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The effect of systemic lupus erythematosus on sexual function in women: an updated meta-analysis based on cross-sectional studies

Maoyu Liu^{1†}, Jianguo Dou^{2†} and Qianqian Wang^{1*} 

Abstract

Background: Systemic lupus erythematosus (SLE), a chronic systemic autoimmune disease, often affects different organs and tissues. It can be effectively managed using drugs; however, attention should be paid to the patient's quality of life. This study aimed to evaluate the effect of SLE on female sexual function based on current literature.

Methods: The PubMed, Embase, and Cochrane Library databases were searched for eligible studies published up to November 9, 2021. This review included all English studies that compared the sexual function between women with SLE and healthy women. A meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.

Results: A total of 367 records were retrieved from 3 electronic databases. Five studies that involved 710 women with SLE and 2059 healthy women were finally included in this meta-analysis. The result indicated a significant decrease (mean difference = -1.74 , 95% confidence interval -3.14 to -0.34 , $p = 0.02$) in the total scores of the Female Sexual Function Index in women with SLE, implying that healthy women had better sexual function than those with SLE.

Conclusion: The results of our study indicated that SLE could negatively affect the quality of sexual life in terms of desire, arousal, and pain. Thus, close attention should be paid to the sexual function of women with SLE.

Trial registration: This study was registered in the International Prospective Register of Systematic Reviews (registration number: CRD42021290439).

Keywords: Systemic lupus erythematosus, Sexual function, Meta-analysis

Introduction

Systemic lupus erythematosus (SLE), a chronic systemic autoimmune disease, often affects different organs and tissues [1]. In North America, the estimated incidence rate of SLE is 23 patients per 100,000 people. SLE is more

common in African-Americans, Hispanics, and Asians than in the Caucasian population [2]. It primarily affects women in the age group of 15–40 years. In China, the incidence rate of SLE ranges from 31 to 70 patients per 100,000 people, and the male-to-female ratio is 1:9 [3].

SLE can be effectively managed with drugs; however, attention should be paid to the patient's quality of life (QoL). Sexual life is an important component of people's QoL, and sexual behavior is considered an indispensable part of personal behavior [4]. Several chronic diseases have been reported to negatively affect sexual function, a finding that is frequently neglected in clinical practice [5]. Regarding SLE, studies have reported that the factors

[†]Maoyu Liu and Jianguo Dou contributed equally and should share first authorship

*Correspondence: wangqianqian@hospital.cqmu.edu.cn

¹ Department of Obstetrics and Gynecology, The Second Affiliated Hospital of Chongqing Medical University, No. 74 Linjiang Road, Yuzhong District, Chongqing 400000, China
Full list of author information is available at the end of the article



affecting patients' sexual function may be caused by the disease itself, mental health disorders (e.g., depression and anxiety), and drug treatment [6, 7]. Previous meta-analyses have revealed that SLE has potential adverse effects on the sexual function in women with SLE; however, no further analysis of specific performance and treatment has been conducted [8, 9].

This study aimed to evaluate the effect of SLE on female sexual function based on current literature, with the hope of investigating methods for improving the sexual function of patients with SLE and attracting the attention of clinicians.

Methods

We conducted a meta-analysis according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines [10]. This study was registered in the International Prospective Register of Systematic Reviews (registration number: CRD42021290439).

Search strategy

A systematic literature search of three electronic databases, i.e., PubMed, Embase, and Cochrane Library, for studies published until November 9, 2021 was performed. All studies published in English were searched using the following keywords according to their description in MeSH: ("systemic lupus erythematosus" [Title/Abstract] OR "SLE" [Title/Abstract] OR "lupus" [Title/Abstract]) AND ("Sexual" [Title/Abstract] OR "sexual function" [Title/Abstract] OR "sexual desire" [Title/Abstract]) AND ("female" [Title/Abstract] OR "woman" [Title/Abstract] OR "women" [Title/Abstract]). The studies included in previous meta-analyses were also searched.

