Erectile function and connective tissue diseases. Prevalence of erectile dysfunction in German men with systemic sclerosis compared to other connective tissue diseases and healthy subjects

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ABSTRACT

Objective. *Women are more frequently affected by connective tissue diseases like systemic sclerosis (SSc). Therefore, few studies exist on male-specific complaints. This study aimed to investigate the prevalence and associated factors of erectile dysfunction (ED) in SSc compared with other connective tissue diseases (CTD) and healthy controls.*

Methods. *64 patients were analysed and compared with 123 age-matched HC. The 15–item International Index for Erectile Function (IIEF) questionnaire was used to assess sexual function. The prevalence of depression was quantified by using the validated Beck Depression Inventory (BDI).*

Results. *Mean age was 52.3 years (SD 10.75) for SSc, 52.9 years (SD 11.01) for patients with other CTD and 52.6 (SD 12.37) for HC. Mean IIEF-15 score was 13.6 for SSc, 11.7 for other CTD and 23.6 for HC. ED was significantly more frequent in patients with SSc (55.0%) and other CTD (54.4%) than in HC (12.7%) ($p<0.001$) and correlated with diseases severity. The mean BDI score was 10.8 for SSc/CTD and 5.4 for HC ($p<0.001$). With 36.6%, SSc patients suffered more often from a depression than patients with other CTD (17.4%) and HC (6.3%). We found a significant correlation between the IIEF-15 and depression classified by BDI ($r= -0.527$; $p<0.001$).*

Conclusion. *This is the first study to show increased prevalence of ED, especially severe ED, in men with SSc compared to other CTD and age-matched HC. Physicians should be aware of this influence on sexual health and its correlation to depression and disease severity.*

Introduction

Systemic sclerosis (SSc) is a heterogeneous autoimmune disease with various organ manifestations and impact on different areas of daily life. Although the pathogenesis is not fully understood, SSc is dominated by a complex interrelation between vascular, immunologic and fibrotic processes (1). The disease affects the skin as well as many internal organs, such as the gastrointestinal tract, the cardiopulmonary system, the musculoskeletal system and the kidney function (2). Patients with SSc can be subdivided into two main categories, limited and diffuse cutaneous (dc) (3). Patients with dcSSc more often suffer from severe organ involvement and early progression (4). The incidence and prevalence of SSc range from 3.7 and 31 per million in the UK to 43 and 341 per million in Italy. SSc predominates in women with a female to male ratio of 9.7 : 1 (5), but male patients often have a more aggressive course of disease (6). Erectile dysfunction (ED) is the inability to attain and/or maintain an erection sufficient to perform sexual intercourse. Goldstein *et al*. reports an overall prevalence in German adults of 44.9% and an overall average age of 56 years (7). The largest European multicentre population-based study of ageing men reported a prevalence of ED up to 64% depending on different age subgroups with an average of 30% (8). Nevertheless several large multinational studies have estimated the prevalence of ED in young men to be as high as 30% (9). Beside the main causes of vasculopathy and arteriosclerosis, psychogenic, neurogenic, endocrine and urological causes have been linked to the development of ED. However,

pathogenesis is often a combination of physical and psychological factors and both are closely associated with increasing age (8, 10).

Depression is a known comorbidity in patients with chronic diseases such as SSc. Patients with SSc frequently meet criteria for psychiatric disorders (11, 12). The lifetime prevalence for a depression in healthy people is 13.3% (9% for men, 17.1% for women). The mean age at onset is 30.4 years (13). Recent studies discussed an increased prevalence of ED in patients with SSc and found an association between SSc and depression (14), whereas other groups were unable to compare the increased prevalence to other connective tissue diseases (CTD) and healthy controls.

Thus, the aim of this study was to examine the prevalence of ED and sexual dysfunction (SDF) as well as depression with validated questionnaires in patients with SSc and compare the results to patients with other CTD and HC.

