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

Maoyu Liu¹†, Jianguo Dou²† and Qianqian Wang¹*

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...
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 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 (I²) and chi-squared (χ²) tests. I² was considered acceptable for I² <50%, and the meta-analysis was conducted using a fixed-effects model. For I² ≥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 (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 I² among the studies was significant, and a random effects model was used (p <0.00001, I² =95%) (Fig. 2).
FSFI scores
The results indicated a significant decrease (MD = −1.74, 95% CI −3.14 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% CI −0.63 to −0.04, p = 0.03) (Fig. 4A), arousal (MD = −0.36, 95% CI −0.62 to −0.10, p = 0.006) (Fig. 4B), and pain (MD = −0.50, 95% CI −0.87 to −0.13, p = 0.009) (Fig. 4C). Moreover, there was no statistical difference in lubrication (MD = −0.25, 95% CI −0.72 to 0.22, p = 0.30) (Fig. 4D), orgasm (MD = −0.12, 95% CI −0.35 to 0.11, p = 0.32) (Fig. 4E), and satisfaction (MD = −0.10, 95% CI −0.24 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 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).
| Study       | Research type       | Number of Participant | Inclusion indicators                      | Age, mean ± SD years | Assessment | Cases of sexual dysfunction |
|-------------|---------------------|-----------------------|-------------------------------------------|-----------------------|------------|-----------------------------|
|             |                     |                       |                                           | SLE                   | Control    | SLE                         |
| Tseng et al | 2011                | Cross-sectional study | 279, 1580 Sexual dysfunction, Civil status, Depression | 37.5 ± 10.2          | 34.8 ± 8.5 | FSFI 85                     |
| Morales et al | 2013              | Cross-sectional study | 65, 55 Sexual dysfunction, Civil status   | 39.03 ± 10.83       | 35.73 ± 11.25 | FSFI 28                     |
| Moghadam et al | 2019            | Cross-sectional study | 170, 170 Sexual dysfunction, Civil status, Depression | 37.64 ± 7.96        | 33.77 ± 6.64 | FSFI 146                     |
| Dorgham et al | 2020              | Cross-sectional study | 94, 98 Sexual dysfunction                | 32.5 ± 5.6          | 29.3 ± 6.3  | FSFI 73                     |
| 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                     |

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            | Yes              | Yes          | Yes            | Yes          | Yes        |
| unexposed subjects (cases and controls) or refer to previous       |                  |              |                |              |            |
| publications                                                        |                  |              |                |              |            |
| 3. Indicate time period used for identifying patients              | Yes              | No           | Yes            | Yes          | Yes        |
| 4. Indicate whether or not subjects were consecutive if not        | Yes              | Yes          | Yes            | Yes          | Yes        |
| population-based                                                   |                  |              |                |              |            |
| 5. Indicate if evaluators of subjective components of study        | Yes              | Yes          | Yes            | Yes          | Yes        |
| were masked to other aspects of the status of the participants     |                  |              |                |              |            |
| 6. Describe any assessments undertaken for quality assurance       | Yes              | Yes          | Yes            | Yes          | Yes        |
| purposes (e.g., test/retest of primary outcome measures)           |                  |              |                |              |            |
| 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     | Unclear          | Unclear      | Unclear        | Unclear      | Unclear    |
| analysis                                                            |                  |              |                |              |            |
| 10. Summarize patient response rates and completeness of data      | Yes              | Yes          | Yes            | Yes          | Yes        |
| collection                                                         |                  |              |                |              |            |
| 11. Clarify what follow-up, if any, was expected and the           | Unclear          | Unclear      | Unclear        | Unclear      | Unclear    |
| percentage of patients for which incomplete data or follow-up      |                  |              |                |              |            |
| was obtained                                                       |                  |              |                |              |            |
| 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 groups.