Inclusion and exclusion criteria

The studies were selected using Endnote X9 tools. The inclusion criteria: (1) articles comparing the sexual function between women with SLE and healthy women and (2) articles in the English language. The exclusion criteria: publications that were unextractable or whose data were unavailable for analyses were excluded (conference abstract, case series, and duplicated data). All studies and data were selected and extracted, respectively. Any disagreement regarding data extraction was resolved by a third independent reviewer through mutual discussion.

Data extraction and quality assessment

Data from the included studies were extracted independently and any disagreement about data extraction was resolved by a third reviewer through

mutual discussion. The authors of these studies were contacted via mail, if necessary.

All the included studies were cross-sectional, and their qualities were evaluated by the Agency for Healthcare Research and Quality [11] using an 11-point Likert scale (0–3, low quality; 4–7, medium quality; and 8–11, high quality).

Outcomes of interest

The main outcomes included the Female Sexual Function Index (FSFI) scores and sexual function. Depression and single status were additional outcomes.

Statistical analysis

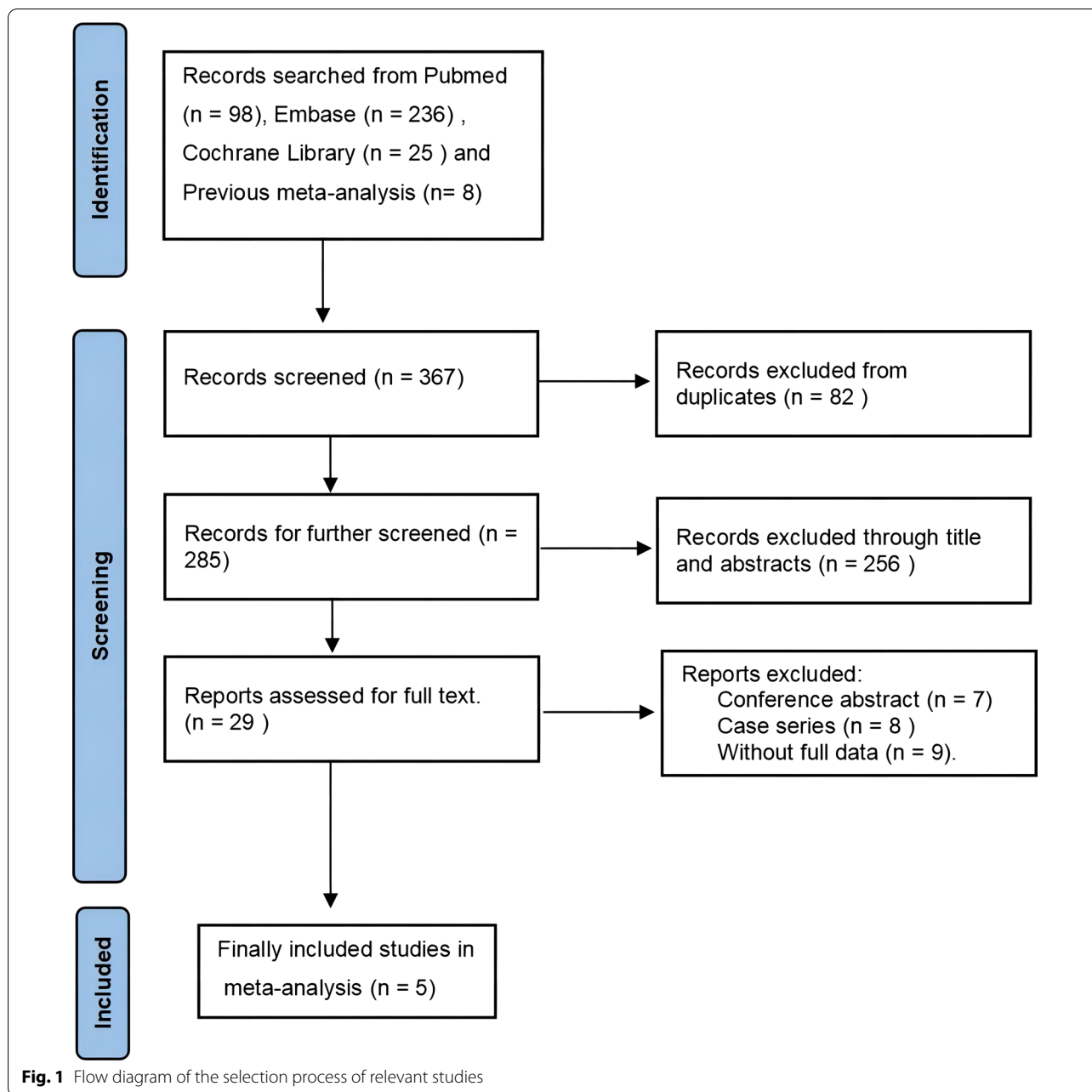
All data analyses were conducted using RevMan, version 5.3 (Cochrane Collaboration) and Stata SE, ver. 14.0 tools. The continuous and dichotomous variables were expressed as mean difference (MD) and odds ratio (OR), respectively. A *P* value of <0.05 was considered statistically significant. Additionally, heterogeneities among the studies were assessed using the heterogeneity (I^2) and chi-squared (χ^2) tests. I^2 was considered acceptable for $I^2 < 50\%$, and the meta-analysis was conducted using a fixed-effects model. For $I^2 \geq 50\%$, a random effects model was used. Furthermore, a sensitivity analysis was employed to test the stability of the results.

