Frequency and Analysis of Factors Closely Associated with the Development of Depressive Symptoms in Patients with Scleroderma

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ABSTRACT. ***Objective.*** To examine the frequency of depressive symptoms and also to identify factors closely associated with their development in patients with scleroderma (systemic sclerosis, SSc).

Methods. We evaluated 50 patients with SSc for factors associated with depressive symptoms using the following established scales: the Beck Depression Inventory (BDI); the Rheumatology Attitude Index for measuring helplessness; the Sense of Coherence (SOC) scale (a measure of an individual's resilience in the face of stress and capacity to cope with it); the modified Health Assessment Questionnaire for physical disability, working, and social function; support domains of Arthritis Impact Measurement Scales version 2; and a visual analog pain scale. In addition, disease severity of SSc, including skin thickness and internal organ involvement, was also examined in each patient. Multiple regression analysis was used to determine which factors correlated with depressive symptoms.

Results. Depressive symptoms ranging from mild to severe state were seen in 46% of the patients. Total BDI scores were significantly correlated with low working ability, low social activity, low SOC, pain, and helplessness, and not associated with disease severity variables including skin score and internal organ involvement. Multiple regression analysis showed that a high level of helplessness and a low level of SOC might be closely associated with depressive symptoms in SSc.

Conclusion. Our results indicate that depressive symptoms are frequent in SSc patients. Medical staffs should pay attention to the possible risk factors for depressive symptoms, such as patient's helplessness and SOC. (J Rheumatol 2003;30:1782–7)

Key Indexing Terms:
SCLERODERMA DEPRESSION SENSE OF COHERENCE HELPLESSNESS

Systemic sclerosis (SSc) is a multisystem connective tissue disease characterized by inflammatory, fibrotic, and degenerative changes in the skin (scleroderma), peripheral circulation, synovium, skeletal muscle, and certain internal organs in varying degrees of severity[1,2]. At present, the pathogenesis of SSc is unknown, and there have been few truly effective therapies identified for SSc. Therefore, the disease may often cause not only decreased physical function but also various psychosocial problems, and quality of life (QOL) may decrease gradually during a long disease course.

Depressive state or depression is increasingly recognized as a significant problem in systemic rheumatic diseases, since depressive state is an important factor causing decreased QOL. Depression was reported to be common in patients with rheumatoid arthritis (RA), with a prevalence rate of 31%[3]. In SSc, there have been only a few reports concerning depression. Roca, *et al* reported that 26 of 54 SSc patients had mild depressive symptoms, and an additional 9 had moderate to severe symptoms[4]. However, there have been no detailed reports on the characteristics, predictors, and management of depression in patients with SSc.

The purpose of our study was to examine the frequency of depressive symptoms, and to elucidate the factors closely associated with their development in patients with SSc.

MATERIALS AND METHODS

Patients. All of the patients were diagnosed with definite SSc according to the American College of Rheumatology (ACR, formerly American Rheumatism Association) criteria for classification of scleroderma[5], and followed at the Rheumatology Clinic of Saga Medical School Hospital and affiliated hospitals. Fifty patients were enrolled in the study, and all gave informed consent. In some patients with overlapping disease, RA and systemic lupus erythematosus (SLE) were diagnosed according to ACR classification criteria[6,7], and Sjögren's syndrome (SS) was diagnosed according to European criteria[8].

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Study instruments. The self-report measures used in this study included the Beck Depression Inventory (BDI)[9], the Rheumatology Attitude Index (RAI)[10], the Sense of Coherence (SOC) scale[11,12], the modified Health Assessment Questionnaire (mHAQ)[13], Arthritis Impact Measurement Scales version 2 (AIMS2)[14], and the 100 mm visual analog pain scale. In addition, modified Rodnan skin score[15], disease severity scale for SSc[16], joint tenderness and swelling counts, and laboratory data were obtained from patients' physicians and medical records. Also, the range of active handspread[17] and the maximal oral aperture[17] were measured in each patient.

BDI is a 21 item self-report measure of cognitive, affective, and somatic symptoms of depression[9], of which reliability and validity have been verified[4,18-20]. This measure has been widely used for assessing depressive symptoms in patients with various diseases such as type 2 diabetes mellitus[21], RA[18,20], and SSc[4]. Higher BDI scores indicate more severe depressive state. According to BDI scores, depressive states were classified into 4 categories[4,9], as follows: 0–10: normal; 11–16: depressive mood; 17–20: mild depressive symptoms; 21–26: moderate depressive symptoms; > 26: severe depressive symptoms.

