Prevalence of Sexual Dysfunction in People With Systemic Sclerosis and the Associated Risk Factors: A Systematic Review

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ABSTRACT

Introduction: The association between systemic sclerosis (SSc) and sexual dysfunction was controversial.

Aim: To explore the impacts of SSc on sexual function, the prevalence of sexual dysfunction in patients with SSc and associated risk factors.

Methods: A systematic review of all published studies was performed. Studies exploring the association between SSc and sexual function were retrieved from PubMed, Web of Science, and EBSCO. All retrieved papers were selected according to the inclusion and exclusion criteria.

Main Outcome Measure: The impacts of SSc on sexual function, the prevalence of sexual dysfunction in males and females with SSc and associated risk factors.

Results: A total 12 studies were included in this study. The prevalence of sexual dysfunction in SSc males and SSc females were 76.9−81.4% and 46.7−86.6%, respectively. But the direct impacts of SSc on sexual function were controversial. EULAR SSc activity score ≥3, the number of complications ≥2, and the presence of anticardiolipin antibody and anti U1 ribonucleoprotein antibody in males and resistive index (RI) and the systolic/diastolic (S/D) ratio of clitoral blood in females have potential to be SSc-specific risk factors for sexual dysfunction.

Clinical Implications: Clinicians need to pay more attention to the impacts of SSc on sexual function of patients especially in those with risk factors.

Strengths & Limitations: Systematically explored the prevalence of sexual dysfunction in SSc males and females, and the risk factors of sexual dysfunction for SSc were explored innovatively. However, there were some limitations in included studies prevented exploring the impacts of SSc on sexual function deeply.

Conclusion: Sexual dysfunction may be an important symptom of SSc, many risk factors may be associated with sexual dysfunction in males and females with SSc. **Gao R, Qing P, Sun X, et al. Prevalence of Sexual Dysfunction in People With Systemic Sclerosis and the Associated Risk Factors: A Systematic Review. Sex Med 2021;9:100392**.

Key Words: Systemic Sclerosis; SSc; Sexual Dysfunction; Systematic Review

INTRODUCTION

Sexual function is closely associated with quality of life, and sexual satisfaction affects the family and social lives of men and women. Many diseases have been found to be related to sexual dysfunction and have greatly troubled patients. Unfortunately, clinicians and researchers still tend to pay more attention to the diagnosis and treatment of diseases, of all kinds, while ignoring the improvements of quality-of-life. Autoimmune diseases affect quality of life in many ways, people have begun to pay attention to its impacts on sexual function in recent years.[1−3] For instance, ankylosing spondylitis, atopic dermatitis, and psoriasis have been indicated to be associated with male sexual dysfunction, especially erectile dysfunction (ED), in previous studies.[4−6] Systemic sclerosis (SSc) is a chronic autoimmune disease characterized by

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endothelial dysfunction, microvascular damage and fibrosis of the skin and internal organs.[7] As reported, the prevalence of SSc was varies from 254 cases per million to 296 per million.[8,9] The peak age of SSc onset was 55−69 years and the incidence was 4.7 times higher in women than in men.[10] Previous studies found that SSc might impair the sexual function of both females and males, but there are not enough studies to confirm this conclusion, nor is it clear what the credible risk factors for sexual dysfunction are in patients with SSc.[11−14] The mechanism of SSc on sexual dysfunction in males and females was also unclear due to the limitation of studies published previously. For males, ED seems to be a main manifestation of sexual dysfunction, and it has been regarded to be related to vascular, fibrotic, neurological, and psychological factors[15,16]; for females, sexual dysfunction may be embodied in sexual desire disorders, arousal disorders, lubrication disorders, orgasm disorders, sexual satisfaction disorders, and sexual pain due to physical and mental reasons.[17−20]

What is the prevalence of sexual dysfunction in SSc males and females, respectively? What are the risk factors for sexual dysfunction in SSc males and females? There has been few systematic review or meta-analysis on this topic before. The present study was designed to explore the prevalence of sexual dysfunction in SSc patients, the impacts of SSc on sexual function and the associated risk factors, through a systematic review.

MATERIAL AND METHODS

The present systematic review was performed according to the PRISMA guideline[21] and was approved by ethics committee of West China Second University Hospital. Its time range for retrieval spanned from the establishment of the databases to September 1, 2020. The PubMed (from 1996), Web of Science (from 1900), and EBSCO (from 1975) databases were searched using "systemic sclerosis," "sexual function" and "erectile function," among other keywords. Detailed literature retrieval strategies were shown in Supplementary Table 1. Then, 2 of the authors (R.G. and X.S.) selected the retrieved literature independently according to the inclusion and exclusion criteria developed collectively. The references of included studies were also selected to find papers that had been ignored. If there were any disagreements, discussion with the third author (L.Q.) was used to reach a final result (Figure 1).

