pain outcomes	Post-treatment and 6-mo follow-up	Significant improvements (pre- to post-treatment) in sexual functioning and distress; these improvements were maintained at 6-mo follow-up; no significant improvement in sexual pain scores (FSFI pain subscale)	Dropout at 6 mo: 6 of 25; no comparison group (not randomized, no concealment); not blinded; other treatments potentially followed by participants are not documented; no a priori sample size calculation
Brotto et al[26]	Prospective cohort study	132	Women with PVD	MVP: duration 10–12 wk; 2 1-h educational seminar in group lead by gynecologist (pathophysiology of PVD, sexual function and pain	Pain intensity during intercourse (VAS), sexual function and distress (FSFI, FSDS)	After treatment and 2- to 3-mo follow up (a portion of the sample was follow for 6 mo)	Significant decrease of pain after treatment and results remained at follow-up; 54% (71 of 132) of women indicated that their pain had decreased	Dropout after treatment 16 of 132; dropout at follow-up 48 of 132 (36%); relatively large attrition; no comparison group (not randomized, no

(continued)

Table 1. Continued

Study	Design	N	Population	Intervention	Outcomes	Duration of follow-up	Results	Comments
				management); individual gynecologist consultation to discuss specific issue with each woman (medical management); gynecologist also met the women at the end of the program for discharge appointment; 3 2-h session with psychologist (integrating psychological skills training and mindfulness); 3 1-h sessions with physical therapist (BF, pelvic floor relaxation, dilator, home exercises); referral to physical therapist for further follow-up if necessary; PT did not involve any manual release techniques to address hypertonicity of pelvic floor			since starting the MVP; all domains of sexual function improved after treatment and results were maintained at follow-up (sexual desire, sexual arousal, lubrication, orgasm, sexual satisfaction, overall sexual functioning); significant decrease in sex-related distress after treatment and gains were maintained at follow-up	concealment; not blinded; other ongoing treatments (medical management); no a priori sample size calculation
Danielsson et al[27]	RCT	46	Women with VVS (ie, PVD)	EMG BF (n = 23) and Glazer protocol for 4 mo; monthly supervised sessions; home BF 3 times daily; topical lidocaine (n = 23) 2% and 5% for 4 mo	Pain intensity during intercourse (VAS), pain intensity during cotton-swab test (VAS), pressure pain (vulvar algesiometer), sexual functioning (questionnaire developed)	After treatment, 6-mo and 12-mo follow-up	Decrease in pain (VAS) for the 2 groups, non-significant difference between groups; significant increase in pain thresholds at 2 vestibular sites and for 2 treatment groups at 12-mo follow-up vs baseline; non-significant difference between groups; self-reported	Dropout at 12 mo: 5 of 23 in BF group, 4 of 23 in lidocaine group; randomized; concealment unclear; evaluator not blinded; sample size calculation provided and predetermined sample was obtained

(continued)

Table 1. Continued

Study	Design	N	Population	Intervention	Outcomes	Duration of follow-up	Results	Comments
							improvement: 2 of 23 reported complete cure, 12 of 23 reported improvement with BF, 2 of 23 reported complete cure and 10 of 23 reported improvement with lidocaine; significant improvement in sexual functionating in 2 groups; low adherence to BF: 0 performed exercises 3 times a daily, 10 of 18 (56%) performed them twice daily, and the rest performed them once daily	
Downey and Frederick[28]	Case report	1	Woman with VVS (ie, PVD)	PT 8 sessions (n = 8) over 10 wk; EMG assisted pelvic muscle rehabilitation including relaxation and strengthening, soft tissue massage and stretching, home exercise program (pelvic floor contractions)	Pain intensity (NRS; by palpation)	2 mo	NRS score = 8.5 of 10 before treatment, score = 0 at follow-up	No comparison group (not randomized, no concealment); not blinded (evaluator not blinded and involved in treatment)
Fisher[29]	Case report	1	Woman patient with dyspareunia and overactivity of pfms	PT at 3 sessions over 9 wk including education, teaching of muscle control, manual therapy, vaginal self-dilation techniques at home	Pain during intercourse (NRS)	After treatment	NRS score = 10 of 10 before treatment, NRS score = 0 at follow-up	No comparison group (not randomized, no concealment); not blinded (evaluator not blinded and involved in treatment)
Fowler[30]	Prospective study	85	Women with VVS (ie, PVD; Friedrich criteria)	Hypo-contactant vulvar therapy (≥4 mo), which includes avoidance of irritants, use of lubricant, emollient, and hydration cream, and use of dilator (3 times/wk)	Change in dyspareunia	6–36 mo	17 of 85 (21%) reported complete response, 48 of 85 (56%) reported partial response, 20 of 85 reported no response, 60% reported improvement of ≥1	Not clear if there was any dropout; no comparison group (not randomized, no concealment); not blinded; non-validated outcomes; variation in treatment and follow-up duration; other ongoing treatment for

(continued)

Table 1. Continued

Study	Design	N	Population	Intervention	Outcomes	Duration of follow-up	Results	Comments
							level on Marinoff scale	some women; no a priori sample size calculation
Forth et al[31]	Pilot prospective study	21	Women with vulvodynia (15 with VVS and 6 with unprovoked vulvodynia)	PT average of 4 sessions over 3 mo, including various elements such as behavior modification and PFM EMG BF	Pain level and description of pain (MPQ)	3 mo	Pain levels decreased during treatment period vs control period, although it was found non-significant	Dropout 7 of 21; no comparison group (not randomized, no concealment); not blinded; variation in treatment duration; no sample size calculation; insufficient statistical power reported
Gentilcore-Saulnier et al[9]	Prospective study	22	Women with PVD (n = 11; Friedrich criteria) and women without provoked vestibulodynia (control group; n = 11)	PT program (8 sessions) including digital intravaginal techniques (techniques of soft tissue mobilization, stretching, and desensitization), insertion techniques using dilators, pelvic floor SEMG BF, electrical muscle stimulation, education, and home exercises	Superficial and deep PFM SEMG tonic activity and phasic activity in response to painful pressure stimulus, PFM digital assessment variables (tone, flexibility, relaxation capacity, and strength), pain intensity during intravaginal assessment	4 wk	Women with PVD reported having significantly lower pain ratings after treatment and there was no difference in reported pain between PVD and control groups	No dropout; no randomization, no concealment; not blinded; no a priori sample size calculation
Glazer et al[32]	Case report	1	Woman with VVS (ie, PVD)	EMG BF at home for 24 wk, treatment followed in real time remotely using a web platform (telemedicine)	Pain intensity (NRS), pelvic floor SEMG data (vaginal sensor)	After treatment	NRS score = 8 of 10 before treatment, score = 0 at follow-up	No comparison group (not randomized, no concealment); not blinded (evaluator was treatment provider)
Glazer et al[33]	Prospective study	33	Women with VVS (ie, PVD), some participants had unprovoked pain	EMG BF; 6 BF sessions with therapist; home BF-assisted PFM rehabilitation exercises (average = 16 wk, twice daily)	Pain intensity (NRS)	6 mo	Subjective reports of pain decreased average of 83%; 17 of 33 patients (52%) reported pain-free intercourse at 6-month follow-up, 22 of 28 who had abstained from	No dropout reported; no comparison group (not randomized, no concealment); not blinded (evaluator was treatment provider); other ongoing treatment for some women