RAI is a 5 item self-report questionnaire that assesses perceived learned helplessness that characterizes deficits resulting from exposure to uncontrollable events[10]. Higher RAI scores indicate increased levels of helplessness.

The SOC-13 scale includes 13 items that relate to various aspects of an individual's life. The SOC scale was originally developed by Antonovsky, and he concluded that the sense of coherence may be interpreted as a trait, a stable dispositional orientation of a person, in contrast to a state, which may fluctuate substantially[11,12]. The SOC scale is essentially a measure of an individual's resilience in the face of stress and capacity to cope with it. The SOC is related to both coping and depression, but is very different from either. While conventional coping measures assess preferences for particular coping strategies, the SOC essentially measures an individual's capacity to respond to stressors by the appropriate application of a variety of coping and other strategies[12].

The mHAQ is an 8 item self-report questionnaire that assesses the patient's level of difficulty with activities of daily living (ADL)[13]. Some questions of AIMS2 concerning working abilities (4 items), social function (5 items), and support from family and friends (4 items) were used to cover aspects of broader health status[14]. In the mHAQ and AIMS2, a high score means low ability or decreased activity. The 100 mm visual analog pain scale was designed to assess the severity of pain. For this scale, each patient was asked to place a mark between terminal points designated either no pain or pain as bad as it could be.

Skin thickness was quantified using the modified Rodnan skin thickness score technique in which skin thickness was assessed clinically in each of 17 body surface areas on a 0–3 scale: 0: normal, 1: mild thickness, 2: moderate thickness, and 3: severe thickness (maximum score of 51)[15].

The disease severity scale for SSc was designed to assess organ-specific severity of 9 systems such as general, peripheral vascular, skin, joint/tendon, muscle, gastrointestinal tract, lung, heart, and kidney[16] according to Medsger's definition. Briefly, for the general system, hematocrit (Ht) was used (0: normal Ht; 1: Ht 33.0–36.9%; 2: Ht 29.0–32.9%; 3: Ht 25.0–28.9%; and 4: Ht > 25.0%). For the peripheral vascular system, the score was based upon the presence of the following: Raynaud's phenomenon: 1; digital pitting scars: 2; digital tip ulcerations: 3; or digital gangrene: 4; and absence of any above symptom: 0. For the evaluation of skin, the total skin score (TSS) described above was used (severity score 0: TSS = 0; 1: TSS = 1–14; 2: TSS = 15–29; 3: TSS = 30–39; and 4: TSS ≥ 40). For scoring the joint/tendon system, finger-to-palm (FTP) distance in flexion was measured (0: FTP = 0–0.9 cm; 1: FTP = 1.0–1.9 cm; 2: FTP = 2.0–3.9 cm; 3: FTP = 4.0–4.9 cm; and 4: FTP ≥ 5.0 cm). For scoring the muscle system, proximal muscle strength was tested (0: no proximal weakness; 1: mild proximal weakness; 2: moderate proximal weakness; 3: severe proximal weakness; and 4: ambulation aids required). For the gastrointestinal tract, we evaluated distal esophageal and small bowel hypomotility (0: normal function; 1: distal esophageal hypoperistalsis and/or small bowel series abnormal; 2: distal esophageal aperistalsis and/or antibiotics required for bacterial overgrowth; 3: malabsorption syndrome and/or episodes of pseudoobstruction; and 4: hyperalimentation required). For the lung, chest radiography, pulmonary function tests, echocardiogram, and/or right heart catheterization were tested [0: normal; 1: diffusing capacity for carbon monoxide (DLCO) 70–80%, forced vital capacity (FVC) 70–80%, rales and/or fibrosis on radiograph; 2: DLCO 50–69%, FVC 50–69%, and/or mild pulmonary hypertension; 3: DLCO < 50%, FVC < 50%, moderate to severe pulmonary hypertension; and 4: oxygen required]. For the heart, electrocardiogram, echocardiogram, and/or chest radiograph were used [0: normal; 1: presence of conduction defect and/or left ventricular ejection fraction (LVEF) 45–49%; 2: arrhythmia, ventricular enlargement and/or LVEF 40–44%; 3: LVEF < 40%; and 4: congestive heart failure and/or arrhythmia requiring therapy]. For the kidney, we measured serum creatinine and urine (0: normal; 1: serum creatinine 1.3–1.6 mg/dl and/or urine protein 2+; 2: serum creatinine 1.7–2.9 mg/dl and/or urine protein 3–4+; 3: serum creatinine > 3.0 mg/dl; and 4: dialysis required).

