



The negative effect of urologic chronic pelvic pain syndrome on female sexual function: a systematic review and meta-analysis

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Received: 14 January 2019 / Accepted: 10 May 2019 / Published online: 21 June 2019
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Abstract

Introduction and hypothesis To explore the effect of urologic chronic pelvic pain syndrome (UCPPS) on female sexual function. **Methods** Database searches were conducted in PubMed, EMBASE, the Cochrane Library, and Google Scholar for published literature using the Female Sexual Function Index (FSFI) or reporting the prevalence of dyspareunia. Data extraction and quality evaluation were performed on the literature that met the inclusion criteria, and a meta-analysis was performed using STATA 12.0 and RevMan5.3 software to calculate the mean differences (MD) and odds ratios (OR) and their 95% confidence intervals (CI). **Results** A total of nine case-control studies enrolling 4965 subjects were investigated. The present meta-analysis results demonstrated a strong correlation between UCPPS and dyspareunia (OR = 11.27, 95% CI: 5.15–24.67, $P < 0.00001$). The UCPPS group had significantly lower scores in each domain of the FSFI compared with the healthy control group: total score (MD = -11.35, 95% CI: -14.54–-8.16, $P < 0.00001$); desire (MD = -1.04, 95% CI: -1.20–-0.88, $P < 0.00001$); arousal (MD = -1.78, 95% CI: -2.36–-1.20, $P < 0.00001$); lubrication (MD = -2.11, 95% CI: -2.49–-1.73, $P < 0.00001$); orgasm (MD = -1.50, 95% CI: -1.72–-1.28, $P < 0.00001$); satisfaction (MD = -1.54, 95% CI: -1.97–-1.12, $P < 0.00001$); pain (MD = -2.89, 95% CI: -3.63–-2.14, $P < 0.00001$).

Conclusions UCPPS had a significantly negative effect on female sexual function, particularly in the lubrication, pain, and total score domains. In addition, UCPPS patients had a significantly higher risk of dyspareunia. Psychosocial variables may be a potential pathogenesis of female sexual dysfunction (FSD). Future well-designed research is called for to develop a comprehensive estimate of the association between UCPPS and FSD.

Keywords Urologic chronic pelvic pain syndrome · Female sexual dysfunction · Female Sexual Function Index · Dyspareunia · Meta-analysis

Introduction

Urologic chronic pelvic pain syndrome (UCPPS) was first proposed by the MAPP research network, established by the NIH in 2008, and includes bladder pain syndrome/interstitial cystitis (BPS/IC), and chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS). As a symptom complex, UCPPS includes a group of landmark symptoms, such as chronic pain or discomfort in the lower abdomen, pelvic area, and/or genitourinary genitalia, usually accompanied by bladder and

lower urinary tract symptoms, even with sexual dysfunction [1]. Increasing evidence suggests that UCPPS negatively affects the quality of life, emotional status, and sexual function of patients and their spouses. However, most studies focus on assessing male sexual function, while female sexual health is often overlooked.

Currently, female sexual dysfunction (FSD) is measured by the Female Sexual Function Index (FSFI), a validated instrument also recommended for use by the MAPP research network [1], providing an overall assessment of six key domains (desire, arousal, lubrication, orgasm, satisfaction, and pain). Each domain scores 0–6 points; an FSFI total score is 2–36 points, with higher scores indicating better function [2]. Wiegel et al. suggested that an FSFI total score of 26.55 is the best cutoff for FSD [3]. Nevertheless, the score alone does not make it clear which specific domain of FSFI is most negatively affected or the severity of sexual impairment in each domain.

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The present study aims to focus on female sexual health, evaluate the significant effect of UCPPS on female sexual function, and explore the potential pathogenesis of FSD in a structured manner. We also discuss the important concept of UCPPS as a symptom complex.

Materials and methods

The present study followed the Meta-analysis of Observational Studies in Epidemiology (MOOSE) checklist for reporting [4].