(continued)

Table 1. Continued

Study	Design	N	Population	Intervention	Outcomes	Duration of follow-up	Results	Comments
							intercourse before treatment had resumed intercourse after treatment; improvements were maintained at 6-mo follow-up; fully compliant (100%)	(27 took amitriptyline); no a priori sample size calculation
Goetsch[34]	Prospective study	111	Women with VVS (ie, PVD; ISSVD criteria)	Surgery combined with PT (49% had PT treatment) and/or dilatators (limited details provided for PT treatment; therapists more often used manual technique than BF)	Improvement (corrected, improved, not improved, worse)	Average = 3 mo to 4.2 y, maximum = 14 y	Improvement (dyspareunia): corrected in 73 of 109 (67%), improved in 22 of 109 (20%), not improved in 10 of 109 (9%), worse in 4 of 109 (4%); 50% with continuing dyspareunia had PFM tensions; portion of subjects with normalized vestibule sensation but failure of PT to fully correct dyspareunia was only 10%	Dropout 2 of 111; no comparison group (not randomized, no concealment); not blinded; non-validated outcomes; variation in PT treatment provided (modalities, duration); variation in follow-up duration; no a priori sample size calculation
Goldfinger et al[35]	Prospective study	13	Women with PVD (Friedrich criteria)	PT program (8 sessions) including digital intravaginal techniques (techniques of soft tissue mobilization, stretching, and desensitization), insertion techniques using dilators, pelvic floor SEMG BF, electrical muscle stimulation, education, and home exercises	Vestibular pain (vulvalgesiometer; 0–10); pain intensity during intercourse (NRS); sexual function (FSFI, sexual esteem subscale of Sexuality Scale); improvement (from 1 = complete cure to 6 = pain is worse)	After treatment and 3-mo follow-up	Significant improvements in pain intensity, pain threshold, and sexual function; improvement at follow-up: complete cure for 2 of 13 (15%), great improvement for 8 of 13 (61%); this defined successful outcome in 10 of 13 women (77%)	No dropout; no comparison group (not randomized, no concealment); not blinded; no a priori sample size calculation
Goldfinger et al[36]	Pilot RCT	20	Women with PVD	Treatment entailed 8 supervised sessions of 1.5 h duration (8–24 wk); PT protocol (n = 10): education, PFM	Pain intensity during intercourse (NRS), pain during cotton-swab test, MPQ, FSFI, degree of vulvar pain	After treatment and 6 mo	Non-significance was found between the 2 groups in all reported outcomes; there were significant improvements for	No dropout reported; missing data for gynecologic examination (pain for cotton-swab test) dealt with "last

(continued)

Table 1. Continued

Study	Design	N	Population	Intervention	Outcomes	Duration of follow-up	Results	Comments
				exercises, manual techniques, SEMG BF, progressive vaginal penetration exercises through the use of 4 silicone vaginal dilators of varied diameter, stretches of hip muscles, deep breathing and global body relaxation exercises, and pain management techniques; CBT (n = 10): education, collaborative reconceptualization of PVD as multifactorial pain condition, desensitization exercises including instructions on how to perform genital self-exploration at home, diaphragmatic breathing and other relaxation techniques, techniques for increasing sexual desire and arousal, sexual communication skills training, cognitive restructuring, and instructions on carrying out PFM exercises and on using 4 silicone vaginal dilators to perform progressive vaginal penetration exercises at home (same dilators as used in PT)	improvement from 1 (complete cure) to 6 (pain is worse)		pain intensity in average intercourse attempts across the 2 treatments groups from before to after treatment that were maintained at 6-mo follow-up; only PT group showed significant decreases in pain during cotton-swab test from before to after treatment; by 6-mo follow-up, the 2 treatment groups demonstrated significant decreases; there were significant decreases in MPQ sensory and affective pain rating indices from before treatment to 6-mo follow-up in CBT group; PT group showed no significant changes in their affective ratings, and although the sensory ratings improved from before to after treatment, they were not maintained to the 6-mo follow-up; neither treatment group had significant increases in overall sexual functioning from before to after treatment; CBT group had significant increase at 6 mo; improvement at 6 mo (>50% decrease) in PT (8 of 10, 80%) and CBT (6 of 10, 60%) groups; non-significant between groups	observation carried forward"; randomized; concealment unclear; no blinding of evaluator; no a priori sample size calculation; sample size insufficient for treatment comparison; protocol registry NCT02494934

(continued)

Table 1. Continued

Study	Design	N	Population	Intervention	Outcomes	Duration of follow-up	Results	Comments
Granot et al[37]	Prospective study (non-randomized trial; women chose their treatments)	90	Women with PVD (Friedrich criteria)	Vestibulectomy (n = 33), non-surgical treatments (n = 31; 1 of the following treatments): BF (n = 5), CBT (n = 15), or hypoallergenic agents (n = 11; no details provided), no treatment (n = 26)	Percentage of decrease of pain (100-point scale, 0 = no pain decrease to and 100 = complete improvement); improvement defined as >30% decrease	8 mo	Vestibulectomy showed greater effectiveness; most (n = 26) of the 33 women in vestibulectomy group reported a significant improvement (pain decrease = 65.7 ± 26%); in non-surgical treatment group, 15 of the 31 women reported a decrease in vulvar pain; only 3 of the 26 women in no-treatment group reported an improvement	Dropout 4 of 94; not randomized, no concealment; no blinding (participant or evaluator); difference in baseline characteristic between groups unknown; treatment selection bias; limited information provided on non-surgical treatment (number of sessions, supervision with health professional, etc); no a priori sample size calculation
Hartmann and Nelson[38]	Retrospective study	24	9 women with VVS (ie, PVD; ISSVD criteria), 15 women with dysesthetic vulvodynia	PT: average 15 visits over 44 wk; all patients with VVS underwent manual therapy and PFM exercises; most also had BF, electrical stimulation, and joint mobilization	Pain intensity (NRS), pain intensity during intercourse (NRS), percentage of overall improvement	Unclear (0–3 y)	When questioned about vulvar symptoms, quality-of-life issues, and sexual functioning (before and after PT intervention), women's responses showed statistically significant improvement in all areas of concern: 71% of women treated reported >50% improvement in overall symptom decreases, 62% of women reported an overall improvement in sexual functioning	Dropout 73% returned questionnaires; no comparison group (not randomized, no concealment); not blinded (self-reported outcome); variation in treatment modalities and duration; variation in follow-up duration; no a priori sample size calculation
Holland[39]	Case report	1	Woman with dyspareunia	31 PT sessions over 1 y; soft tissue mobilization, myofascial release, muscle energy techniques, BF, strengthening, and stabilizing exercises	Pain intensity and frequency	After treatment	Pain with intercourse was reportedly absent after treatment	No comparison group (not randomized, no concealment); not blinded (evaluator involved in treatment)

(continued)