Inclusion and Exclusion Criteria

Inclusion criteria: (1) study types include cohort studies, case-control studies or cross-sectional; (2) studied explored the association between SSc and sexual dysfunction; (3) patients with SSc was diagnosed by precise diagnostic criteria; (4) sexual function was assessed by a validated tool or questionnaire, which was confirmed by published literature; (5) outcomes contain the prevalence of sexual dysfunction in SSc patients and other associated risk factors.

Exclusion criteria: (1) patients were diagnosed with other accompanying diseases; (2) the results are inconsistent with the purpose of this study; (3) patients in which drug intervention was administered; (4) data of outcomes were not reported.

Data Extraction

Two authors (R.G. and P.Q.) extracted information from the included studies independently according to a standardized information collection form designed in advance by all the author. The information extracted included first authors, year of publication, study type, patient genders, outcome indicators related to sexual function, results and conclusions. If there was any disagreement regarding information extraction, the third author (L.Q.) would discuss with the 2 authors to reach a final conclusion.

RESULTS

The flow of literature research and inclusion was shown in Figure 1. Computer retrieval from online databases was performed and searched 58 literature from PubMed, 240 from Web of Science, and 48 from EBSCO. A total of 270 literature was selected after excluding duplicates, and 12 studies (3 related to males and 9 related to females) were ultimately included in this present systematic review. Eleven of 12 studies explored the risk factors of sexual dysfunction in patients with SSc.

Male Sexual Dysfunction

Three studies explored the prevalence of sexual dysfunction in males with SSc[15,22,23] and 2 explored the associated risk factors,[15,22] all of them focused on ED. The 5-Item International Index for Erectile Function (IIEF-5) was used to investigate the degree of male ED, where lower scores represent poor sexual function and an IIEF-5 score ≤7 is regarded as severe ED.[24]

The Prevalence of Sexual Dysfunction in SSc Males and the Impacts of SSc on Male Sexual Function. According to the included studies, the prevalence of sexual dysfunction in SSc males was varies from 76.9% to 81.4% (Table 1). Keck et al investigated 78 men with SSc, and 60 of these 78 Men with SSc were diagnosed with ED (22 mild; 19 mild to moderate; 8 moderate; 11 severe).[22] Hong et al explored the ED risk in men with SSc compared to rheumatoid arthritis (RA) patients matched for demographic characteristics; 81% of the men in the SSc group and 48% in the RA group had ED, and there was a significant statistical difference between the 2 groups.[23] Foocharoen et al conducted a prospective study of the multinational EULAR Scleroderma Trial and Research database by amending its electronic data-entry system, and the results indicated that only 23 of 130 patients with SSc (17.7%) had a normal IIEF-5 score and that 30.8%, 10.8%, 20.0%, and 19.2% of all patients had severe, moderate, mild to moderate, and mild ED, respectively.[15] Although there was considerable heterogeneity between the included studies, this limited evidence indicated that ED may be an important symptom in men with SSc. However, the impacts