Results

A total of 367 records were retrieved from the 3 aforementioned electronic databases. Five studies that involved 710 women with SLE and 2,059 healthy women were finally included in the meta-analysis [12–16]. The flow diagram for study selection is presented in Fig. 1. The FSFI, which included 6 separate areas and consisted of 19 items, was used to assess sexual function. The total score ranged from 2 to 36, and desire (1.2–6), arousal (0–6), lubrication (0–6), orgasm (0–6), satisfaction (0.8–6), and pain (0–6) were determined. A high score indicated better sexual function, and a total score of <26.55 indicated sexual impairment [17, 18]. The basic characteristics of each study are presented in Table 1. The quality of the included studies was evaluated in Table 2. All the included studies were cross-sectional, and the sexual function evaluation scale remained consistent.

Sexual dysfunction

All five studies compared the sexual function between the control group (healthy women) and SLE group (women with SLE). The difference in the prevalence of sexual dysfunction in the two groups exhibited no statistical significance (OR 2.13, 95% confidence interval [CI], 0.70–6.49, $p=0.18$). The I^2 among the studies was significant, and



a random effects model was used ($p < 0.00001$, $I^2 = 95\%$) (Fig. 2).

FSFI scores

The results indicated a significant decrease ($MD = -1.74$, $95\% \text{ CI} = -3.14 \text{ to } -0.34$, $p = 0.02$) in the total FSFI scores in the SLE group (Fig. 3), implying that the control group experienced better sexual function than the SLE group. Furthermore, the sexual function of the SLE group exhibited a significant decrease in desire ($MD = -0.33$, $95\% \text{ CI} = -0.63 \text{ to } -0.04$, $p = 0.03$) (Fig. 4A), arousal

($MD = -0.36$, $95\% \text{ CI} = -0.62 \text{ to } -0.10$, $p = 0.006$) (Fig. 4B), and pain ($MD = -0.50$, $95\% \text{ CI} = -0.87 \text{ to } -0.13$, $p = 0.009$) (Fig. 4C). Moreover, there was no statistical difference in lubrication ($MD = -0.25$, $95\% \text{ CI} = -0.72 \text{ to } 0.22$, $p = 0.30$) (Fig. 4D), orgasm ($MD = -0.12$, $95\% \text{ CI} = -0.35 \text{ to } 0.11$, $p = 0.32$) (Fig. 4E), and satisfaction ($MD = -0.10$, $95\% \text{ CI} = -0.24 \text{ to } 0.04$, $p = 0.15$) (Fig. 4F).