Table 1. Continued

Study	Design	N	Population	Intervention	Outcomes	Duration of follow-up	Results	Comments
Idama and Pring[40]	Prospective cohort	18	Women with superficial dyspareunia	Self-vaginal dilatations: verbal and written instructions were provided; 10–15 min with dilator inserted once or twice daily; treatment duration not reported	Interview-reported improvement	Unclear	14 patients (77.8%) reported improved outcome, 13 (72.2%) claimed complete relief and satisfaction with therapy	Dropout 1 of 18; no comparison group (not randomized, no concealment); not blinded (evaluator was treatment provider); follow-up and treatment duration not reported; non-validated outcomes; other ongoing treatment for some women; no a priori sample size calculation
Kalina[41]	Case report	1	Woman with dyspareunia	8 PT sessions over 8 wk: external and intravaginal soft tissue mobilization and home program including self-scar mobilization, stretching exercises, relaxation training, and use of vaginal dilator	Pain intensity (VAS)	After treatment	VAS pain score = 8 of 10 before treatment; score = 0 after 8 sessions	No comparison group (not randomized, no concealment); evaluator not blinded and involved in treatment
Lindström and Kvist[42]	Prospective cohort	60	Women with PVD (Friedrich criteria)	CBT, desensitizing, and PFM exercises; 10 60-min sessions once a week for 10 wk of CBT including education on PVD and sexual function; home exercises included insertion of woman's or partner's fingers and training to feel tension and relaxation in PFMs, use of tampons during menstruation was encouraged	Occurrence of dyspareunia (from 1 to 7 = never; 1 question of MFSQ)	after treatment and 6 mo	Significant increase in MFSQ from baseline to after treatment; women reported decreased pain occurrence; all improvements were reported to be sustained at 6 mo	No dropout reported but missing data (n = 0–9 participants depending on questions); no comparison group (not randomized no concealment); not blinded (self-reported outcome); protocol registry ISRCTN40416405; a priori sample size calculation was provided; predetermined sample was obtained

(continued)

Table 1. Continued

Study	Design	N	Population	Intervention	Outcomes	Duration of follow-up	Results	Comments
Mackenzie[43]	Qualitative retrospective study	5	Women with dyspareunia	Trigger point massage as part of PT treatment	Interview	Unclear	All participant reported improvement in their symptoms	No comparison group (not randomized no concealment, no blinding); no details provided on treatment (eg, modalities included, number of sessions, duration); non-validated outcomes; no a priori sample size calculation
McKay et al[44]	Prospective cohort	29	Women with VVS (ie, PVD; Friedrich criteria, level 2–3 on Marinoff scale)	EMG BF of PFMs (Glazer protocol): 4–6 monthly supervised sessions; 8 repetitions of 3-s contraction, 12-s rest; 8 repetitions of 8-s contraction, 12-s rest; 1 repetition of 60-s contraction; home exercises twice daily: home trainer BF device and specific instructions were given to perform BF-assisted PFM rehabilitation exercises; patients received monthly evaluations of PFMs to ensure and motivate compliance and to monitor improvement and symptom changes	Pain characterized as negligible, mild, or no improvement; pain intensity also evaluated on a scale from 1 (least) to 10 (most); self-reported presence of sexual activity before and after treatment	After treatment and 6-mo follow-up (12 mo after beginning of treatment)	Pain during intercourse was negligible for 15 of 29 (51%), mild for 9 of 29 (31%), no improvement for 5 of 29 (17%); pain intensity (1–10) reported at follow-up excluded women with no improvement; 20 of 29 women (69%) resumed sexual intercourse	It appears that the following number of participants was not included in analysis (pain intensity): 18 of 29 after treatment, 25 of 29 at 6-mo follow-up; no comparison group (not randomized, no concealment); not blinded (evaluator was treatment provider); non-validated outcomes; variation in treatment duration; no a priori sample size calculation
Miletta and Bogliatto[45]	Prospective cohort study, preliminary results	14	Women with PVD (ISSVD 2003 criteria)	Multimodal PT, managed by trained midwife (10 30-min sessions) including PFM, BF, perineal massage, manual treatment of trigger points, postural	Pain intensity (vas)	4 mo	9 of 14 patients reported improvement in vulvar and sexual pain with good relief (decrease of 2–3 points for VAS score); 3 patients	Dropout 2 of 14; no comparison group (not randomized, no concealment); not blinded; preliminary results; no a priori sample size calculation

(continued)

Table 1. Continued

Study	Design	N	Population	Intervention	Outcomes	Duration of follow-up	Results	Comments
				evaluation, global relax technique (yoga), auto-training at home			referred to any significant effect; results briefly reported	
Munday et al[46]	Qualitative retrospective study	29	Women with PVD and some had mixed vestibulodynia (ISSVD 2003 criteria)	Multidisciplinary program; women participated in all or some treatment modalities; medical modalities (topical steroid, amitriptyline); low oxalate diet; psychotherapy; PT consisting of education, voiding pattern, PFM therapy, self-massage for desensitization, interferential therapy, TENS, BF	Interview (evaluator not related to clinical team)	Unknown	27 of 29 reported significant benefit; 9 of 29 were pain free; 15 of 19 who received PT identified this treatment as part of their recovery	Number of patients who refused to participate is not reported; no comparison group (not randomized, no concealment, no blinding); non-validated outcomes; treatment variation (modalities and duration) for each participant; details on treatment limited; no a priori sample size calculation
Murina et al[47]	Prospective cohort study	15	Women with PVD	Amielle vaginal dilators as an adjuvant, standardized instruction for 8 wk at 3 times/wk, dilatator of progressive size for 10 min, 3 series of 8 movements; participants underwent $\geq$1 of different treatments including TENS, vestibular infiltration, BF, amitriptyline, and pregabalin	Marinoff scale, FSFI	Immediately after treatment	Significant improvement in Marinoff scale and FSFI from baseline to after treatment ($P < .01$)	No dropout reported; no comparison group (not randomized, no concealment); not blinded (unclear if evaluator was involved in treatment); other ongoing treatment; no a priori sample size calculation
Murina et al[48]	RCT	40	Women with PVD (Friedrich criteria)	20 sessions twice weekly of active TENS or sham treatment delivered through vaginal probe (inserted	Pain intensity (VAS), SF-MPQ, Marinoff scale, FSFI	Immediately after treatment and 3-mo follow-up	VAS and SF-MPQ scores improved significantly in active TENS group after treatment and at follow-up, but not in	No dropout reported; randomized, no concealment; double-blinded (patients and assessors seemed to be blinded; therapist

(continued)