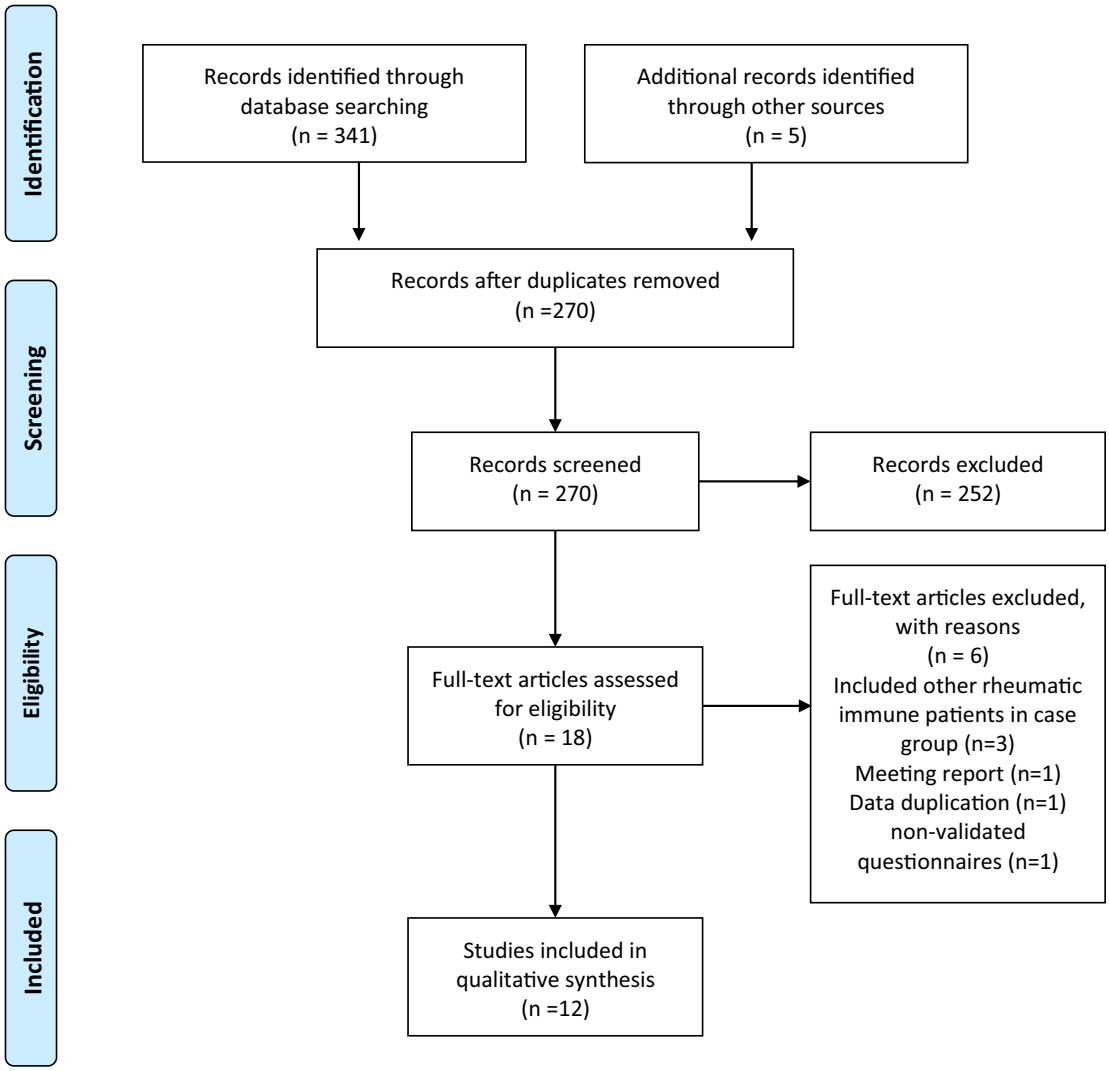

Figure 1. Flow of literature research and inclusion in this study.

of SSc itself on sexual function were not clear because there were no healthy males as control groups in included studies. It's worth to declare that two studies are based on the same database,[15,22] so the patients included in these 2 studies may be duplicate, which may overstate our results. These results must be interpreted with caution.

The Associated Risk Factors. Keck et al found that age was potential risk factor of ED in SSc males (P = 0.002), but did not found the association of ED with nailfold patterns, digital ulcers, pulmonary arterial hypertension or scleroderma patterns in SSc males.[22] Foocharoen et al explored the risk factors for ED in patients with SSc based on lifestyle, comorbidities, demographics, and disease characteristics. According to the results, alcohol consumption (>2 units/day), European Alliance of Associations for Rheumatology (EULAR) SSc activity score ≥3, the number of complications ≥2 and some antibodies were potential risk factors for patients with SSc developing ED, as explored by the included studies. Complications mentioned contain lung complications (forced vital capacity < 80%, systolic pulmonary arterial pressure > 40 mm Hg), central nervous system problems, prostatic disease, muscle atrophy, and renal crisis. The associated antibodies contain anticardiolipin antibody (ACA) and anti U1 ribonucleoprotein antibody (U1 RNP). The number of comorbidities ≥2 was also potential risk factor of ED in SSc males.[15] Potential risk factor(s) of ED in SSc males among included studies were shown in Table 1.