Secondary outcomes

The secondary outcomes included depression and single status. Between the control and SLE groups, no

Table 1 Characteristics and quality of included studies

Study	Research type	Number of Participant	Inclusion indicators		Age, mean ± SD years		Assessment		Cases of sexual dysfunction	
			SLE	Control	SLE	Control	SLE	Control	SLE	Control
Tseng et al	2011	Cross-sectional study	279	1580	Sexual dysfunction, Civil status, Depression	37.5 ± 10.2	34.8 ± 8.5	FSFI	85	408
Morales et al	2013	Cross-sectional study	65	55	Sexual dysfunction, Civil status	39.03 ± 10.83	35.73 ± 11.25	FSFI	28	15
Moghadam et al	2019	Cross-sectional study	170	170	Sexual dysfunction, Civil status, Depression	37.64 ± 7.96	33.77 ± 6.64	FSFI	146	45
Dorgham et al	2020	Cross-sectional study	94	98	Sexual dysfunction	32.5 ± 5.6	29.3 ± 6.3	FSFI	73	81
Serna-Peña et al	2021	Cross-sectional study	102	156	Sexual dysfunction, Civil status, Depression	36.3 ± 11.6	33.2 ± 10.8	FSFI	18	27

FSFI: Female Sexual Function Index; SLE: Systemic lupus erythematosus

Table 2 The quality of included studies were evaluated by the Agency for Healthcare Research and Quality

Item	Serna-Peña 2021	Dorgham 2020	Moghadam 2019	Morales 2013	Tseng 2011
1. Define the source of information (survey, record review)	Yes	Yes	Yes	Yes	Yes
2. List inclusion and exclusion criteria for exposed and unexposed subjects (cases and controls) or refer to previous publications	Yes	Yes	Yes	Yes	Yes
3. Indicate time period used for identifying patients	Yes	No	Yes	Yes	Yes
4. Indicate whether or not subjects were consecutive if not population-based	Yes	Yes	Yes	Yes	Yes
5. Indicate if evaluators of subjective components of study were masked to other aspects of the status of the participants	Yes	Yes	Yes	Yes	Yes
6. Describe any assessments undertaken for quality assurance purposes (e.g., test/retest of primary outcome measurements)	Yes	Yes	Yes	Yes	Yes
7. Explain any patient exclusions from analysis	Yes	Yes	Yes	Yes	Yes
8. Describe how confounding was assessed and/or controlled	Yes	Yes	Yes	Yes	Yes
9. If applicable, explain how missing data were handled in the analysis	Unclear	Unclear	Unclear	Unclear	Unclear
10. Summarize patient response rates and completeness of data collection	Yes	Yes	Yes	Yes	Yes
11. Clarify what follow-up, if any, was expected and the percentage of patients for which incomplete data or follow-up was obtained	Unclear	Unclear	Unclear	Unclear	Unclear
Total score	9	8	9	9	9

The score ranges of 0–3, 4–7, and 8–11 indicate low, medium, and high quality, respectively