Table 1. Continued

Study	Design	N	Population	Intervention	Outcomes	Duration of follow-up	Results	Comments
				20 mm); active TENS (n = 20) consisted of symmetrical biphasic wave generated by calibrated dual-channel TENS unit of YSY-EST device; each session entailed 15 min of 10-Hz frequency and 50-ms pulse duration followed by 15 min of 50-Hz frequency and 100-μs pulse duration; placebo (n = 20) consisted of non-active electrical stimulation, 2 sets of 3-s stimulation (2-Hz frequency, 2-μs pulse duration) followed by 15-min pause			placebo group; Marinoff dyspareunia scale and FSFI also showed significant improvement; no statistical analysis for between-group differences	not blinded); statistical analysis comparing intragroup changes but no between-group comparisons reported; a priori sample size calculation was provided; predetermined sample was obtained
Murina et al[49]	RCT	20	Women with PVD (Friedrich criteria)	Oral palmitoyl ethanolamide 400 mg + transpolydatin 40 mg twice daily for 60 d + TENS (n = 10), placebo twice daily for 60 d + TENS (n = 10); domiciliary TENS, average sessions 26.7, 6–7 teaching sessions with therapist; vaginal probe (inserted 20 mm); each session entailed 15 min of 10-Hz frequency and 50-ms pulse duration followed by 15 min of 50-Hz frequency and 100-μs pulse duration	Pain intensity (VAS), Marinoff dyspareunia scale (0–3)	2 mo after treatment	Significant decrease of pain (pain intensity and Marinoff scale) in 2 groups; non-significant between-group differences; regression analysis was performed and showed that efficacy was higher in women with shorter duration of PVD symptoms	No dropout reported; randomized, no concealment; double blinded (patient and assessor); unclear if treatment provider was blinded; it is difficult to evaluate the contribution of TENS in this study because all participants received TENS; no a priori sample size calculation

(continued)

Table 1. Continued

Study	Design	N	Population	Intervention	Outcomes	Duration of follow-up	Results	Comments
Nappi et al[50]	Prospective study	29	Vestibular pain inducing dyspareunia (n = 20), vaginismus (n = 9)	Electrical stimulation 20-min session once a week for 10 wk, current at vestibular area and at vaginal introitus using a small rounded probe, 1- to 4Hz biphasic current of frequency, pulse width 0.1-0.3 ms, and intensity 0–70 ma, with individually adapted on-off (10–20 s) cycles; home exercises were PFM exercises 3 times/wk for 20 min	Pain intensity (VAS), sexual function (FSFS)	Immediately after treatment	Significant decrease in VAS score for pain ($P < .001$); significant improvement of FSFI total score and FSFI pain score ($P < .001$)	No dropout reported; no comparison group (not randomized, no concealment); not blinded; scores reported in graph; other treatment ongoing (home PFM exercises); no a priori sample size calculation
Olszewski[51]	Case study	1	Postpartum woman with provoked vestibulodynia, stress urinary incontinence, and constipation	9 PT sessions over 3-mo period including education, manual therapy, dilator, and BF and home exercises	Pain intensity (NRS)	After treatment	NRS pain intensity during intercourse score from 7 to 0 of 10	No comparison group (not randomized, no concealment); evaluator not blinded and involved in treatment
Smith and Gillmer[52]	Prospective cohort	10	Superficial dyspareunia and secondary vaginismus (5 childbirth trauma, 1 lichen, 1 vaginismus after infection, 1 atrophy, 2 vaginismus for non-identified reason)	Amielle dilators; no details provided for modalities and duration	Self-reported success (1 = treatment unfavorable to 6 = completely favorable)	Unclear	All patients reported improvement (score ≥ 2); 90% reported some improvement or complete cure; cure was reported in 2 of 10	Dropout 1 of 10; no comparison group (not randomized, no concealment); not blinded; non-validated scale; results only descriptive; treatment (duration and modalities) not described; duration of follow-up not specified; no a priori sample size calculation
Spoelstra et al[53]	Retrospective study	64	Women with PVD	Multifaceted and multidisciplinary therapeutic approach of education, vaginal EMG BF, PFM PT, home exercises, inert cream, hygienic protocol, and, if needed, individual	Vulvar pain (VAS); pretreatment score assessed retrospectively; sexual functioning (FSFI; only post-treatment score compared with norm database); sexually	3–7 y	Significant decrease of pain after treatment (decrease of 3.6 of 10, SD = 3.9); decrease in vulvar pain after individualized, multifaceted treatment was	64 of 70 returned questionnaires; no comparison group (not randomized, no concealment); not blinded; variation in treatment modality and duration; variation in follow-up duration;

(continued)

Table 1. Continued

Study	Design	N	Population	Intervention	Outcomes	Duration of follow-up	Results	Comments
				sexological counseling and sexological partner-relationship therapy, vestibulectomy	related personal distress (FSDS; only post-treatment score compared with norm database)		reported by 81% (n = 52 of 70)	no a priori sample size calculation
Tommola et al[54]	Prospective study (2 groups, non-randomized)	66	Women with PVD (Friedrich criteria)	Vestibulectomy (n = 39), conservative treatment (PT with BF, sexual counseling; n = 27); no further details provided	Pain intensity during intercourse (VAS), sexual function (MFSQ)	Vestibulectomy median 44 mo, conservative treatment 77 mo	Dyspareunia decreased significantly in the 2 groups; VAS score decreased 66.7% in surgery group and 78.1% in conservative treatment group ($P = .407$); long-term sexual well-being did not differ between the 2 groups ($P = .718$)	No dropout reported; no comparison group (not randomized, no concealment); not blinded; limited information on treatment; other ongoing treatment for some women; participants already had conservative interventions; follow-up durations differed between the 2 groups; no a priori sample size calculation
Vallinga et al[55]	Prospective study	39	Women with PVD refractory to behavioral treatment as reported by Weijmar Schultz et al[56]	Domiciliary TENS as additional therapy: vulvar electrode, 80-Hz frequency, 50- to 180-μs pulse duration (according to participant's tolerance), pulse intensity set to maximal level that was still comfortable; participants had 1–2 teaching session with physical therapist; 90-min stimulation daily (divided in 2–3 sessions) for 12–16 wk (treatment could be interrupted at 6–8 wk if the effect was satisfactory)	Pain intensity; vulvar pain (VAS), sexual function (FSFI), sexual distress (FSDS)	Immediately after treatment; study also included follow-up assessment; some women at this time point underwent vestibulectomy	Vulvar VAS pain scores after treatment (median = 3.4) were lower than at baseline (median = 8.0); sexual functioning and distress showed significant improvement; we did not include follow up assessment because it was difficult to evaluate whether the effects were attributable to TENS or vestibulectomy	No dropout reported; no comparison group (not randomized, no concealment); not blinded; variation in treatment and follow-up duration; other ongoing treatment for some women; no a priori sample size calculation

(continued)

Table 1. Continued

Study	Design	N	Population	Intervention	Outcomes	Duration of follow-up	Results	Comments
Weijmar Schultz et al[56]	RCT (study 1) and prospective arm (study 2)	RCT (n = 14), prospective (n = 34)	Women with VVS (ie, PVD)	Study 1 (RCT), behavioral treatment (n = 7): education (sexual function, hygienic advices), PFM exercises (with physical therapist if necessary), dilatator, sexological counseling if necessary (mean duration = 17 mo, 13 sessions); surgery followed by behavioral treatment (same as above; n = 7; mean duration = 11 mo, 13 sessions); study 2 (prospective; same treatment as above but women were given choice): behavioral treatment (n = 28; mean duration = 13 mo, 10 sessions); surgery followed by behavioral treatment (n = 6; mean duration = 18 mo, 13 sessions)	Improvement (1 complaint disappeared to 5 complaints worsened)	Average 3 y after treatment (8–56 mo)	Study 1: non-significant difference between the 2 groups; behavioral treatment 3 of 7 complaints disappeared, 2 of 7 complaints diminished, 1 of 7 no change; surgery followed by behavioral treatment 3 of 7 complaints disappeared, 3 of 7 complaints diminished, 1 of 7 no change; study 2: non-significant difference between the 2 groups; behavioral treatment 10 of 28 complaints disappeared, 8 of 28 complaints diminished, 9 of 28 no change; surgery followed by behavioral treatment 3 of 6 complaints disappeared, 2 of 6 complaints diminished, 1 of 6 no change	No dropout reported; randomized, no concealment; not blinded (phone interview); non-validated outcomes; variation in treatment duration (but the 2 groups were similar); variation in follow-up duration; no a priori sample size calculation