Search strategy

Database searches were conducted in the PubMed, EMBASE, Cochrane Library, and Google Scholar databases for relevant published literature up to December 2018. An English language restriction was imposed. The following key words and medical subject headings (MeSH) were used as search terms: “urologic chronic pelvic pain syndrome,” “UCPPS,” “interstitial cystitis/bladder pain syndrome,” “IC/BPS,” “chronic pelvic pain syndrome,” “female sexual dysfunction,” “female sexual function index,” “FSFI,” and “dyspareunia.” This process was performed iteratively until no additional articles could be identified. The references cited in the literature were manually retrieved.

Selection criteria

The inclusion criteria followed the PICOS principle: female with a diagnosis of IC/BPS or CPPS, with urologic symptoms presenting a majority of the time during any 3 days in the past 6 months (in the case of CPPS) or in the most recent 3 months (for IC/BPS); at least 18 years old; reporting a non-zero score for bladder and/or pelvic region pain, pressure, or discomfort during the past 2 weeks. The sexual function assessment must have been done using the FSFI. Outcome measurement included FSFI total score, six domain (desire, arousal, lubrication, orgasm, satisfaction, and pain) scores, and the prevalence of dyspareunia. The study types selected were observational studies, including case-control studies, retrospective cohort studies, and cross-sectional studies. Incomplete or erroneous data, duplicate studies, reviews, case reports, editorial comments, letters from readers, abstracts of conferences, and animal experiments were excluded.

Data extraction

Two authors independently extracted and cross-checked the following data: first author, publication year, nation, study type, data source, ethnicity, sample size, mean age, outcome, diagnostic criteria, and quality scores. In case of a

disagreement, discrepancies were resolved through discussion or third-party ruling.

Quality evaluation

In this study, the risk of bias was assessed by the Newcastle-Ottawa Scale (NOS), which was recommended by the Cochrane Collaboration [5]. Each included case-control study was judged on eight items and categorized into three groups: selection, comparability, and exposure, respectively. Stars were awarded for each quality item; the stars served as a quick visual assessment. A study was awarded a maximum of one star for each numbered item within the selection and exposure categories. A maximum of two stars could be given for the comparability. Stars were awarded such that the highest quality studies were awarded up to nine stars. A score ≤ 5 was regarded as low quality.