Female Sexual Dysfunction

Six studies explored the prevalence of sexual dysfunction in SSc females, 5 studies[25–29] explored the impacts of SSc on female sexual function and all studies explored the associated risk factor(s). Eight studies evaluated female sexual function via the Female Sexual Functioning Index (FSFI),[25,26,28–32] and one used the Illness Scale-Self-Report (PAIS-SR).[33]

Table 1. Information of studies about the association between SSc and male sexual dysfunction

Author	Year	Study type	No. of study population		Criteria of sexual dysfunction	Prevalence of sexual dysfunction in SSc males (%)	Potential risk factor(s)	
			SSc patients	Healthy controls			Significant	Nonsignificant
Keck et al	2014	Cross-sectional study	78	—	IIEF-5 score < 22	76.9	Age	Disease classification, nailfold capillary abnormalities, digital ulcers, pulmonary arterial hypertension
Hong et al	2004	Case-control study	43	—	IIEF-5 score < 22	81.4	No*	No*
Foocharoen et al	2012	Prospective cohort study	130	—	IIEF-5 score < 22	80.8	Alcohol consumption, number of comorbidities, ACA-positive, UI RNP-positive, EULAR SSc activity score ≥ 3	Diabetes, depression, hypertension, hypercholesterolemia, antinuclear antibodies

ACA = anticardiolipin antibody; EULAR = European Alliance of Associations for Rheumatology; IIEF-5 = 5-Item International Index for Erectile Function; SSc = systemic sclerosis; UI RNP = anti UI ribonucleoprotein antibody.
*No potential risk factor of sexual dysfunction among SSc males was explored in this study.

The Prevalence of Sexual Dysfunction in SSc Females and the Impacts of SSc on Female Sexual Dysfunction

According to the included studies, the prevalence of sexual dysfunction in SSc females was varies from 46.7% to 86.6% (Table 2). However, the diagnostic criteria of sexual dysfunction were of difference in different studies, so this point must be interpreted with caution. The impacts of SSc itself on sexual function after adjusting for possible confounding factors were also different among included studies. Ucar et al showed that total FSFI scores in SSc females was 15.27 ± 7.2 and in control group was 25.63 ± 7.86, there was significant statistical difference (P = 0.0001)[25]; Schouffoer et al showed that total FSFI score and the subscale scores for lubrication, orgasm, arousal, and pain were significantly lower in patients with SSc ($P < 0.05$)[26]; Levis et al indicated that patients with SSc had lower sexual activity and higher rates of sexual dysfunction than healthy women, after adjusting for age, marital status and education level (P = 0.012 and $P < 0.001$)[27]; Gigante et al found that there was significant statistical difference in total FSFI scores between the 2 groups (P = 0.026), too.[28] However, Maddali et al showed that compared to controls, patients with SSc had a lower FSFI desire subscale score (P = 0.035), but there were no significant differences in total FSFI score and all the other subscale scores (including arousal, lubrication, orgasm, satisfaction, and pain) between women with SSc and controls.[29] The differences among the results of the included studies may be due to the small sample sizes and limited research types of each study.

The Associated Risk Factors. Disease characteristics (long duration and dcSSc), high levels of marital dissatisfaction, psychological scales (PDSBE, HADS-Depression, SF-36, CHFDS, WHOQOL-BREF-Psychological health domain) and clitoral blood flow (high resistive index and systolic/diastolic ratio) were potentially related to sexual dysfunction in women with SSc. For disease characteristics, 2 studies indicated that long duration of disease was potential risk factor of SSc females developing low sexual function scores,[26,32] and one study showed that females with diffused cutaneous SSc (dcSSc) were more likely to developing low sexual function scores.[33] It is worth to notice that the above correlations were not found in other 4 studies.[25,26,28,31] Two studies[26,27] indicated that low marital satisfaction was a significant risk factor of sexual dysfunction in SSc females. Psychological health was also an important associated factor of sexual dysfunction in women with SSc, and it was investigated in 4 studies.[26,29,31,32] Lower scores for social functioning (SF), emotional role difficulties (RE) and mental health (MH) in the MOS item short form health survey (SF-36) were significant factors.[31] Clitoral blood flow were also widely discussed as potential risk factors of sexual dysfunction in women with SSc. One study indicated that the resistive index (RI) and systolic/diastolic (S/D) ratio of clitoral blood are significant risk factors.[30] The potential associated factors of sexual function in SSc females were shown in Table 2.