BF = biofeedback; CBT = cognitive behavioral therapy; EMG = electromyographic; FSDS = Female Sexual Distress Scale; FSFI = Female Sexual Function Index; GCBT = group cognitive behavioral therapy; ISSVD = International Society for the Study of Vulvovaginal Diseases; ITT = intention to treat; MFSQ = McCoy Female Sexuality Questionnaire; MPQ = McGill Pain Questionnaire; MVP = multidisciplinary vulvodynia program; NRS = numerical rating scale; PFM = pelvic floor muscle; PT = physical therapy; PVD = provoked vestibulodynia; RCT = randomized control trial; SEMG = surface electromyography; SF-MPQ = McGill-Melzack Pain Short Form; TENS = transcutaneous electrical nerve stimulation; VAS = visual analog scale; VPI = vestibular pain index; VVS = vulvar vestibulitis.

Table 2. Risk of bias summary

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Backman et al[21]	−	−	−	−	+	?	−
Bergeron et al[22]	+	?	−	+	+	?	+
Bergeron et al[18]	−	−	−	−	+	?	+
Bergeron et al[23]	+	?	−	+	+	+	−
Brotto et al[25]	−	−	−	−	+	?	−
Brotto et al[26]	−	−	−	−	−	?	−
Danielsson et al[27]	+	?	−	−	+	?	+
Downey and Frederick[28]	−	−	−	−	+	?	−
Fisher[29]	−	−	−	−	+	?	−
Fowler[30]	−	−	−	−	+	?	−
Forth et al[31]	−	−	−	−	−	?	−
Gentilcore-Saulnier et al[9]	−	−	−	−	+	?	+
Glazer et al[32]	−	−	−	−	+	?	−
Glazer et al[33]	−	−	−	−	+	?	−
Goetsch[34]	−	−	−	−	+	?	−
Goldfinger et al[35]	−	−	−	−	+	?	+
Goldfinger et al[36]	+	?	−	−	+	+	−
Granot et al[37]	−	−	−	−	+	?	−
Hartmann and Nelson[38]	−	−	−	−	+	?	−
Holland[39]	−	−	−	−	+	?	−
Idama and Pring[40]	−	−	−	−	+	?	−
Kalina[41]	−	−	−	−	+	?	−
Lindström and Kvist[42]	−	−	−	−	+	+	+
Mackenzie[43]	−	−	−	−	+	?	−
McKay et al[44]	−	−	−	−	?	?	−
Miletta and Bogliatto[45]	−	−	−	−	+	?	−
Munday et al[46]	−	−	−	−	?	?	−
Murina et al[47]	−	−	−	−	+	?	−
Murina et al[48]	+	?	+	+	+	?	−
Murina et al[49]	+	?	?	+	+	?	?
Nappi et al[50]	−	−	−	−	+	?	?
Olszewski[51]	−	−	−	−	+	?	−
Smith and Gillmer[52]	−	−	−	−	+	?	−
Spoelstra et al[53]	−	−	−	−	+	?	−
Tommola et al[54]	−	−	−	−	+	?	−
Vallinga et al[55]	−	−	−	−	+	?	−
Weijmar Schultz et al[56]	+	?	−	−	+	?	−

− = high risk of bias; ? = unclear risk of bias; + = low risk of bias.

difficult to draw any conclusion about the effectiveness of biofeedback because only 5 of 31 women in the non-surgical group had received biofeedback.

Bergeron et al[22] conducted an RCT comparing vestibulectomy, EMG biofeedback (Glazer protocol for 12 weeks), and group CBT in women with PVD. The average decrease in pain intensity during intercourse was 35% for biofeedback participants and 34% of women in this group reported great improvement or complete relief of their pain. The intention-to-treat analyses showed no significant differences among the three

groups in pain outcomes. The only exception was the vestibular pain index, which favored the vestibulectomy group. All three treatments also were found equally effective in improving sexual function. Participants had an additional follow-up at 2.5 years, which showed that the gains were maintained and that, in fact, pain intensity was further decreased at long-term follow-up.[24] However, it also was shown that women in the CBT and vestibulectomy groups had greater improvement than women in the biofeedback group. In an RCT by Danielsson et al,[27] biofeedback was compared with lidocaine in 46 women with PVD. They reported a cure in 2 of 23 (9%) and a significant improvement in 12 of 23 (52%) of biofeedback participants at a 12-month follow-up. However, these improvements were not statistically different from those of the lidocaine group. The two latter studies had treatment adherence problems because fewer than 57% adhered to the home biofeedback exercises, which could explain the lower effectiveness observed.[22,27] It should emphasized that, as for the prospective studies, the program was quite demanding because it required home exercises with the vaginal probe inserted twice or thrice daily for 20 minutes. The investigators also hypothesized that success and adherence rates would have been higher if patients had benefited from multimodal physical therapy as opposed to biofeedback alone.[22,27]

In sum, the three prospective studies and one case report, with risk bias mainly attributed to the study design (selection bias, performance bias, and detection bias), showed promising results for the effectiveness of biofeedback in decreasing pain in women with PVD. Two well-designed RCTs further supported these findings, although with less pronounced treatment effects, potentially attributed to the lower adherence to home exercises. They also showed positive effects on sexual function and the overall treatment effects were maintained at longer-term follow-up. However, no significant differences were found in self-reported pain intensity when comparing biofeedback with topical lidocaine, vestibulectomy, and CBT at 6- and 12-month follow-ups. Importantly, none of these studies were designed for conducting non-inferiority analysis and thus might have been underpowered to confirm treatment equivalence. Moreover, long-term follow-up (2.5 years) favored CBT and vestibulectomy over biofeedback for decreasing pain during intercourse.