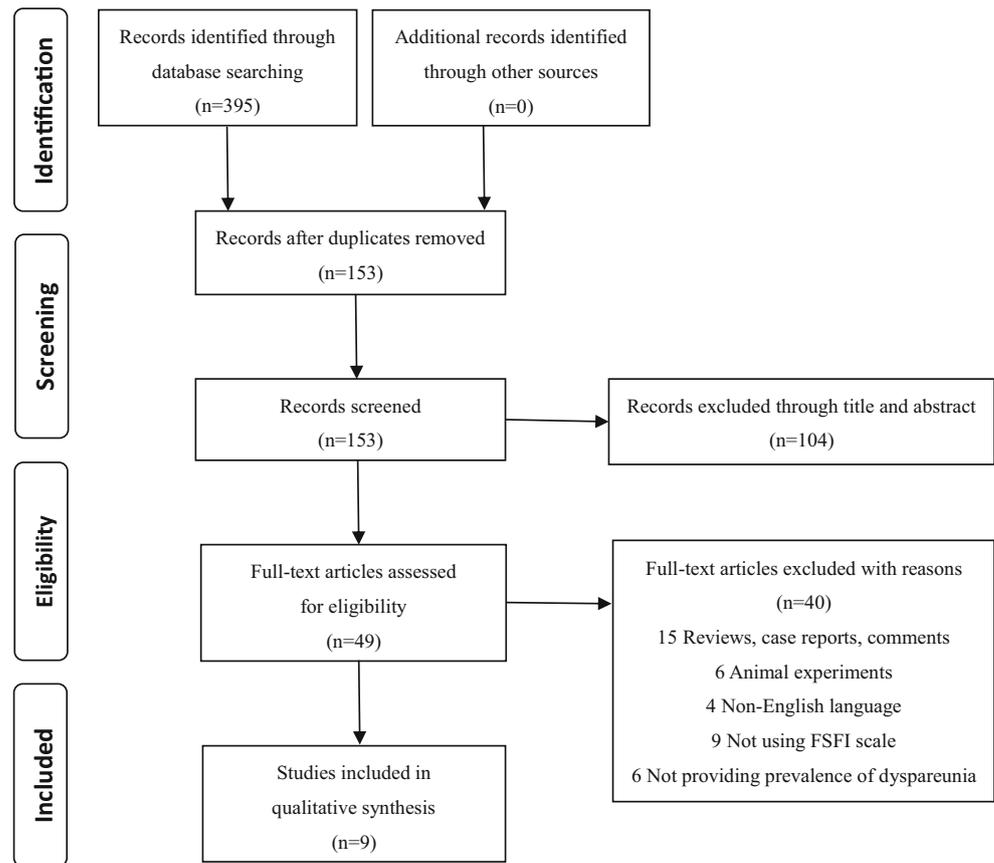
Statistical analysis

STATA 12.0 and Review Manager 5.3 softwares were used to conduct the meta-analysis. The odds ratio (OR) with 95% CI was used for dichotomous data, and the mean difference (MD) with 95% CI was used for continuous data. The I^2 statistic and Cochrane-Q test were used to test the heterogeneity of each study. A test level of $\alpha = 0.1$ and P value < 0.05 were considered statistically significant. Studies with an I^2 statistic of 25–50% were considered to have low heterogeneity; $50% < I^2 \leq 75%$ indicated moderate heterogeneity; $I^2 > 75%$ referred to high heterogeneity. A P value > 0.1 or an I^2 statistic $\leq 50%$ meant that the heterogeneity between the studies was small, and the fixed effect model was used. Otherwise, the random effect model was used.

Results

Search results

The flow diagram for the selection process was shown in Fig. 1. A total of 395 records were detected; 153 of these records were retrieved after excluding 242 duplicated articles, and 104 articles were excluded after scanning the title and abstract. Among the remaining 49 full-text articles assessed for eligibility, 40 articles were excluded. Of the 40 excluded articles, 15 were reviews, case reports, and comments; 4 were in a non-English language; 6 studied animal experiments; 9 did not use the FSFI scale; 6 did not report the prevalence of dyspareunia. Finally, nine studies were included in the qualitative synthesis; they were all case-control studies and written in English [6–14].

Fig. 1 Flow diagram of reference selection process

Characteristics of eligible studies

The general characteristics of the nine eligible case-control studies are presented in Table 1. A total of 4965 subjects were included in the present study. All studies were published between 2001 and 2014. The sample sizes ranged from 86 to 1781. The mean age of the case and control group ranged from 34.8–50.6 and 36.1–50.66, respectively. The overall quality of the included studies was moderate to good, and the range of NOS scores was 5–8, with an average score of 6.5 (Table 2). The included articles mainly came from single-center studies. Four articles came from Europe (Italy, UK) and five from North America (Canada, USA). Six studies evaluated the FSFI total score [6–8, 10, 12, 14], four studies evaluated the FSFI domains (desire, arousal, lubrication, orgasm, satisfaction, and pain) [6, 7, 10, 12], and five studies evaluated dyspareunia [6, 9, 11–13]. Only one study evaluated the FSFI pain domain [14].

Outcome of overall assessment of UCPPS and female sexual function

FSFI total score

Six studies evaluated the FSFI total score [6–8, 10, 12, 14], and the meta-analysis result is shown in Table 3. The result

indicated that patients in the UCPPS group had significantly lower FSFI total scores compared with the healthy control group (MD = -11.35, 95% CI: -14.54–-8.16, $P < 0.00001$). Figure 2a shows the details of the pooled analysis forest plot.

Desire

Four studies evaluated the FSFI desire domain [6, 7, 10, 12], and the meta-analysis result is shown in Table 3. The result indicated that patients in the UCPPS group had significantly lower desire scores compared with the healthy control group (MD = -1.04, 95% CI: -1.20–-0.88, $P < 0.00001$). Figure 2b shows the details of the pooled analysis forest plot.