Methods

Patients were recruited from the rheumatology outpatient clinic at the University Hospital Tuebingen, Germany. The study was approved by the independent research ethics committee of the University of Tuebingen (313/2018BO2). All patients and HC gave written informed consent. All SSc patients fulfilled the criteria for SSc according to the American College of Rheumatology/European League Against Rheumatism (15). The group of other CTD includes patients with systemic lupus erythematosus, myositis, Sjögren's syndrome and mixed connective tissue diseases. All patients with other CTD fulfilled the relevant criteria for classification and were diagnosed by experienced rheumatologists (16, 17). Participants under the age of 18 or with diabetes are not included. Additionally, patients who suffered from a tumour disease of the lower urinary tract, especially of the prostate, as well as patients who received pelvic radiotherapy were excluded. All patients filled out a questionnaire on demographic information, lifestyle, sexual activity, sexual complaints and changes since onset of the disease. Additionally, we used clinical data from the medical record for clinical manifestations and medication.

The 15–item International Index for Erectile Function (IIEF-15) questionnaire, an index of ED severity, with an overall cut-off <14 for ED, was used to assess the sexual function. It has high retest reliability and is validated in several languages (18). The IIEF-15 subdivides five domains of male sexual function (erectile function, orgasmic function, sexual desire, intercourse satisfaction and overall satisfaction). Each domain provides a numerical score that is classified into categories of severity. The cut-off for assessing the severity of erectile function is 26-30 for "no ED", 22-25 for "mild ED", 17-21 for "mild to moderate ED", 11-16 for "moderate ED" and 1-10 for "severe ED" (18, 19). The prevalence of depression was quantified by using the Beck Depression Inventory (BDI) (20, 21). The cut-off for assessing the severity of depression are 0-13 points for no depression, 14-19 for mild depression,

Table I. Baseline characteristics of study patients.
Presentation of patient demographics such as age, disease duration and disease characteristics. Data are represented as absolute number of patients and mean for age, age at onset and disease duration (significant differences in bold).

	Patients with SSc, n	Patients with other CTD, n	*p*-value
Age, mean years (SD)	52.3 (10.8)	52.9 (11.0)	0.822
Age at onset, mean years (SD)	45.8 (10.7)	40.8 (14.8)	0.122
Disease duration, mean years (SD)	6.6 (5.4)	10.9 (9.8)	**0.015**
Alcohol consumer	25	17	0.296
History of smoking	28	14	0.459
Arthralgia	20	12	0.924
Arthritis	5	13	**0.001**
Raynaud's phenomenon	36	5	**0.001**
mRSS (SD)	9.7 (9.5)	6 (n=1)	
Sclerodactyly	28	1	**0.001**
Digital ulcers	24	2	**0.001**
Telangiectasia	22	0	**0.001**
Gastrointestinal manifestations	23	5	**0.008**
Pulmonary manifestations (ILD or PAH)	29	8	**0.005**
Cardiac manifestations	14	6	0.504
Renal manifestations	0	6	**0.001**
Total	41	23	

SSc: systemic sclerosis; CTD: connective tissue diseases; mRSS: modified Rodnan Skin Score; ILD: interstitial lung disease; PAH: pulmonary arterial hypertension.

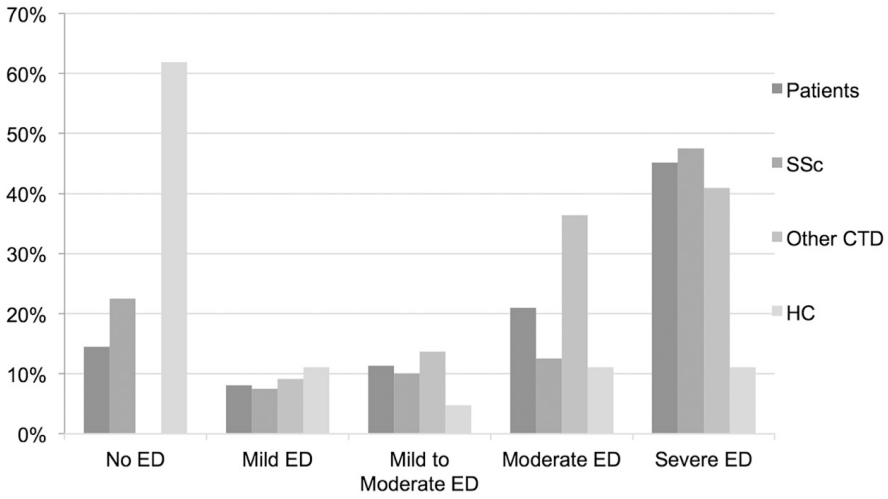

Fig. 1. Prevalence and severity of erectile dysfunction (ED). Comparison between all patients (systemic sclerosis (SSc) and other connective tissue diseases (CTD)), patients' subgroups and age-matched healthy controls showing that SSc patients suffer significantly more often from ED, especially from severe ED, than patients with other CTD and HC.