Dilators and Insertion Techniques

The use of vaginal dilators can help women with dyspareunia to control their fear of pain and promote pelvic floor relaxation during insertion. The dilators also might prove beneficial to elongate shortened PFMs and improve flexibility and tissue viscoelastic properties. Three prospective studies with small samples (N = 10−18) reported promising results for decreasing dyspareunia. Idama and Pring[40] found complete relief from pain in 72% of participants as measured by an interview after home self-insertion treatments (N = 18). In the same population, Smith et al[52] reported substantial improvement or cure in 90% of women using a homemade scale (N = 10). It should be emphasized that these two studies used non-validated outcomes for documenting treatment effect, thus limiting the generalization of the high percentage of effectiveness obtained. Murina et al[47] studied the effect of adding dilators in 15 women with PVD after one of the following treatments: electrical stimulation, vestibular infiltration, biofeedback, amitriptyline, or pregabalin. An overall treatment effect for pain intensity and sexual function was observed after treatment using validated outcomes. However, it is not possible to discriminate to the extent to which the dilators contributed to these changes.[47]

The risk biases in these studies are related to the absence of a comparison group (selection bias, performance bias, and detection bias) and the small samples. The findings showed that dilators might be a promising modality for decreasing dyspareunia. However, little is known about the duration of treatment required because the information was omitted in two studies[40,52] and one trial used dilators in conjunction with other treatments.[47]

Electrical Stimulation

Electrical stimulation is a therapeutic modality widely used in physical therapy and, based on the parameters used, it can act on pain through several mechanisms, including the improvement of muscle proprioception, the increase in local blood circulation, the decrease of nociceptive signal flows (ie, gate control theory), and the secretion of endorphins.[60] The available studies focused on sensory stimulation using external vulvar electrodes[55] or a probe inserted partway in the vaginal cavity (20 mm) to apply stimulation to the vestibule area.[48−50] Two prospective studies showed a significant improvement in dyspareunia and sexual function in women with PVD after domiciliary electrical stimulation[55] and in-clinic electrical stimulation combined with home PFM exercises.[50] An RCT by Murina et al[48] involving 40 women with PVD showed that in-clinic transcutaneous electrical nerve stimulation (TENS) yielded significant improvement in pain and sexual function, whereas sham current resulted in non-significant changes. It should be noted that comparisons between groups were not reported in this study. These positive findings suggest that electrical stimulation can be a worthwhile component of treatment. Pursuing this perspective, Murina et al[49] undertook an RCT comparing oral palmitoyl ethanolamide and transpolydatin with placebo in 20 women with PVD who were receiving domiciliary TENS.[49] Because the two groups similarly improved in their dyspareunia, the investigators attributed these changes to the addition of TENS. However, such a conclusion could be ascertained only with a placebo-controlled trial.

For the other modalities reviewed, the risks of bias are mainly related to the absence of a comparison group. For the two RCTs available, the lack of between-group comparison analysis[48] or the fact that the two groups received TENS treatment[49] limits the interpretation of findings. Notwithstanding these limitations and the wide variation in electrical stimulation parameters studied, the available evidence showed positive benefit, as measured with

validated outcomes, for using electrical stimulation in women with PVD.

According to the protocol study registry, another ongoing RCT is comparing vaginal diazepam combined with TENS with placebo and TENS.[50] Based on the chronic pain literature[61] and a case report in women with unprovoked vulvodynia,[62] innovative treatments such as transcranial direct-current stimulation also could be considered. Such treatment relies on recent evidence suggesting a centralization of pain in women with PVD.[7] An RCT protocol was recently published indicating an ongoing study evaluating the efficacy of a transcranial direct-current stimulation compared with sham stimulation in women with PVD (published protocol[63] and NCT02543593[64]).

Manual Therapy

Manual therapy, including stretching, massage, and myofascial techniques, is typically considered the cornerstone of physical therapy interventions. It aims to facilitate muscle relaxation, release tensions and trigger points, improve blood circulation and mobility in the pelvic-perineal region, adjust postural imbalances, and increase the vaginal opening and desensitize the area.[65] As discussed in the following section, most studies included manual therapy as part of multimodal interventions. However, the present search did not show any studies evaluating manual therapy as an isolated modality in the selected population. Because several studies have shown positive results in other populations such as abdominopelvic adhesion,[66] interstitial cystitis,[67,68] and urologic chronic pelvic pain,[69] future studies should focus on this therapeutic approach in women with PVD.

Education

Although education is a common component of multimodal physical therapy treatment and CBT,[9,18,22,36,51,53] it has been rarely studied as a single isolated modality. Education can encompass several topics, namely advice concerning vulvar hygiene habits, avoidance of irritants, behavior modification, stress decreasing techniques, and education about sexual function and pain pathophysiology. Fowler[30] conducted a prospective study including 85 women with PVD assessing the efficacy of an education program consisting mainly of avoidance of irritants and use of dilators. Fowler reported that 21% of participants (17 of 85) had a complete response and 56% (48 of 85) had a partial response after 6 to 36 months of treatment. It should be noted that the definitions used for "complete" and "partial" response were not clearly described. In another prospective study, Brotto et al[25] evaluated the effect of three 1-hour educational seminars in 25 women with PVD. Based on validated measurements, significant effects on sexual function and distress were observed after treatment and maintained at 6-month follow-up. Outcome measurements evaluating pain intensity were not included in the study. Because these seminars included information about management options, the participants might have been more prone to seek other treatments, which were not documented in the study. Overall, these two prospective studies support the relevance of education in the treatment of women with PVD. The risk of biases in these studies are mainly related to the design (lack of control group), the absence of validated pain outcome measurements, and use of other ongoing treatments.

Multimodal Physical Therapy

Multimodal interventions most closely represent current practice in physical therapy in women with PVD.[17] Of the 15 studies focusing on multimodal physical therapy, 5 are case reports, 3 are retrospective, 5 are prospective, and 1 is a pilot RCT. All case report studies showed complete resolution of pain, as measured by numerical rating or visual analog scales, in their single-case participant after manual therapy, stretching, PFM control exercises with or without biofeedback, and education.[28,29,39,41,51]

The three retrospective studies also supported the effectiveness of multimodal physical therapy for alleviating pain during intercourse.[18,38,43] In a retrospective study by Bergeron et al,[18] 71% of women (25 of 35) with PVD reported greater than moderate improvement in their pain condition, as measured by a non-validated seven-point scale (ranging from "a lot worse" to "complete relief of pain"). Significant changes in sexual function also were found. This treatment consisted of education, biofeedback, manual techniques, dilators and insertion techniques, and electrical stimulation. Obtaining similar results, Hartmann and Nelson[38] found that 71% of women reported greater than 50% improvement in pain on a numerical rating scale and 62% reported an overall improvement in sexual functioning. However, this sample was more diversified, including 9 women with PVD and 15 with unprovoked vulvodynia. Despite variation in treatments provided, the core modalities were similar to those of Bergeron et al.[18] MacKenzie[43] conducted a qualitative retrospective study in five women with dyspareunia who undertook trigger point massage as part of their physical therapy intervention. The outcomes were collected by interview and all participants reported an improvement in their pain symptoms.

The five prospective studies showed similar results compared with those yielded by retrospective designs. Using validated measurements, Goldfinger et al[35] found significant improvements in pain intensity, pain threshold, and sexual function in 13 women with PVD after eight weekly sessions of multimodal physical therapy. Consisting of education, PFM exercises, manual techniques, EMG biofeedback, dilators and insertion techniques, stretches of the hip muscles, deep breathing, and global body relaxation exercises, this intervention was successful in 77% of participants (complete cure in 2 of 13 [15%] and great improvement in 8 of 13 [61%]). In the same sample, Gentilcore-Saulnier et al[9] extended their analyses to investigate muscle function and found significant improvements in PFM tone, flexibility, and relaxation capacity and a decrease in pain intensity associated with intravaginal assessment. Corroborating similar effectiveness, Miletta and Bogliatto[45] found that 64% of

participants (9 of 14) had a clinically relevant decrease of pain (visual analog scale score = ≥2−3 of 10) after 10 sessions of physical therapy modalities provided by a midwife (PFM training, biofeedback, perineal massage, manual treatment of trigger points, postural evaluation, and global relax technique). Forth et al[31] observed a decrease of pain assessed by the McGill Pain Questionnaire; however, the changes did not reach statistical significance. The investigators argued that the lack of statistical power due to an insufficient sample size and the limited number of treatment sessions might explain their non-significant results. Interestingly, Tommola et al[54] carried out a prospective non-randomized study comparing vestibulectomy with physical therapy. Limited information was provided concerning the physical therapy intervention, namely the modalities included and the numbers of session undertaken. Pain intensity, evaluated by a visual analog scale, decreased by 67% in the surgery group and by 78% in the physical therapy group. The difference between the two groups was not statistically significant, suggesting that response to surgery was comparable to that achieved by physical therapy.