Arousal

Four studies evaluated the FSFI arousal domain [6, 7, 10, 12], and the meta-analysis result is shown in Table 3. The result indicated that patients in the UCPPS group had significantly lower arousal scores compared with the healthy control group (MD = -1.78, 95% CI: -2.36–-1.20, $P < 0.00001$). Figure 2c shows the details of the pooled analysis forest plot.

Table 1 Clinical and demographic characteristics in eligible references

Reference	Publish year	Nation	Study type	Data source	Ethnicity	Sample size (total/case/control)	Mean age (range) (case/control)	Outcome	Diagnostic criteria	NOS scores
Schrepf et al.	2014	America	Case-control	Multi-center (MAPP research network)	Mixed	86/58/28	41.1 ± 14.8/ 42.9 ± 13.1	FSFI total score FSFI Pain	IC/BPS diagnosis by NIDDK	8
Gardella et al.	2011	Italy	Case-control	Single-center (San Matteo Hospital)	Caucasian	235/47/188	38.2 ± 11.3/ 37.9 ± 11.6	Dyspareunia% FSFI total score DALOSP	IC/BPS diagnosis by NIDDK	5
Nickel et al.	2011	Canada	Case-control	Multi-center (nine participating sites)	Mixed	324/207/117	49.6 ± 15.1/ 47.8 ± 13.5	FSFI total score	IC/BPS diagnosis by NIDDK	8
Warren et al.	2011	America	Case-control	Multi-center (national urology and urogynecology organizations)	Mixed	625/312/313	42.3/ 42.9	Dyspareunia%	IC/BPS diagnosis by AUA guideline	6
Zaslau et al.	2008	America	Case-control	Single-center	Mixed	685/554/131	38.0 ± 10.7/ 39.7 ± 13.2	FSFI total score FSFI DALOSP	NA	5
Gardella et al.	2008	Italy	Case-control	Single-center (San Matteo Hospital)	Caucasian	94/47/47	38.7 ± 12/ 38.2 ± 10.5	FSFI total score FSFI DALOSP	IC/BPS diagnosis by NIDDK	8
Ottom et al.	2007	Canada	Case-control	Single-center	Mixed	97/75/22	38.0 ± 13.0/ 43.0 ± 7.0	Dyspareunia% FSFI total score FSFI DALOSP	IC/BPS diagnosis by suggestive history and physical examination	7
Peters et al.	2007	Italy	Case-control	Single-center	Mixed	1038/215/823	50.6 ± 14.8/ 50.66 ± 14.4	Dyspareunia%	IC/BPS diagnosis by NIDDK	6
Zondervan et al.	2001	UK	Case-control	Single-center	Caucasian	1781/432/1346	34.8 ± 9.0/ 36.1 ± 8.5	Dyspareunia%	CPP diagnosis by symptom	6

FSFI Female Sexual Function Index; *DALOSP* desire, arousal, lubrication, orgasm, satisfaction, pain; *IC/BPS* interstitial cystitis/painful bladder syndrome; *CPP* chronic pelvic pain; *MAPP* The Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network; *NIDDK* National Institute of Diabetes and Digestive and Kidney Diseases; *AUA* American Urological Association; *NOS* Newcastle-Ottawa Scale; *NA* not available

Table 2 Newcastle-Ottawa quality assessment scale for case-control studies

Reference	Selection			Comparability ^a		Exposure		Quality scores ^b
	Definition of cases	Representativeness of cases	Selection of controls	Definition of controls	Basis of the design or analysis	Ascertainment of exposure	Same method of ascertainment for cases and controls	
Schrepf et al. 2014	★	★	★	★	★★	★	★	8
Gardella et al. 2011	★	–	★	★	★	–	★	5
Nickel et al. 2011	★	★	★	★	★★	★	★	8
Warren et al. 2011	★	★	★	★	–	★	★	6
Zaslau et al. 2008	★	–	★	–	★	★	★	5
Gardella et al. 2008	★	★	★	★	★★	★	★	8
Ottom et al. 2007	★	★	★	★	★	★	★	7
Peters et al. 2007	★	★	★	★	★	–	★	6
Zondervan et al. 2001	★	★	–	★	★★	–	★	6