**A** Desire (A), arousal (B), pain (C), lubrication (D), orgasm (E) and satisfaction (F)

#### SLE Study or Subgroup

| SLE Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | Mean Difference IV, Random, 95% CI Year |
|-----------------------|------|----|-------|------|----|-------|--------|----------------------------------------|
| Tseng 2011            | 3.1  | 0.9| 171   | 3.2  | 0.8| 930   | 32.2%  | -0.10 [-0.25, 0.05] 2011               |
| Morales 2013          | 3.24 | 1.49| 65    | 4.09 | 1.19| 55    | 18.1%  | -0.65 [-1.33, -0.37] 2013              |
| Moghadam 2019         | 3.07 | 1.16| 170   | 3.52 | 1.22| 170   | 27.6%  | -0.45 [-0.70, -0.20] 2019              |
| Dorgham 2020          | 3.3  | 1.2 | 194   | 3.4  | 1.5 | 98    | 21.9%  | -0.10 [-0.48, 0.28] 2020              |

**Total (95% CI)**

| 500 | 1253 | 100.0% |

Heterogeneity: Tau² = 0.06; Chi² = 12.74, df = 3 (P = 0.005); I² = 76%

Test for overall effect: Z = 2.22 (P = 0.03)

#### SLE Study or Subgroup

| SLE Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | Mean Difference IV, Random, 95% CI Year |
|-----------------------|------|----|-------|------|----|-------|--------|----------------------------------------|
| Tseng 2011            | 4.4  | 1.1 | 171   | 4.6  | 1.1 | 930   | 36.8%  | -0.20 [-0.39, -0.02] 2011               |
| Morales 2013          | 4.11 | 2.03| 65    | 5.06 | 1.81| 55    | 17.0%  | -0.95 [-1.64, -0.26] 2013              |
| Moghadam 2019         | 2.58 | 1.18| 170   | 2.87 | 4.79| 170   | 15.5%  | -0.31 [-1.05, 0.43] 2019               |
| Dorgham 2020          | 3.8  | 1.1 | 194   | 4.5  | 1.2 | 98    | 30.8%  | -0.70 [-1.03, -0.37] 2020              |

**Total (95% CI)**

| 500 | 1253 | 100.0% |

Heterogeneity: Tau² = 0.03; Chi² = 4.28, df = 2 (P = 0.12); I² = 53%

Test for overall effect: Z = 2.73 (P = 0.006)

#### SLE Study or Subgroup

| SLE Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | Mean Difference IV, Random, 95% CI Year |
|-----------------------|------|----|-------|------|----|-------|--------|----------------------------------------|
| Tseng 2011            | 4.8  | 0.9 | 171   | 5.0  | 0.9 | 930   | 31.2%  | -0.20 [-0.35, -0.05] 2011               |
| Morales 2013          | 3.8  | 1.3 | 65    | 4.78 | 1.56| 55    | 20.6%  | -0.98 [-1.60, -0.36] 2013              |
| Moghadam 2019         | 3.99 | 1.5 | 170   | 4.46 | 4.1 | 170   | 19.9%  | -0.49 [-1.15, 0.17] 2019               |
| Dorgham 2020          | 4.3  | 1.1 | 194   | 3.9  | 1.1 | 98    | 28.3%  | 0.40 [0.09, 0.71] 2020                 |

**Total (95% CI)**

| 500 | 1253 | 100.0% |

Heterogeneity: Tau² = 0.18; Chi² = 20.24, df = 3 (P = 0.0002); I² = 85%

Test for overall effect: Z = 1.03 (P = 0.30)

#### SLE Study or Subgroup

| SLE Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | Mean Difference IV, Random, 95% CI Year |
|-----------------------|------|----|-------|------|----|-------|--------|----------------------------------------|
| Tseng 2011            | 4.6  | 1.1 | 171   | 4.7  | 1.1 | 930   | 40.1%  | -0.10 [-0.26, 0.06] 2011               |
| Morales 2013          | 4.22 | 1.85| 65    | 4.84 | 1.62| 55    | 11.0%  | -0.62 [-1.24, 0.00] 2013              |
| Moghadam 2019         | 3.95 | 1.5 | 170   | 4.09 | 1.63| 170   | 24.8%  | -0.24 [-0.57, 0.09] 2019               |
| Dorgham 2020          | 4.2  | 1.3 | 194   | 4.1  | 1.1 | 98    | 24.1%  | 0.20 [-0.14, 0.54] 2020               |