Table 2. Information of studies about the association between SSc and female sexual dysfunction

Author	Year	Study type	No. of study population		Criteria of sexual dysfunction	Prevalence of sexual dysfunction in SSc females (%)	Potential risk factor(s)	
			SSc patients	Healthy controls			Significant	Nonsignificant
Ucar et al	2018	Case-control study	30	30	Total FSFI score < 22.7	86.6	No	Disease duration, lung involvement
Schouffoer et al	2009	Case-control study	37	37	Total FSFI score < 26.55	70.3	High levels of marital dissatisfaction	Disease classification (lc SSc or dcSSc)
Rosato et al	2013	Case-control study	22	20	FSFI	—	RI and S/D ratio of clitoral blood flow	PSV, EDV and PI of clitoral blood
Maddali et al	2013	Case-control study	46	46	Total FSFI score < 26.55	67.4	PDSBE, HADS-Depression, SF-36, CHFDS	Some other psychological scales
Levis et al	2012	Case-control study	730	180	Total FSFI score < 22.5	61.1	High levels of marital dissatisfaction	No
Knafo et al	2009	Cross-sectional study	138	—	PAIS-SR	—	Disease classification (dcSSc)	No
Impens et al	2009	Cross-sectional study	101	—	FSFI	—	SF-36 score	Disease duration, disease classification (lc SSc or dcSSc)
Gigante et al	2019	Case-control study	15	10	Total FSFI score < 19	46.7	RI and S/D ratio of clitoral blood	Disease duration, serum levels of VEGF
Frikha et al	2014	Cross-sectional study	10	—	Total FSFI score < 26	80.0	Long disease duration, WHOQOL-BREF-Psychological health domain, HADS-Depression	Marriage duration

CHFDS = Cochin Hand Functional Disability Scale; dcSSc = diffuse systemic sclerosis; EDV = end diastolic velocity; FSFI = Female Sexual Functioning Index; HADS = Hospital anxiety and depression scale; lcSSc = limited systemic sclerosis; PAIS-SR = Illness Scale-Self-Report; PDSBE = Disability Sexual and Body Esteem Scale; PI = pulsatile index; PSV = peak systolic velocity; RI = resistive index; S/D = systolic/diastolic; SF-36 = Medical Outcomes Study Short Form-36 health survey; SSc = systemic sclerosis; VEGF = vascular endothelial growth factor; WHOQOL-BREF = World Health Organization Quality of Life.

DISCUSSION

Sexual dysfunction is a common disease that troubles 40% of women in the United States, and it is reported that 150 million men worldwide are affected by ED.[34,35] Due to a lack of international consensus on sexual dysfunction, however, the incidences or prevalence reported in different studies are different, and the epidemiological characteristics are unclear.[36] Many studies think that sexual dysfunction can be classified into 4 categories: (1) sexual desire disorders, (2) sexual arousal disorders (sexual arousal disorders in females and male ED), (3) orgasmic disorders (inhibited male or female orgasm and premature ejaculation in males), and (4) sexual pain disorders (dyspareunia and vaginismus).[37,38] SSc is an autoimmune disease that is characterized by fibrosis of the skin and internal organs, as well as vasculopathy, and it has a high morbidity and mortality.[39] In recent years, with the development of treatments, the prognosis for patients with SSc has been greatly improved, and their quality of life has become a widely studied issue. But the impacts of SSc on sexual function are often ignored. Some studies report that patients with SSc might suffer sexual dysfunction in higher proportions, but there is little persuasive evidence on this issue, although such evidence would be significant for improving the quality of life of patients with SSc.[11,15,22,25,26,29,40]

A systematic review was performed in this study to explore the impacts of SSc on sexual function and the prevalence of sexual dysfunction in patients with SSc. For males with SSc, ED is the most studied symptom. Based on these studies, we can conclude that ED is an important symptom in men with SSc, but case-control or cohort studies with larger samples are still needed to verify whether or not SSc itself is independently predictive of the sexual dysfunction. For women with SSc, the manifestation of sexual dysfunction is complex, and sexual function scales, such as the FSFI, were thus selected to represent outcomes in the included studies. Four studies[25,26,29] indicated that women with SSc have lower total FSFI scores than healthy women, but one embodied that only FSFI desire subscale score was statistically different between women with SSc and controls,[29] only one study[28] showed that there was no statistical differences between the FSFI scores of women with SSc and healthy women. The inconsistency of these results may be due to the small sample sizes and the difference of criteria of impaired sexual function among included studies. The impacts of SSc on sexual function in females require further study, as the present evidence is insufficient.