Stars are awarded such that the highest quality studies are awarded up to nine stars

A maximum of one star for each numbered item within the Selection and Exposure categories

^a A maximum of two stars can be given for Comparability categories

^b One star ★ for one score

Table 3 Results of meta-analysis for female sexual function

Outcomes of interest	Studies, no.	UCPPS, no.	Control, no.	MD/OR[(95%CI)	P value*	Effect model	Heterogeneity			
							χ^2	df	I ² , %	P value
FSFI-Desire	4	712	371	-1.04(-1.20,-0.88)	<0.00001	Fixed	0.72	3	0	0.87
FSFI-Arousal	4	712	371	-1.78(-2.36,-1.20)	<0.00001	Random	19.36	3	85	0.0002
FSFI-Lubrication	4	712	371	-2.11(-2.49,-1.73)	<0.00001	Fixed	7.4	3	59	0.06
FSFI-Orgasm	4	712	371	-1.50(-1.72,-1.28)	<0.00001	Fixed	4.08	3	26	0.25
FSFI-Satisfaction	4	712	371	-1.54(-1.97,-1.12)	<0.00001	Random	9.09	3	67	0.03
FSFI-Pain	5	770	399	-2.89(-3.63,-2.14)	<0.00001	Random	39.55	4	90	<0.00001
FSFI total score	6	977	516	-11.35(-14.54,-8.16)	<0.00001	Random	45.15	5	89	<0.00001
Dyspareunia%	5	1043	2515	11.27(5.15,24.67)	<0.00001	Random	40.98	4	90	<0.00001

FSFI Female Sexual Function Index; MD mean difference; OR odds ratio

Lubrication

Four studies evaluated the FSFI lubrication domain [6, 7, 10, 12], and the meta-analysis result is shown in Table 3. The result indicated that patients in the UCPPS group had significantly lower lubrication scores compared with the healthy control group (MD = -2.11, 95% CI: -2.49– -1.73, $P < 0.00001$). Figure 2d shows the details of the pooled analysis forest plot.

Orgasm

Four studies evaluated the FSFI orgasm domain [6, 7, 10, 12], and the meta-analysis result is shown in Table 3. The result indicated that patients in the UCPPS group had significantly lower orgasm scores compared with the healthy control group (MD = -1.50, 95% CI: -1.72– -1.28, $P < 0.00001$). Figure 2e shows the details of the pooled analysis forest plot.

Satisfaction

Four studies evaluated the FSFI satisfaction domain [6, 7, 10, 12], and the meta-analysis result is shown in Table 3. The results indicated that patients in the UCPPS group had significantly lower satisfaction scores compared with the healthy control group (MD = -1.54, 95% CI: -1.97– -1.12, $P < 0.00001$). Figure 2f shows the details of the pooled analysis forest plot.

Pain

Five studies evaluated the FSFI pain domain [6, 7, 10, 12, 14], and the meta-analysis result is shown in Table 3. The results indicated that patients in the UCPPS group had significantly lower pain scores compared with the healthy control group (MD = -2.89, 95% CI: -3.63– -2.14, $P < 0.00001$). Figure 2g shows the details of the pooled analysis forest plot.