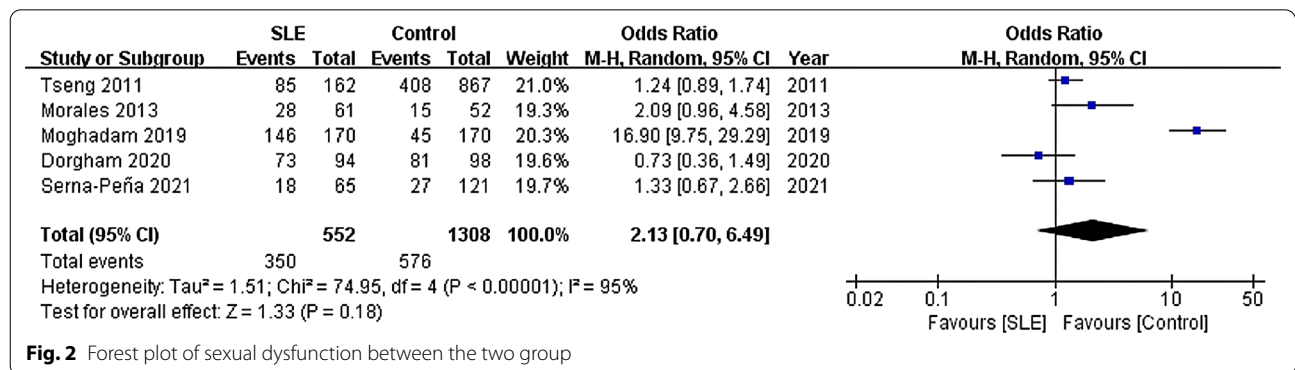


Fig. 2 Forest plot of sexual dysfunction between the two group

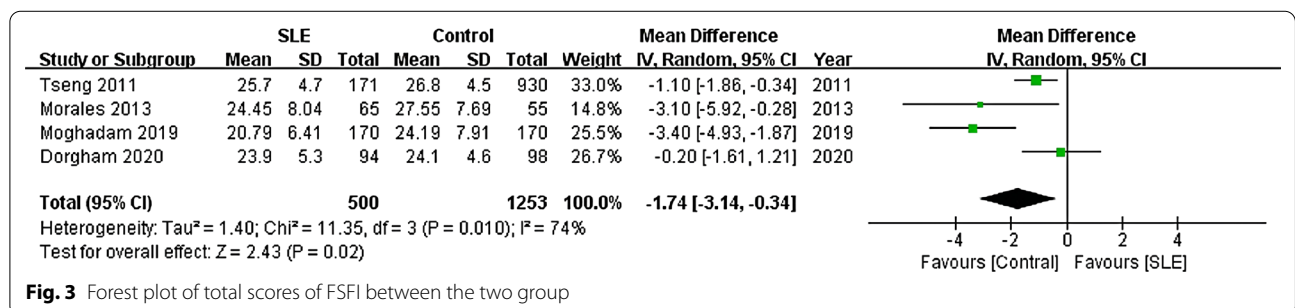


Fig. 3 Forest plot of total scores of FSFI between the two group

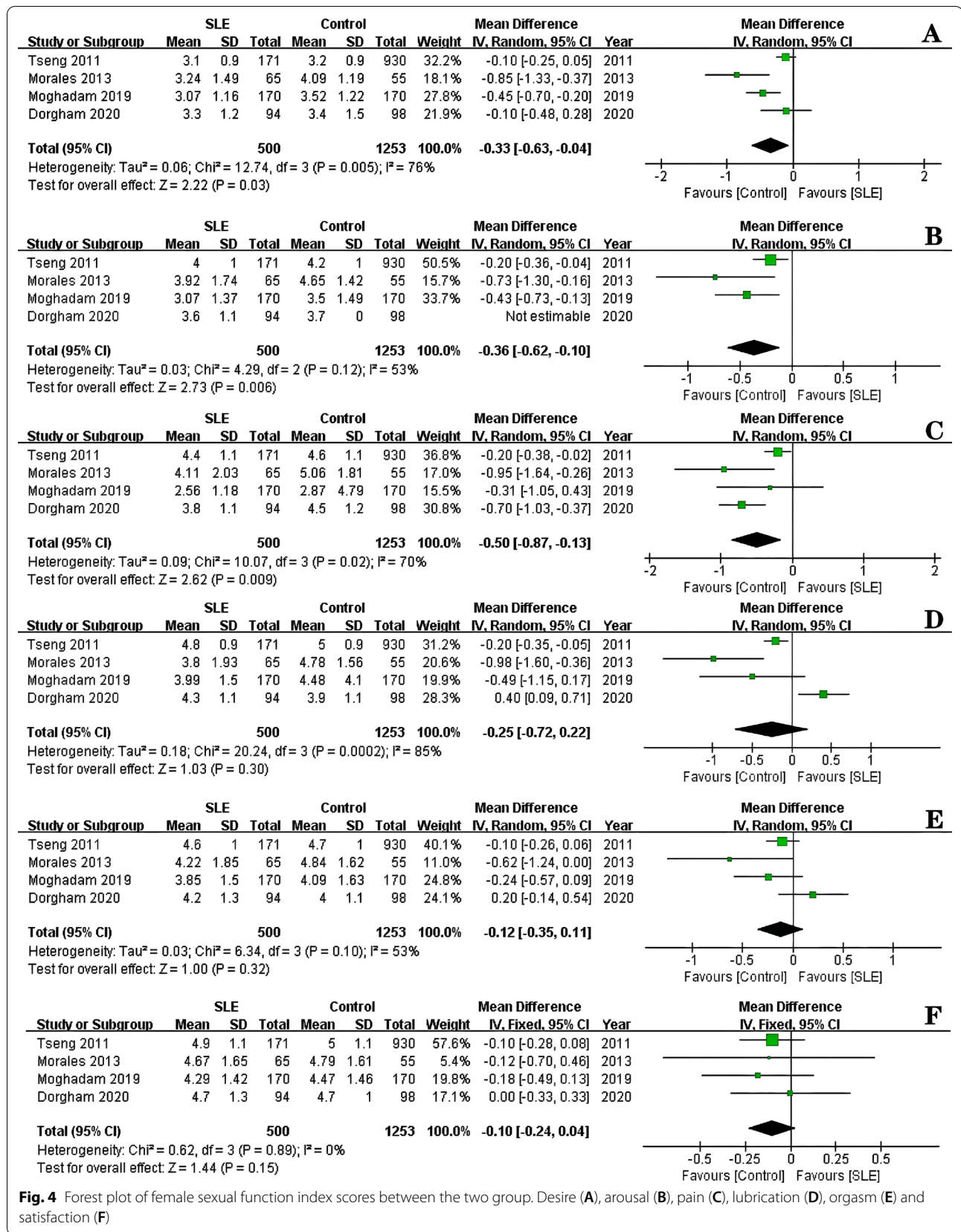


Fig. 4 Forest plot of female sexual function index scores between the two group. Desire (A), arousal (B), pain (C), lubrication (D), orgasm (E) and satisfaction (F)

statistical differences were observed in depression (OR 3.80, 95% CI 0.86–16.80, $p=0.08$) (Fig. 5a) and single status (OR = 0.93, 95% CI 0.74–1.17, $p=0.55$) (Fig. 5b).

Sensitivity analysis

Sensitivity analysis was conducted by excluding each study and recalculating the pooled odds risk estimate. Analysis of sexual dysfunction was conducted (Fig. 6a), and the total FSFI scores were determined (Fig. 6b). The results indicated no remarkable change in the overall results after the exclusion of each study from the main analysis.

Discussion

After significant progress in the SLE treatment, more attention should be focused on improving the patients’ QoL. Sexual function is an important part of the QoL of individuals, which should not be ignored [19]. Our study mainly evaluated the effects of life status and depression in both the SLE and control groups. The results indicated that the prevalence of female sexual dysfunction between the two groups did not exhibit a significant difference, which was not reported in previous meta-analyses [8, 9]. Our studies also demonstrated that the FSFI scores of the SLE group in terms of desire, arousal, pain, and total scores statistically significantly declined. This implies that the sexual function of the SLE group decreased.