20-28 for moderate depression and 29-63 for severe depression (22).

For the statistical analysis, SPSS Statistics (v. 25.0.0.1, IBM, Armonk, NY, USA) was used and the results are presented as mean values and standard deviation for metric variables and percentages for categorical variables. Mean values of metric variables were analysed by using t-test for independent samples. To compare categorical variables, Pearson's Chi-squared test was used. With frequencies of five or lower Fisher's exact test was applied. The Pearson correlation coefficient was used for correlations. *p*-values <0.05 were considered statistically significant.

Results

We analysed data from 64 male patients (41 SSc and 23 other CTD) and compared them to 123 age-matched HC. Mean age was 52.3 years (SD 10.75) for SSc, 52.9 years (SD 11.01) for patients with other CTD and 52.6 (SD 12.37) for HC. Mean disease duration was 6.6 years (SD 5.4) for SSc and 10.9 years for other CTD (SD 9.8). In the disease group, 87.8% (n=36) of the patients with SSc and 56.5% (n=13) of the patients with other CTD stated that they live in a relationship whereas in HC 95.3% (n=61) were. The mean number of children was 1.2 (SD 1.15) for SSc and 1.0 (SD 1.04) for other CTD, whereas for HC it was 1.6 (SD 1.01). Patient demographics such as age, disease duration and disease characteristics are shown in Table I.

Patients had significantly less sexual intercourse, with 39% of SSc and 34.8% of CTD, compared with HC with 82.8%. Complaints related to disease were named as the most frequent cause. Moreover, 41.5% of patients with SSc and 43.5% with other CTD described a decreased libido and 22.0% of patients with SSc and 21.7% with other CTD changes in self-confidence since the onset of disease. SDF was significantly more frequent in patients, with 42.5% (SSc) and 23.8% (other CTD), compared to HC with 4.7%.

Of the 64 patients with SSc and other CTD only 14.1% (n=9) had a normal IIEF-15 score (≥ 25). Two men had not been engaged in any sexual activity prior to filling out the IIEF-15 questionnaire and could therefore not be attributed. The mean score of all patients with 12.9 (SSc with 13.6 and other CTD with 11.7) was significantly lower than in HC with 23.6 (p<0.001). ED was significantly more frequent in patients with SSc with 55.0% and patients with other CTD with 54.4% than in HC with 12.7% (p<0.001). The largest group of both SSc and other CTD had severe ED as shown in Figure 1.

Severe ED was significantly more prevalent in SSc with 47.5% and other

Table II. Comparison of patients with and without erectile dysfunction (ED). ED is associated with increasing age and disease severity in terms of cutaneous, gastrointestinal or cardiac manifestation. Data are represented as absolute and mean for age and disease duration (significant differences in bold).

	All patients, n			SSc patients, n		
	No ED	ED	*p*-value	No ED	ED	*p*-value
Age, mean years	48.2	55.7	**0.022**	48.5	55.6	**0.049**
Disease duration, mean years	8.8	7.7	0.587	7.0	6.4	0.714
History of smoking	17	23	0.462	11	16	0.309
Alcohol consumer	20	21	0.424	12	12	0.436
IIEF-15 score	54.4	17.2	**<0.001**	59.8	15.8	**<0.001**
Erectile function	22.0	5.5	**<0.001**	24.3	4.8	**<0.001**
Orgasmic function	8.6	3.0	**<0.001**	9.22	2.0	**<0.001**
Sexual desire	7.0	4.7	**<0.001**	7.4	4.9	**0.001**
Intercourse satisfaction	9.3	0.5	**<0.001**	10.7	0.4	**<0.001**
Overall satisfaction	7.5	3.9	**<0.001**	8.2	3.8	**<0.001**
mRSS	5.8	13.8	**0.005**	**4.5**	**13.1**	**0.002**
Digital ulcers	10	15	0.502	9	14	0.385
Raynaud's phenomenon	20	20	0.302	17	18	0.230
Sclerodactyly	11	17	0.399	10	17	0.145
Telangiectasia	5	17	**0.008**	**5**	**17**	**0.002**
Arthritis	6	10	0.475	3	1	0.204
Arthralgia	10	20	0.070	6	13	0.105
Joint involvement	13	23	0.092	7	13	0.204
Gastrointestinal manifestations	7	21	**0.004**	7	16	**0.031**
Pulmonary manifestations (ILD or PAH)	14	21	0.352	10	18	0.071
Cardiac manifestations	5	13	0.079	**2**	**11**	**0.009**
Renal manifestations	1	5	0.140	0	0	
Arterial Hypertension	12	13	0.784	9	7	0.291