The more significant objective of this study was to systematically review the risk factors for sexual dysfunction in patients with SSc to serve as a reference throughout the prevention of sexual dysfunction in patients with SSc. For men with SSc, it seems that age, alcohol consumption (>2 units/day), EULAR SSc activity score ≥3, the number of complications ≥2 and some antibodies (ACA, U1 RNP) are potential risk factors for sexual dysfunction. According to American Urological Association's guidelines, age, alcohol consumption, smoking, diabetes mellitus, hypertension, dyslipidemia, depression, obesity, and a sedentary lifestyle are well-recognized, independent risk factors for ED.[41] Thus, only EULAR SSc activity score ≥3, the number of complications ≥2 and some antibodies (ACA, U1 RNP) have potential to be specific risk factors for ED in men with SSc. More high-quality studies with larger sample sizes are needed, however, to confirm this opinion.

For women with SSc, marital dissatisfaction, resistive index (RI) and the systolic/diastolic (S/D) ratio of clitoral blood seem to be associated factors based on the present studies; however, opinions on other factors such as the duration of disease and the pattern of disease are inconsistent in different studies. In addition, vaginal and skin pain in patients with SSc may be one reason for sexual dysfunction.[42] Clinical features of SSc such as Raynaud's phenomenon, joint contractures, gastrointestinal manifestations, and ulcers also contribute to pain and physical discomfort, which also affects sexual satisfaction. Other symptoms, such as stiffness, reduced capacity for exercise and muscle weakness may disturb the sex lives of patients. All of these factors may impair female sexual functions to some degree.[43] It is worth to noting that sexual dysfunction in women is closely related to psychological health, and depression seems to be a convincing risk factor of sexual dysfunction in women with SSc. Lower scores of social functioning (SF), emotional role difficulties (RE) and mental health (MH) in SF-36 are also possible risk factors, according to one cross-sectional study.[31] According to the guidelines on female sexual dysfunction of The American College of Obstetricians and Gynecologists, female sexual dysfunction consists of various conditions characterized by desire, arousal, orgasm or pain, and many factors such as anxiety disorder, diabetes, marital dissatisfaction, depression, female genital mutilation, and genitourinary syndrome throughout menopause are common risks of female sexual dysfunction.[44] Thus, only resistive index (RI) and the systolic/diastolic (S/D) ratio of clitoral blood have potential to be specific risk factors of sexual dysfunction in SSc females.

The differences in risk factors of patients with SSc between men and women may be related to the different formation mechanisms of sexual dysfunction. Female sexual function can be easily disturbed by states of psychological health, and many psychological disorders, such as depression, anxiety and lower body esteem, have the potential to affect sexual function in different ways. In addition, SSc may cause physiological changes in the reproductive system and other systems, manifested as vaginal dryness, pain and other forms of discomfort, all of which can affect sexual experience and thus affect the sex lives of patients with SSc. Sexual arousal functions in males (ED) seem to be less susceptible to psychological health than those of women, as they are more related to physiological and pathological changes caused by the disease. Of course, the mechanisms by which SSc affect sexual function are complex, and this opinion must be validated by future studies.

Although this study reviewed the results of these present studies and drew a comprehensive conclusion, the presence of certain limitations means that these results still need to be carefully interpreted. First, there are still no clear criteria for the classification and diagnosis of sexual dysfunction, the considerable heterogeneity among the included studies decreases the reliability of this systematic review. Second, the direct impacts of SSc on sexual function after adjusting for other factors were little explored in previous studies, so we cannot understand the impacts of SSc on sexual function systematically. We cannot expound whether the effects of SSc on sexual function are direct or are realized through other symptoms. Finally, because the causes and clinical manifestations of sexual dysfunction are complex, great differences exist in the potential risk factors explored by the studies included in this review. This study, however, can also serve as inspiration for clinicians. On the one hand, paying greater attention to the sexual function of patients with SSc is meaningful because sexual function impairs are important symptoms of SSc. On the other hand, clinicians can identify patients with impaired sexual function as early as possible by these risk factors and initiate early intervention. Studies with large samples are necessary to explore the direct impacts of SSc on sexual function and to investigate more exact risk factors in the future.

CONCLUSION

Based on available evidence, the prevalence of sexual dysfunction in SSc males and SSc females were 76.9−81.4% and 46.7−86.6%. Sexual dysfunction appears to be an important and noteworthy symptom in patients with SSc. Except for the common risk factors, EULAR SSc activity score ≥3, the number of complications ≥2 and some antibodies (ACA, U1 RNP) have potential to be specific risk factors for sexual dysfunction in SSc males; and resistive index (RI) and the systolic/diastolic (S/D) ratio of clitoral blood have potential to be specific risk factors of sexual dysfunction in SSc females. However, there were some limitations in included studies prevented exploring the impacts of SSc on sexual function deeply.