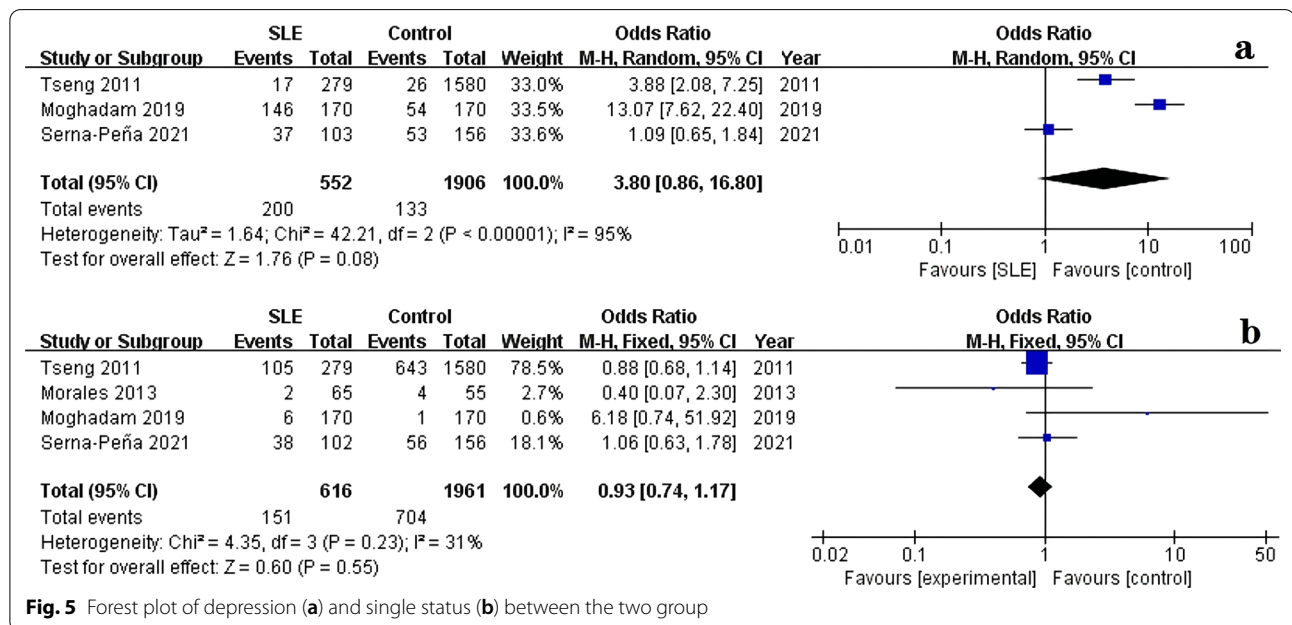


Fig. 5 Forest plot of depression (a) and single status (b) between the two group

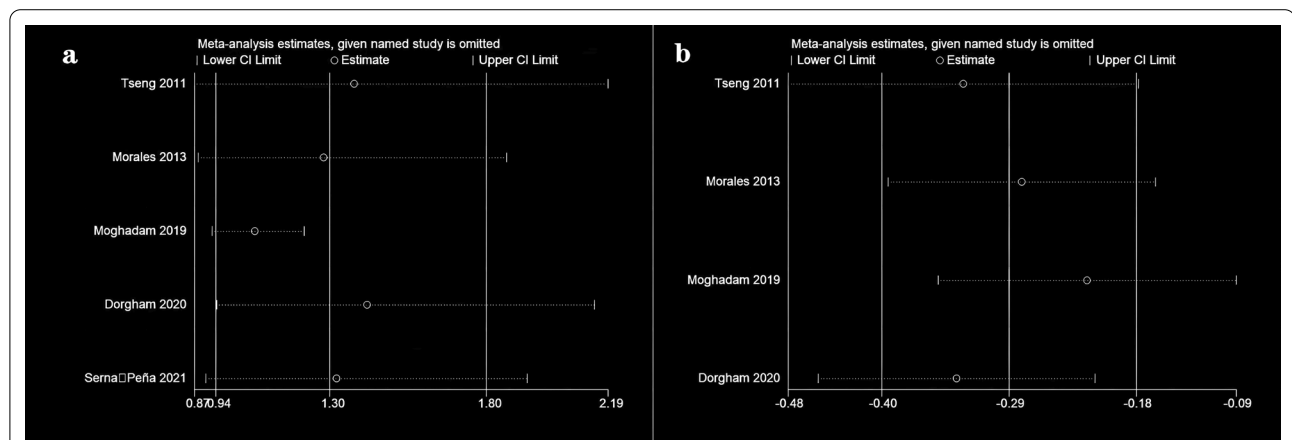


Fig. 6 Sensitivity analysis between the two group of sexual dysfunction (a) and the total scores of FSFI (b)