Only one pilot RCT investigated multimodal physical therapy compared with CBT in women with PVD.[15] The two treatments showed a significant decrease in pain intensity, as measured by a numerical rating scale. A decrease in pain greater than 50% was observed in 80% of participants (8 of 10) in the physical therapy group and in 60% (6 of 10) in the CBT group. However, as argued by the investigators, insufficient statistical power might have prevented the detection of differences between the two interventions.

For isolated modalities, the methodologic limitations of the studies on multimodal physical therapy are mainly related to study design (eg, no control group, no randomization, no blinding) and to small samples. Despite some variations in treatment, some modalities are used more consistently across studies, namely education, PFM exercises, manual techniques, surface EMG biofeedback, and stretching and insertion techniques. Treatment duration and frequency vary widely, from 3 to 8 sessions and over 8 to 12 weeks[28,29,41,51] to 15 to 31 sessions over 1 year 6 months.[38,39] Overall, the present findings suggest that multimodal physical therapy is effective for decreasing pain and improving sexual function in women with PVD. Large RCTs should be carried out to confirm these preliminary findings.

Three registered RCT protocols investigating multimodal physical therapy were found. First, Morin et al[70,71] recently completed the recruitment of a large sample of 212 women with PVD to evaluate the efficacy of multimodal physical therapy compared with an overnight topical application of lidocaine (published protocol[70] and NCT01455350[71]). The last two ongoing RCTs are investigating a treatment algorithm in which women are allocated to treatments, including physical therapy, according to vulvodynia subtypes (ie, hypertonic PFM dysfunction, hormonally mediated PVD, neuro-proliferative PVD; NCT02712814[72] and NCT02892214[73]). Despite these research efforts aimed at offering personalized treatment to women with PVD, further studies need to be conducted to better understand PVD etiology and to validate PVD subtyping.

Multidisciplinary and Multimodality Approaches

Multidisciplinary and multimodality approaches have been increasingly proposed to deal with chronic vulvar pain conditions.[15,74] Indeed, from the perspective that the etiology of PVD is multifactorial, it can be hypothesized that a combined approach would better address all the factors contributing to the pain and associated psychosexual and relational difficulties and thus be more beneficial to patients. Until now, four prospective and two retrospective studies have evaluated physical therapy modalities in conjunction with psychosexual and/or medical treatments.

In a prospective study conducted by Goetsch,[34] the effectiveness of vestibulectomy combined with physical therapy and/or dilatators was investigated in 111 women with PVD. Goetsch found that 67% of participants (73 of 109) had their dyspareunia completely resolved and 20% (22 of 109) reported improvement as measured by a non-validated four-point improvement scale. Interestingly, Goetsch reported that, of the women with continued dyspareunia, 50% had PFM tensions. Goetsch also found that the portion of participants with normalized vestibule sensation but failure of physical therapy to fully correct dyspareunia was only 10%. Sexual function was not examined. Although limited information was provided on the modalities used and the duration of treatment, with the only information that the physical therapists involved were prone to using manual therapy, these findings support the addition of physical therapy to surgery.

Two prospective studies evaluated psychosexual approaches in conjunction with desensitization and insertion techniques. In a study by Backman et al,[21] psychosexual therapy (average = 12 sessions) was combined with desensitization and insertion techniques taught by a midwife (average = 12 sessions). Using non-validated outcome measurements, they found that 79% of women (19 of 24) with PVD were cured or reported great improvement. General sexual functioning was reported as much improved for 63% of women (15 of 24) as measured by a homemade questionnaire. In a study by Lindström and Kvist,[42] all treatment components including CBT and home desensitizing techniques were dispensed by a psychotherapist during 10 weekly sessions. Using the McCoy Female Sexuality Questionnaire as a primary outcome, they found a significant improvement in sexual function after treatment, which was maintained at 6-month follow-up. Significant changes in pain were evaluated using a single question about pain occurrence during intercourse.

Two retrospective studies and one prospective study evaluated a broader multidisciplinary treatment involving gynecologists, physical therapists, and psychotherapists and sex therapists. Munday et al[46] conducted a qualitative retrospective study in

29 women with provoked and mixed vestibulodynia. Women participated in all or some treatment modalities of their multidisciplinary program including medical modalities (eg, topical steroid, amitriptyline), a low-oxalate diet, psychotherapy, and physical therapy. The latter consisted of education, voiding pattern, PFM training, self-massage for desensitization, interferential therapy, TENS, and biofeedback. Results, obtained by an interview, showed that 93% of participants (27 of 29) reported a significant benefit and that 31% (9 of 29) were pain free. Interestingly, 15 of the 19 women who received physical therapy identified this treatment as a significant part of their recovery. Also using a retrospective design, Spoelstra et al[53] found that 81% of participants (52 of 70) had a decrease of pain intensity, measured by a visual analog scale, after the multidisciplinary program, which included surgical intervention, education, biofeedback, pelvic floor physical therapy, home exercises, and sexual counseling in women with persistent symptoms. In a larger cohort involving 132 women with PVD, Brotto et al[26] investigated prospectively the effectiveness of a multidisciplinary program over 10 to 12 weeks including two educational seminars and medical management by a gynecologist, three psychology sessions, and three physical therapy sessions (biofeedback, PFM relaxation, dilators, and home exercises). It should be emphasized that the physical therapy treatment did not include any manual therapy or myofascial release techniques. Using validated measurements, significant improvements in pain, sexual functioning, and sexual distress were observed and the gains were maintained at the 2- to 3-month follow-up. Overall, 54% of women (71 of 132) indicated that their pain had decreased since starting the program. Weijmar Schultz et al[56] presented a two-arm study, one randomized arm and one prospective non-randomized arm. The two arms aimed at comparing behavioral multimodal treatment (education, PFM exercises, dilators, and physical therapy and sexual counseling, if necessary) to behavioral treatment preceded by vestibulectomy. Using non-standardized outcomes, a cure rate of 36% (10 of 28) to 43% (3 of 7) and an improvement rate of 64% (18 of 28) to 71% (5 of 7) were observed in behavioral therapy in the two study arms, which were found not to be significantly different than the group also undergoing surgery, showing a cure rate of 43% (3 of 7) to 50% (3 of 6) and an improvement rate of 83% (5 of 6) to 86% (6 of 7). This small study suggested that most women were effectively treated with behavioral therapy and that surgery did not appear to yield further benefit.