Dyspareunia

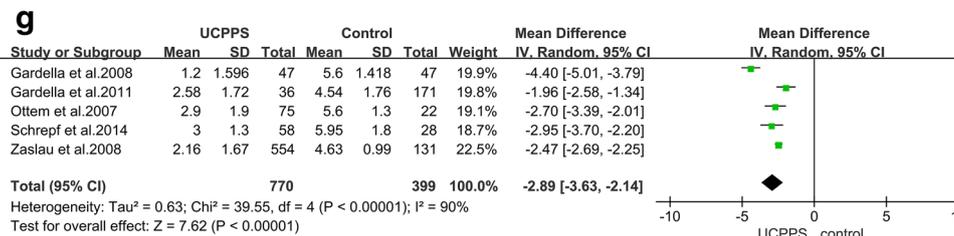
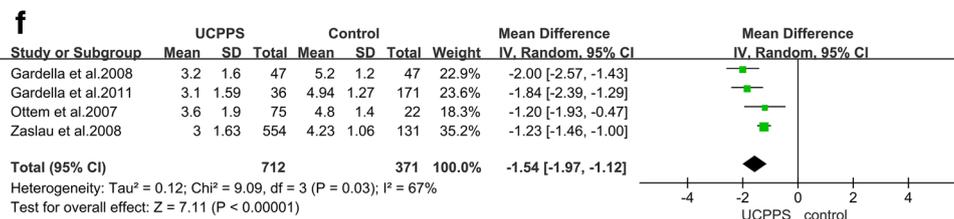
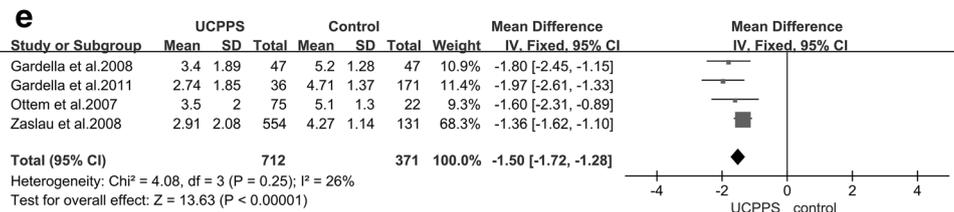
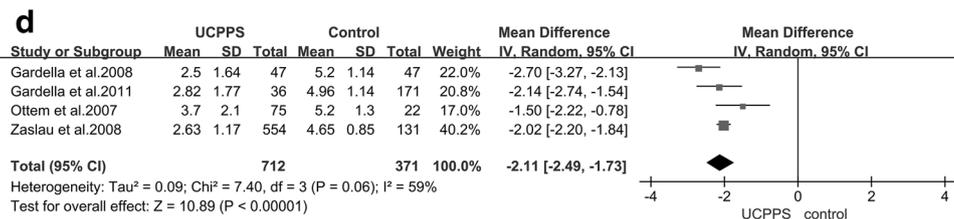
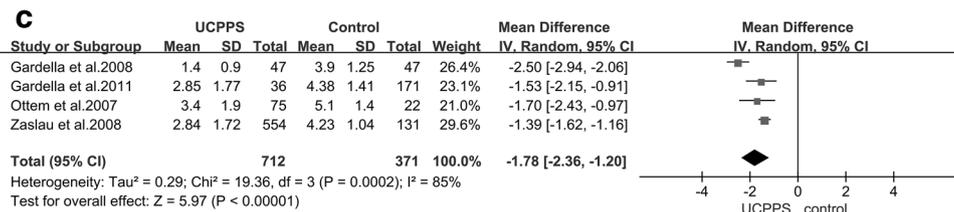
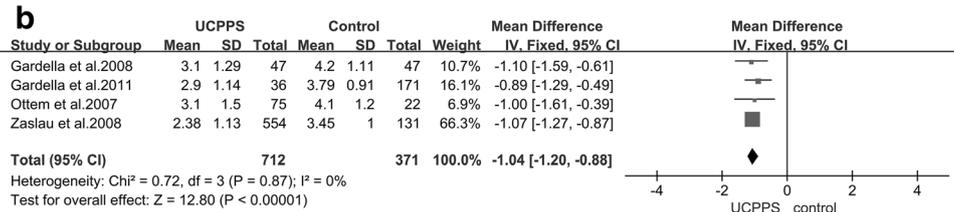
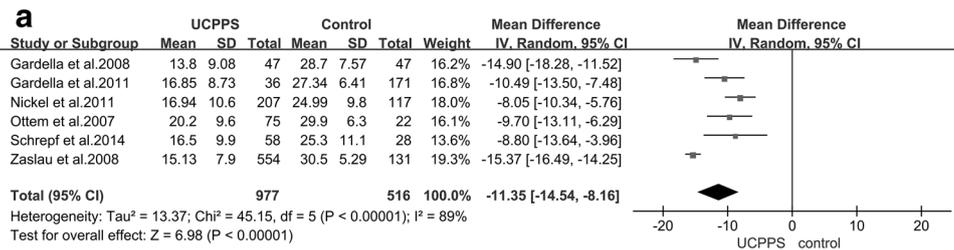
Five studies evaluated dyspareunia [6, 9, 11–13], and the meta-analysis result is shown in Table 3. The results indicated a strong correlation between the UCPPS group and dyspareunia (OR = 11.27, 95% CI: 5.15–24.67, $P < 0.00001$). UCPPS patients had a significantly higher risk of suffering dyspareunia compared with the healthy control group. Figure 3 shows the details of the pooled analysis forest plot.