The pathogenesis of SLE is complex and multifactorial. The sexual function of the SLE group was affected by depression, disease activity and severity, marital status, and education. [16, 20]. The clinical manifestations of the skin and joints in patients with SLE have a negative impact on body image, interest, and desire [16]. Thus, the diagnosis of SLE may cause disease-related stress and an inactive sexual life [21], which may result in low desire and arousal scores. Oktem, et al., reported that estrogen may affect the sexual function of women with SLE owing to the involvement of the ovary in autoimmune oophoritis [22]. Meanwhile, the use of immunosuppressants (e.g., cyclophosphamide) to treat patients with SLE might have a gonadal toxicity effect, which may considerably reduce the number of primary and stimulating follicles, resulting in ovarian failure [23]. Low estrogen levels result in physiological changes in the vulva and vagina, including vaginal dryness, irritation, burning, and pain during sexual intercourse. These symptoms can adversely affect sexual pain scores [24, 25].

The use of estrogen hormone replacement therapy for the treatment of sexual dysfunction in women with SLE remains controversial. Several studies support the fact that proper estrogen supplementation could improve the sexual function of women with ovarian insufficiency at the perimenopausal and postmenopausal stages, and women who have previously undergone oophorectomy [26–29]. However, a few authors have argued that estrogen might enhance autoimmunity, thereby exacerbating the risk of SLE [30, 31]. A recent study found that hormone therapy is effective in the treatment of menopausal symptoms and has an extremely low impact on SLE activity and thrombosis [32]. The possibility of topical estrogen use for the treatment of sexual dysfunction in women with SLE is a promising area for future research; however, no relevant studies have been reported thus far.

Rheumatologists tend to ignore the evaluation of sexual function in patients with SLE [16]. Overall, our meta-analysis revealed that SLE had a potential impact on sexual QoL. However, no relevant randomized controlled trial has been found to report such an impact. Thus, this problem needs to be investigated further.

This study had several limitations that should be acknowledged. First, a publication bias test was not conducted because the number of studies was insufficient. Second, all data on sexual function were collected via self-report, which might have caused a reporting bias. Third, heterogeneities were observed in the study, although the stability of the results was tested using a sensitivity analysis. This heterogeneity may have resulted from differences in various aspects such as race, culture, income, and education. To address these

concerns and identify relevant studies, larger sample size, multicenter, long-term randomized controlled trials are required in the future.

Conclusion

Our study demonstrated that the FSFI scores of the SLE group exhibited a statistically significant decline in desire, arousal, pain, and total scores. Thus, SLE had a potentially adverse effect on sexual function. Fortunately, there was no significant difference in the prevalence of sexual dysfunction between the two groups. More attention should be paid to the sexual function of women with SLE.

Acknowledgements

Not applicable.

Author contributions

MYL, JGD and QQW contributed to the conception and design this study. MYL, QQW and JGD were responsible for the development of the methodology and data interpretation. JGD analyzed and interpreted the data. MYL wrote the paper. QQW revised the paper. MYL and JGD contributed equally and should share first authorship. All authors read and approved the final paper. All authors read and approved the final manuscript.

Funding

None.

Availability of data and materials

All the data presented in this study can be found in online electronic databases. Further inquiries can be directed to the corresponding author/s.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author details

¹Department of Obstetrics and Gynecology, The Second Affiliated Hospital of Chongqing Medical University, No. 74 Linjiang Road, Yuzhong District, Chongqing 400000, China. ²Department of Urology, The People's Hospital of Dazu, Chongqing, China.

Received: 4 March 2022 Accepted: 29 June 2022

Published online: 04 July 2022

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