SSc: systemic sclerosis; CTD: connective tissue diseases; ED: erectile dysfunction; IIEF: international index of erectile function; mRSS: modified Rodnan Skin Score; ILD: interstitial lung disease; PAH: pulmonary arterial hypertension.

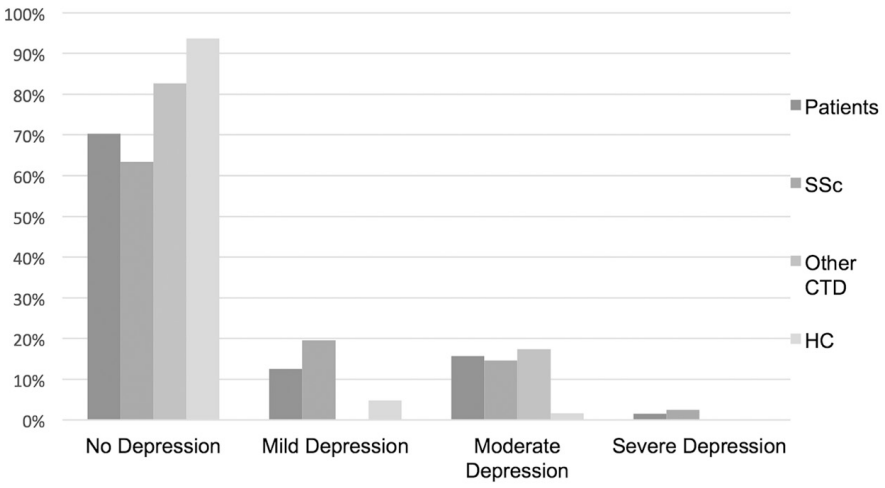

Fig. 2. Prevalence and severity of depression classified by the Beck Depression Inventory. Comparison between patients (systemic sclerosis (SSc) and other connective tissue diseases (CTD)), patients' subgroups and age-matched healthy controls showing that SSc patients were affected more often by a depression than other CTD and healthy controls (HC).

CTD with 40.9% compared with HC with 11.1%. Moreover, we found in 54.8% of all patients a disturbed orgasmic function. Most patients had reduced sexual desire and overall desire, with only 11.5% of all patients who did not find any deviations in sexual desire and 13.1% in overall satisfaction, respectively.

Differences in patients with and without ED are demonstrated in Table II. Patients with ED were significantly older than subjects without ED. The mean disease duration was little longer in patients with ED. The presence of ED was significantly associated with more severe organ involvement in SSc and participants with ED had significant higher modified Rodnan skin scores (mRSS), significantly more telangiectasias, gastrointestinal and cardiac manifestations.

About half of the patients (51.2% with SSc and 52.2% with other CTD) presume themselves to have an ED. However, only 23.4% (19.5% with SSc and 30.4% with other CTD) ever consulted a physician. Despite SDF and ED was more prevalent in patients, 65.6% (61.0% with SSc and 73.9% with other CTD) consider sexuality to be relevant. Even though 42.3% (24.1% with SSc and 56.5% with other CTD) of the patients would like their physicians to ask for sexual function, only 21.9% (19.5% with SSc and 26.1% with other CTD) reported their physicians ever asked them questions regarding their sexual history. Medical treatment or other treatment options like vacuum devices were only used by 20.3%.