**Total (95% CI)**

| 500 | 1253 | 100.0% |

Heterogeneity: Tau² = 0.18; Chi² = 6.24, df = 3 (P = 0.10); I² = 53%

Test for overall effect: Z = 1.00 (P = 0.32)

#### SLE Study or Subgroup

| SLE Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | Mean Difference IV, Fixed, 95% CI Year |
|-----------------------|------|----|-------|------|----|-------|--------|----------------------------------------|
| Tseng 2011            | 4.9  | 1.1 | 171   | 5.1  | 1.1 | 930   | 57.8%  | -0.10 [-0.28, 0.08] 2011               |
| Morales 2013          | 4.67 | 1.65| 65    | 4.79 | 1.81| 55    | 5.4%   | -0.12 [-0.70, 0.46] 2013              |
| Moghadam 2019         | 4.28 | 1.42| 170   | 4.47 | 1.46| 170   | 19.9%  | -0.18 [-0.49, 0.13] 2019               |
| Dorgham 2020          | 4.7  | 1.3 | 194   | 4.7  | 1   | 98    | 17.1%  | 0.00 [-0.33, 0.33] 2020               |

**Total (95% CI)**

| 500 | 1253 | 100.0% |

Heterogeneity: Chi² = 0.82, df = 3 (P = 0.89); I² = 0%

Test for overall effect: Z = 1.44 (P = 0.15)
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.

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

| Study or Subgroup | SLE Events | Control Events | Total | Weight | Odds Ratio M-H, Random, 95% CI | Year |
|-------------------|------------|----------------|-------|--------|-------------------------------|------|
| Tseng 2011        | 17         | 279            | 26    | 1580   | 33.0%                         | 3.88 [2.08, 7.25] | 2011 |
| Moghadam 2019     | 146        | 170            | 54    | 170    | 33.5%                         | 13.07 [7.42, 22.40] | 2019 |
| Serna-Peña 2021   | 37         | 103            | 53    | 156    | 33.6%                         | 1.09 [0.65, 1.84]  | 2021 |
| **Total (95% CI)**| **552**    | **1906**       | **200**| 133    | **3.80 [0.86, 16.80]**        |      |

Total events: 200
Heterogeneity: Tau^2 = 1.64, Chi^2 = 42.21, df = 2 (P < 0.00001), I^2 = 95%
Test for overall effect: Z = 1.76 (P = 0.08)

| Study or Subgroup | SLE Events | Control Events | Total | Weight | Odds Ratio M-H, Fixed, 95% CI | Year |
|-------------------|------------|----------------|-------|--------|-------------------------------|------|
| Tseng 2011        | 105        | 279            | 643   | 1580   | 78.5%                         | 0.98 [0.68, 1.41] | 2011 |
| Morales 2013      | 2          | 65             | 4     | 55     | 2.7%                          | 0.40 [0.07, 2.30]  | 2013 |
| Moghadam 2019     | 6          | 170            | 1     | 170    | 0.6%                          | 6.19 [0.74, 51.92] | 2019 |
| Serna-Peña 2021   | 38         | 102            | 56    | 156    | 18.1%                         | 1.06 [0.63, 1.78]  | 2021 |
| **Total (95% CI)**| **616**    | **1961**       | **151**| 704    | **0.93 [0.74, 1.17]**         |      |

Total events: 151
Heterogeneity: Chi^2 = 4.25, df = 3 (P = 0.23), I^2 = 31%
Test for overall effect: Z = 0.80 (P = 0.55)

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)
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. Öktem, et al., reported that estrogen may affect the sexual function of women with SLE owing to the involvement of the ovary in autoimmune arthritis [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.

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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.

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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.

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