Discussion

The association between female pelvic pain and female sexual function has been reported among different samples [15–17]. However, the outcomes were not in agreement, and integrated reporting was needed. To the best of our knowledge, the present study is the first attempt to evaluate the significant effect of UCPPS on sexual function in female patients. The meta-analysis results demonstrated that women with UCPPS have significantly lower scores in each FSFI domain compared with the healthy control group, particularly in the lubrication, pain, and total score domains, which indicated that UCPPS negatively affects female sexual function. In addition, the results also demonstrated a strong correlation between UCPPS and dyspareunia.

For a long time, the mechanism of UCPPS has been uncertain. Research in the last decade has found that UCPPS and other non-urollogic-associated syndromes (NUAS), such as fibromyalgia, irritable bowel syndrome, chronic fatigue syndrome, endometriosis, and vulvar pain, share a similar chronic pain status, with varying degrees of psychologic or psychiatric

Fig. 2 Forest plots showing meta-analysis results of the Female Sexual Function Index (FSFI) domains in urologic chronic pelvic pain syndrome (UCPPS) patients and healthy controls. **a** Total scores; **b** desire; **c** arousal; **d** lubrication; **e** orgasm; **f** satisfaction; **g** pain



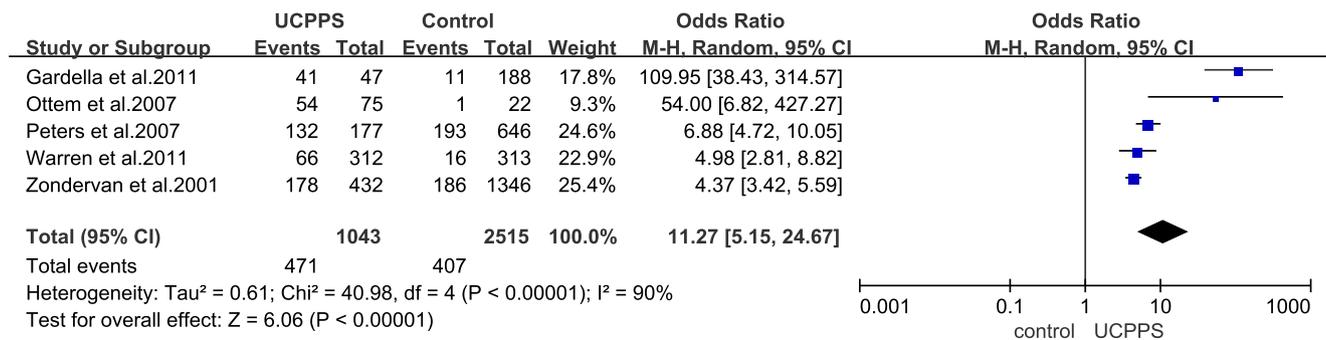


Fig. 3 Forest plot showing meta-analysis results of dyspareunia in urologic chronic pelvic pain syndrome (UCPPS) patients and healthy controls

symptoms, and the central nervous system may be involved. Central sensitization may be the potential mechanism [18–22], suggesting that UCPPS may not be limited to the bladder or prostate [23].