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STATEMENT OF AUTHORSHIP

Rui Gao and Yihong Yang: Conceptualization; Rui Gao, Pingying Qing, and Xiaochi Sun: Methodology; Xun Zeng, Xiao Hu, and Sirui Zhang: Investigation; Xiaochi Sun and Xun Zeng: Data Curation; Rui Gao and Pingying Qing: Writing − Original Draft; Rui Gao and Yihong Yang: Writing − Review & Editing; Xun Zeng and Lang Qin: Funding Acquisition.

REFERENCES

1. Araujo DB, Borba EF, Abdo CH, et al. Sexual function in rheumatic diseases. **Acta Reumatol Port 2010;35:16–23.**
2. Dorner TE, Berner C, Haider S, et al. Sexual health in patients with rheumatoid arthritis and the association between physical fitness and sexual function: a cross-sectional study. **Rheumatol Int 2018;38:1103–1114.**
3. van Berlo WT, van de Wiel HB, Taal E, et al. Sexual functioning of people with rheumatoid arthritis: a multicenter study. **Clin Rheumatol 2007;26:30–38.**
4. Fan D, Liu L, Ding N, et al. Male sexual dysfunction and ankylosing spondylitis: a systematic review and meta-analysis. **J Rheumatol 2015;42:252–257.**
5. Egeberg A, Hansen PR, Gislason GH, et al. Erectile dysfunction in male adults with atopic dermatitis and psoriasis. **J Sex Med 2017;14:380–386.**
6. Chung SD, Keller JJ, Lin HC. Association of erectile dysfunction with atopic dermatitis: a population-based case-control study. **J Sex Med 2012;9:679–685.**
7. Casale R, Buonocore M, Matucci-Cerinic M. Systemic sclerosis (scleroderma): an integrated challenge in rehabilitation. **Arch Phys Med Rehabil 1997;78:767–773.**
8. Rosa JE, Soriano ER, Narvaez-Ponce L, et al. Incidence and prevalence of systemic sclerosis in a healthcare plan in Buenos Aires. **J Clin Rheumatol 2011;17:59–63.**
9. Monaco ALo, Bruschi M, Corte RLa, et al. Epidemiology of systemic sclerosis in a district of northern Italy. **Clin Exp Rheumatol 2011;29:S10–S14.**
10. Royle JG, Lanyon PC, Grainge MJ, et al. The incidence, prevalence, and survival of systemic sclerosis in the UK Clinical Practice Research Datalink. **Clin Rheumatol 2018;37:2103–2111.**
11. Hermankova B, Spiritovic M, Smucrova H, et al. Sexual health in women and men with systemic sclerosis: a cross-sectional study. **Ann Rheum Dis 2020;79:1103–1104.**
12. Hermankova B, Spiritovic M, Smucrova H, et al. Female sexual dysfunction in patients with systemic sclerosis. **Ann Rheum Dis 2018;77:1098–1099.**
13. Hermankova B, Spiritovic M, Smuerova H, et al. Sexual dysfunction in systemic sclerosis female patients. **Arthr Rheumatol 2018;70:1726.**