All studies, except the one by Weijmar Schultz et al,[56] were not RCTs and therefore quality assessment shows high-risk bias pertaining to selection bias, performance bias, and detection bias. In addition, most of these studies integrated medical treatments, psychological and sex therapy, and physical therapy in a non-standardized manner, such that not all participants received the same combination and duration of interventions. Participants also were allowed to receive other treatments while under study. These limitations prevent drawing conclusions on which component actually contributed to decreasing pain. The search identified an ongoing RCT by Dayan[75] that could help to elucidate whether the addition of educational seminars and CBT to physical therapy treatments potentiate the effectiveness compared with physical therapy alone (NCT01628679).

DISCUSSION

The aim of this systematic review was to critically appraise the literature on the effectiveness of physical therapy modalities in women with PVD. The results indicate that physical therapy modalities including biofeedback, dilators, electrical stimulation, education, multimodal physical therapy, and multidisciplinary approaches were consistently effective across studies for decreasing pain during intercourse and, when measured, improving sexual function. The interpretation of these findings is limited because the evidence is derived from only a handful of RCTs and mainly from prospective, retrospective, and case report studies with high risk of bias.

Of isolated modalities, biofeedback was the most rigorously studied with two well-designed and low-risk bias RCTs. Based on the Glazer protocol, the biofeedback programs entailed home PFM exercises two to three times daily and four to eight supervised sessions over a period of 3 to 4 months.[22,27,33,44] Although superior in the prospective studies, the effectiveness in the RCTs was found to be good because 35% to 50% of women reported improvements in dyspareunia.[22,27] Significant effects on sexual function also were found and, most interestingly, all results were maintained up to 2.5 years.[22,27] Findings suggest that biofeedback has a similar effectiveness as vestibulectomy and CBT for self-reported pain intensity at 6- to 12-month follow-up.[22,27] However, none of these studies were designed and powered to undertake non-inferiority analysis[22,27,32,33,37,44] and long-term results favored CBT and vestibulectomy.[24] Concerning the dilators and insertion techniques, promising results were found by the three small studies suggesting positive effects for decreasing dyspareunia when administered alone or in conjunction with other treatments[40,47,52]; however, the evidence contained limited information on the dosage and duration required. Thus far, these studies have used verbal or written instructions for self-administered dilation. It is not specified which professional gave these instructions; therefore, these studies might have not involved physical therapists. Results could be potentiated with closer supervision, including PFM assessment, to ensure adequate muscle relaxation before insertion. For electrical stimulation, the findings obtained from two prospective studies and two RCTs concur to support beneficial effects of superficial electrical current focusing on sensory pathways to decrease pain.[48–50,55] Despite very positive results, none of these studies provided statistical evidence that electrical stimulation is superior to placebo or a comparison group. Further RCTs are awaited to standardize stimulation protocols and to investigate other types of stimulation such as PFM stimulation and transcranial approaches. For the education programs, favorable benefits were observed.[25,30] However, given that the two prospective studies available allowed other ongoing treatments, it

is not possible to distinguish the treatment effects related to education from those of the other interventions received.

In this literature search, the largest number of studies was dedicated to investigating multimodal physical therapy, which can be expected because it most closely portrays clinical practice. Multimodal physical therapy showed consistent effectiveness across studies, with a significant improvement of pain in 71% to 80% of women with PVD.[18,35,38,54] As opposed to the studies evaluating isolated modalities, most studies evaluating multimodal treatment defined "improvement" more rigorously, using a clinically relevant decrease of pain (ie, decreased score of 2−3 of 10, decrease of 50%).[18,38,45] Therefore, the overall effectiveness of multimodal physical therapy appears to surpass isolated modalities. In line with the survey study of Hartmann et al,[17] some modalities were used more consistently across treatment studies, namely education, PFM exercises, manual techniques, surface EMG biofeedback, and stretching and insertion techniques. Wide variations were found in treatment duration and frequency of supervised sessions, ranging from 3 to 8 sessions over 8 to 12 weeks[28,29,41,51] to 15 to 31 sessions over 1 year 6 months.[38,39] In contrast to physical therapy treatment for urinary incontinence, in which a clear dose-response had been demonstrated,[76] this was not as clear in women with PVD given that a protocol of eight weekly sessions figured among the most successful treatments.[35] Overall, the present findings suggest that multimodal physical therapy has promising effects for decreasing pain in women with PVD. Although less commonly included as a main outcome measurement, sexual function also was found to be improved after physical therapy. Of interest, multimodal PT showed similar effectiveness to vestibulectomy and CBT in a small non-randomized study[54] and a pilot RCT,[15] respectively. Robust RCTs comparing multimodal physical therapy with medical interventions are required to confirm these preliminary indications of success.

Multidisciplinary approaches proposing physical therapy modalities in conjunction with psychosexual and/or medical treatments were found effective in decreasing pain in women with PVD. Physical therapy was shown to be a good adjunct to vestibulectomy in the study by Goetsch.[34] In the small RCT by Weijmar Schultz et al,[56] most women were effectively treated with behavioral therapy combined with physical therapy, whereas surgery did not result in additional benefit. Multidisciplinary programs involving gynecologists, psychologists and sex therapists, and physical therapists also were found effective. Although joining multidisciplinary forces is often the best way to help women with PVD in clinical settings, there is insufficient evidence currently available to conclude a higher success for multidisciplinary approaches. Heterogeneity in the treatments provided, including non-standardized treatments and allowance for other ongoing treatments, also precludes an inference of the findings. It should be pointed out that, before investigating multidisciplinary treatment, future studies should consolidate the effectiveness of single approaches to develop the optimal combined intervention. Moreover, the assessment of multidisciplinary approaches should particularly incorporate cost-effectiveness analysis to foresee the feasibility of implementation in clinical settings.

Several limitations across the studies reviewed impede the interpretation of findings. First, most studies lacked a control or comparison group, which is crucial because spontaneous remission[77] and prominent placebo effects[78] have been demonstrated in women with PVD and in chronic pain populations.[79] This emphasizes the need to prove the superiority of physical therapy modalities over a comparison group using a randomized controlled design. Such a study design is a prerequisite for preventing selection bias, performance bias (blinding of participants and personnel), and detection bias (blinding of outcome assessment), which was a common limitation in most of the studies reviewed. Second, inadequate sample size and non-validated outcome measurements represent an important methodologic shortcoming in the current literature. Lack of validated outcomes hinders comparison of trials and merging of data to investigate treatment effectiveness and, more specifically, which modalities showed a superior effect. The Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) group provided guidance for outcome measurements in chronic pain conditions[80] and these recommendations were recently adapted to women with vulvodynia.[81] They recommend evaluating pain, sexual function, and self-perceived improvement using validated outcomes and extending the assessment to the multiple biopsychosocial aspects of vulvodynia. Third, the literature search focused on common modalities used in physical therapy. Other emerging techniques such as laser therapy, dry needling, and modalities targeting pain centralization[82] will deserve consideration with increasing empirical support.

CONCLUSION

Findings of this review provide preliminary support for the effectiveness of physical therapy modalities in women with PVD. However, considering the high-risk bias related to the retrospective and prospective nature of most of the available research, further studies using robust RCT designs, validated outcomes, sufficient sample sizes, and long-term follow-ups should be undertaken to confirm the effectiveness of these promising approaches.

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SUPPLEMENTARY DATA

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.sxmr.2017.02.003.