The multifactorial character of UCPPS and the various terminologies used have led to two major misunderstandings about the concept of IC/BPS and CP/CPPS. First, the bladder was considered to be the source of IC/BPS, while the prostate the origin of CP/CPPS. Second, IC/BPS was regarded as a female-only disease and CPPS only in males. In fact, CPPS could occur in females [24, 25], and IC/BPS and CP/CPPS may share the same pathophysiologic basis [26]. This is the reason the NIH introduced the concept of UCPPS and emphasized that neither the prostate nor the bladder was a specific terminal organ of the disease [1, 27]. UCPPS as a symptom complex involved multiple systems, organs, and factors. The European Association of Urology (EAU) Guidelines and The European Society for the Study of Interstitial Cystitis (ESSIC) have made the effort to normalize terminologies [28, 29]. Its multifactorial character, various confusing terminologies, and misunderstanding of the concept are enormous obstacles that have impeded scientists in exploring the pathogenesis of the disease and development of treatment and have made UCPPS refractory.

Normal sexual function involves complicated interactions among psychologic, hormonal, neurologic, physiologic, social, and cultural factors and transition from arousal to relaxation, with feelings of contentment, pleasure, and fulfillment. All domains of the FSFI could be affected by UCPPS. The present meta-analysis gives evidence that sexual impairment in the lubrication, pain, and total scores is more severe. Age and abnormal female hormone levels may be the reason for decreased vaginal lubrication. The average age of the UCPPS group in the articles included in this meta-analysis was 42.6 years old (range, 34.6–50.6). They were approaching menopause, a period in which inadequate levels of estrogen may lead to vaginal atrophy, increased vaginal pH, and senile urinary tract infections, which may eventually cause decreased vaginal lubrication.

Suffering from long-standing pain and discomfort increases a patient's psychologic burden, which is often

accompanied by mental and psychologic symptoms, such as depression, anxiety, or stress. The prevalence of depression or anxiety in UCPPS patients was higher than in controls. Pain may also lead to pessimistic, fearful, and disappointing sexual psychologic disorders, and patients may appear to avoid or reduce the frequency of sex, loathe sexual activity, and further induce sexual dysfunction. It is worth noting that the main cause of disease in most patients with sexual dysfunction may be due to psychologic factors, which form a vicious cycle of “painful discomfort-psychotic symptoms-sexual dysfunction.” Sexual topics are considered relatively private in some cultures, and it may be difficult for women to express their sexual dysfunction problems [26]. A significant proportion of patients may remain undetected, and the prevalence of FSD may be underestimated. Psychosocial variables may be one of the potential pathogenic mechanisms of FSD. The MAPP research network has recommended that interdisciplinary approaches to the diagnosis and treatment are more effective than monotherapy [1]. In the future, more valid therapies and treatments are required to break the vicious cycle.

Several limitations in this present study need to be addressed. We only conducted a pooled analysis of the FSFI total score, the scores of six domains, and prevalence of dyspareunia. There were no standard criteria for assessing the scale and diagnosis of FSD. We were unable to fully explain the prevalence of FSD. We also considered the poor reproducibility of the NOS scale, and due to unclear or missing details because of insufficient reporting in the original literature, we may have overestimated the risk of bias [30]. In addition, heterogeneity in arousal, pain, the FSFI total score, and dyspareunia was large, and we did not find all sources of heterogeneity, so we preformed a random effects models. This meta-analysis did not include any randomized controlled trials (RCTs) for interrelated scarcity studies. The included studies were mainly from Europe, Canada, and the USA. We lacked research from Asia and Oceania. We carefully interpreted the results of the meta-analysis. It is expected that more RCTs and well-designed studies will be conducted in the future to further explore the association between UCPPS and FSD.

Conclusions

Females with definite symptoms of UCPPS had worse sexual function than those without the disorder. They scored significantly lower in each domain of the FSFI, particularly in the lubrication, pain, and total score domains. In addition, UCPPS patients had a significantly higher risk of suffering dyspareunia. Aging, reduced estrogen levels, and psychosocial variables may be the potential pathogenic mechanism of FSD. Future well-designed research is called for to develop a comprehensive estimate of the association between UCPPS and FSD.

Acknowledgments We thank Prof. Zhihai Qin for his linguistic assistance and suggestions to improve the manuscript. We thank Prof. Hairong Huang for her assistance with the statistical aspects.

Funding This study was funded by grants from the Natural Science Foundation of Hainan Province (no. 20158296).

Compliance with ethical standards

Conflicts of interest None.

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