14. Jaeger VK, Walker UA. Erectile dysfunction in systemic sclerosis. **Curr Rheumatol Rep 2016;18:49.**
15. Foocharoen C, Tyndall A, Hachulla E, et al. Erectile dysfunction is frequent in systemic sclerosis and associated with severe disease: a study of the EULAR Scleroderma Trial and Research group. **Arthr Res Ther 2012;14:R37.**
16. Gigante A, Navarini L, Margiotta D, et al. Erectile dysfunction: Imbalance between pro-angiogenic and anti-angiogenic factors in systemic sclerosis. **Eur J Intern Med 2018;53:e17–ee8.**
17. Coutinho M, Ruela I, Santiago T, et al. Sexual dysfunction is associated with anxiety and higher body mass index in women with systemic sclerosis. **Clin Exp Rheumatol 2014;32 S50-S.**
18. Frikha F, Masmoudi J, Bahloul Z. Sexual functioning and quality of life among married women with systemic sclerosis. **Ann Rheum Dis 2014;73:1010–1011.**
19. Guerriere JA, Rosen RC, Seibold JR. Quality of life and sexual function in women with systemic sclerosis (SSc). **Arthr Rheum 2001;44 S328-S.**
20. Hermankova B, Spiritovic M, Storkanova H, et al. Sexual Health in 60 Female Patients with Systemic Sclerosis. **Arthr Rheumatol 2019;71:1638.**
21. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. **Bmj 2009;339:b2700.**
22. Keck AD, Foocharoen C, Rosato E, et al. Nailfold capillary abnormalities in erectile dysfunction of systemic sclerosis: a EUSTAR group analysis. **Rheumatology 2014;53:639–643.**
23. Hong P, Pope JE, Ouimet JM, et al. Erectile dysfunction associated with scleroderma: a case-control study of men with scleroderma and rheumatoid arthritis. **J Rheumatol 2004;31: 508–513.**
24. Rosen RC, Riley A, Wagner G, et al. The international index of erectile function (IIEF): a multidimensional scale for assessment of erectile dysfunction. **Urology 1997;49:822–830.**
25. Uçar İ, Turgay B, Küçükşahin O, et al. Sexual dysfunction in patients with systemic sclerosis. **Turk J Med Sci 2018;48: 1104–1108.**
26. Schouffoer AA, van der Marel J, ter Kuile MM, et al. Impaired sexual function in women with systemic sclerosis: a cross-sectional study. **Arthr Rheum Arthr Care Res 2009;61:1601–1608.**
27. Levis B, Burri A, Hudson M, et al. Sexual activity and impairment in women with systemic sclerosis compared to women from a general population sample. **Plos One 2012;7: e52129.**
28. Gigante A, Navarini L, Margiotta D, et al. Female sexual dysfunction in systemic sclerosis: the role of endothelial growth factor and endostatin. **J Scler Relat Disord 2019;4:71–76.**
29. Maddali Bongi S, Del Rosso A, Mikhaylova S, et al. Sexual function in Italian women with systemic sclerosis is affected by disease-related and psychological concerns. **J Rheumatol 2013;40:1697–1705.**
30. Rosato E, Gigante A, Barbano B, et al. Clitoral blood flow in systemic sclerosis women: correlation with disease clinical variables and female sexual dysfunction. **Rheumatology 2013;52:2238–2242.**
31. Impens AJ, Rothman J, Schiopu E, et al. Sexual activity and functioning in female scleroderma patients. **Clin Exp Rheumatol 2009;27:38–43.**
32. Frikha F, Masmoudi J, Saidi N, et al. Sexual dysfunction in married women with Systemic Sclerosis. **Pan African Med J 2014;17:82.**
33. Knafo R, Thombs BD, Jewett L, et al. Not talking about sex: a systematic comparison of sexual impairment in women with systemic sclerosis and other chronic disease samples. **Rheumatology 2009;48:1300–1303.**
34. McKinlay JB. The worldwide prevalence and epidemiology of erectile dysfunction. **Int J Impot Res 2000;12(suppl 4) S6-s11.**
35. Clayton AH, Valladares Juarez EM. Female sexual dysfunction. **Med Clin North Am 2019;103:681–698.**
36. Halvorsen JG, Metz ME. Sexual dysfunction, Part I: classification, etiology, and pathogenesis. **J Am Board Fam Pract 1992;5:51–61.**
37. Lewis RW, Fugl-Meyer KS, Corona G, et al. Definitions/epidemiology/risk factors for sexual dysfunction. **J Sex Med 2010;7:1598–1607.**
38. McCabe MP, Sharlip ID, Lewis R, et al. Risk factors for sexual dysfunction among women and men: a consensus statement from the fourth international consultation on sexual medicine 2015. **J Sex Med 2016;13:153–167.**
39. Denton CP, Khanna D. Systemic sclerosis. **Lancet 2017;390: 1685–1699.**
40. Schmalzing M, Nau LF, Gernert M, et al. Sexual function in German women with systemic sclerosis compared to women with systemic lupus erythematosus and evaluation of a screening test. **Clin Exp Rheumatol 2020;38(suppl 125):59–64.**
41. Burnett AL, Nehra A, Breau RH, et al. Erectile dysfunction: AUA guideline. **J Urol 2018;200:633–641.**
42. Rosato E, Rossi C, Molinaro I, et al. Sexual distress, sexual dysfunction and relationship quality in women with systemic sclerosis: correlation with clinical variables. **Int J Immunopathol Pharmacol 2014;27:279–285.**
43. Knafo R, Haythornthwaite JA, Heinberg L, et al. The association of body image dissatisfaction and pain with reduced sexual function in women with systemic sclerosis. **Rheumatology 2011;50:1125–1130.**
44. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Gynecology. Female sexual dysfunction: ACOG practice bulletin clinical management guidelines for obstetrician-gynecologists, number 213. **Obstet Gynecol 2019;134:e1–e18.**