The mean BDI score of patients was 10.8 and 5.4 for HC ($p<0.001$). Based on the BDI, several patients had a mild to severe depression (Fig. 2). With 36.6%, SSc patients were more often affected by a depression than patients with other CTD with 17.4% and HC with 6.3%. In addition, we were able to demonstrate a significant correlation in SSc patients between overall score in the IIEF-15 and depression classified by BDI (r= -0.527; $p<0.001$).

Discussion

To the best of our knowledge, our study is the first to compare the prevalence of ED in men with SSc to other CTD and age-matched HC using validated questionnaires. As CTD mainly affect women, there are few studies exist on male-specific complaints. For the first time we were able to demonstrate the significantly higher prevalence of ED and SDF in patients with SSc compared with other CTD and HC. Thus, our study offers new knowledge about ED in SSc patients and other CTD. As already shown in a meta-analysis of comorbidities in ED and depressive illness by Liu *et al*., we could confirm the association for patients with SSc and other CTD (14). Risk factors for developing an ED like ageing, alcohol and smoking habits, diabetes, metabolic syndrome, lower urinary tract symptom and cardiovascular disease are well known in the general population (23). We could not certify a difference for smoking or alcohol consumption between participants with or without ED. Diabetes and metabolic syndrome were not explicitly investigated.

SDF was prevalent in 42.5% and over half of SSc patients (55.0%) suffered from ED. These rates illustrate that SDF and ED – like interstitial lung disease or reflux – are part of the disease characteristics of SSc and other CTD and should therefore be treated as such. Up to now only few comparable data exist with the same measurements. A recent study by Hong *et al*. analysed ED in men with rheumatoid arthritis compared with SSc patients and found a prevalence rate for ED of up to 80% for SSc (24). Foocharoen *et al*. found similar results for SSc men. Both of them only used the IIEF-5, a short version of the IIEF-15, with a higher cut-off for ED. Moreover, both studies did not include an age-matched HC and compared only to literature data (24, 25). Nevertheless, there are aspects we can confirm, especially that SSc patients not only have elevated prevalence for ED, they also have more severe ED compared to CTD and HC. The overall prevalence rates for ED in the German (19.2%) as well as the European general population (30%) are somewhat higher than our results for HC. However, the prevalence of ED in patients with SSc is still considerably higher (8, 26). Our study confirms age as an important risk factor for ED development in SSc patients (25). In addition to ED and SDF in men, another study showed that women with SSc and SLE were also more likely to experience SDF (27).

Furthermore, our study shows for the first time an association between SSc severity in terms of mRSS, telangiectasia, gastrointestinal and cardiac manifestations and ED. The correlation between ED and the disease severity highlights the roll of endothelial dysfunction in the pathophysiology of ED and SSc itself (28). As presented by previous investigations, we can confirm ED seems linked to vascular damage in patients with SSc (29, 30). This study demonstrates the gap existing in the field of sexual function. Patients have the desire to focus more on their sexual health; they would like their physicians to pick this out as a theme.

As already known, patients with chronic diseases more often suffer from comorbid depression (12). Depression was more frequent in SSc patients than patients with CTD and HC. Two other studies confirmed the increased prevalence of depression in SSc men, recently (11, 31). Our findings illustrate that patients with a lower score in the IIEF-15 and thus ED, have higher scores in the BDI and therefore are more likely to have a depression.

Our study has both strengths and limitations. It represents the largest analysis of ED and SDF in men with SSc compared to other CTD and HC. The small number of subjects reflects the low sex-specific disease prevalence of SSc. Moreover, it should be noted that the participants completed the questionnaire on their own, as a result of which comprehension problems remained unexplained. On the other hand, anonymity enabled the questions to be answered as honestly as possible. No urological or psychiatric confirmation for ED and depression were performed. In addition, there could be confounding factors like different pharmacological treatments and comorbidities that may impact on ED. In this study we could not clearly distinguish whether ED triggers depression or contrariwise.

In summary, this study demonstrates that ED and SDF are very common in men with SSc and other CTD. They not only suffer more often from ED compared with HC, but also more likely from severe ED. The close correlation between ED and depression highlights the importance of care. Healthcare quality can only be guaranteed with raised awareness and consideration of sexual health. There is a need for studies with a focus on treatment options for patients with SSc/CTD and associated SDF and or ED.

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