As additional assessments for skin and joint/tendon involvement, the following measurements were also taken. Active hand spread was measured from the outermost aspect of the fifth digit to the outermost aspect of the first digit during maximal hand spread[17]. The interlabial distance as oral aperture was also measured with the patient maximally opening the mouth[17]. Joint tenderness and swelling counts were assessed for each joint (maximum 57 for each count).

Laboratory data analyzed inlcuded C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), antinuclear antibody (ANA), anti-Scl-70 antibody, and anticentromere antibody.

Data were analyzed using the SPSS software. For correlation of the variables, Pearson's correlation test was performed when data showed normal distribution, and otherwise Spearman's rank correlation test was done. To examine the relative importance of the factors including demographic features and those measured as above, which were correlated with BDI scores, a step-wise multiple regression analysis was performed.

RESULTS

Patient characteristics (Table 1). Fifty patients completed the study: 41 (82%) were female and 9 (18%) were male. The age range was 33 to 75 years, with a mean of 59.6 years. Disease duration ranged from 1 to 40 years, with a mean of 13.6 years. Twenty-four patients (48%) were employed at the time of the study.

Thirty patients (60%) had limited-type scleroderma in which skin sclerosis was confined to hands and forearms, and 20 (40%) had diffuse-type showing proximal skin sclerosis. Skin thickness score ranged from 0 to 34, and mean score was 11.0 ± 8.6 (SD). More than half of the patients showed gastrointestinal tract or lung involvement, but the heart and kidneys were less involved. Fourteen patients (28%) had at least one rheumatic disease in addition to SSc: 8 patients had RA, one had SLE, 4 had SS, and one patient had SLE and SS.

Findings from the study instruments. The mean score of BDI in SSc patients was 11.8 ± 7.3 (Table 2). Thirteen patients (26%) had total BDI scores between 11 and 16, indicating depressive mood, and 10 (20%) had scores ≥ 17, indicating mild to severe depressive symptoms, according to Beck's[9] and Roca's definitions[4]. Therefore, depressive symptoms including the mildest state were seen in almost half (46%) of our SSc patients.

Table 1. Patient characteristics. Internal organ involvement was defined according to Medsger, *et al*[16].

Variable	N (%)
Sex	
Male	9 (18)
Female	41 (82)
Mean age (yrs)	59.6 ± 11.2
Duration of SSc (yrs)	
1–5	5 (10)
> 5	45 (90)
Skin involvement	
Limited type	30 (60)
Diffuse type	20 (40)
Skin score*	
0	3 (6)
1–14	31 (62)
15–29	15 (30)
30–39	1 (2)
40 <	0 (0)
Internal organ involvement	
General (hematocrit < 33%)	3 (6)
Peripheral vascular	15 (30)
Joint/tendon	
Fist closure ≥ 1.0 cm	11 (22)
Tender joint counts ≥ 1	15 (30)
Muscle	15 (30)
Gastrointestinal tract	26 (52)
Lung	29 (58)
Heart	11 (22)
Kidney	2 (4)

* modified Rodnan's total skin thickness score.

Table 2. Distribution of BDI scores in 50 patients with SSc.

BDI scores	Definition[4,9]	N (%)
0–10	Normal	27 (54)
11–16	Depressive mood	13 (26)
17–20	Mild depressive symptoms	4 (8)
21–26	Moderate depressive symptoms	4 (8)
> 26	Severe depressive symptoms	2 (4)

BDI: Beck depression inventory.

BDI includes questions on cognitive-affective depressive symptoms that are relatively specific for depression[4] and also on somatic depressive symptoms, which may cause overestimation of depressive states due to disease-related somatic symptoms. Considering this possibility, questions concerning cognitive-affective symptoms and those concerning somatic symptoms were analyzed separately. As a result, 9 patients scored at least 10 points on the cognitive-affective subscale alone. Only 8 patients had no cognitive-affective symptoms of depression, and only one had no somatic symptoms of depression.

The total BDI scores showed significant positive correlation with RAI, pain, social function, and working abilities, and negative correlation with SOC (Table 3). When the cognitive-affective symptoms were separately analyzed, RAI ($r = 0.441$, $p < 0.01$) and SOC ($r = –0.641$, $p < 0.01$) were the only variables showing a significant relationship to the cognitive-affective subscale of BDI as well as total BDI (Table 3). In contrast, the other variables such as social function, working ability (AIMS2), and pain showed a significant relationship to somatic but not to cognitive-affective symptoms.

RAI scores, similar to total BDI scores, showed a positive correlation with pain, social function, and working abilities, and a negative correlation with SOC. Many variables for disease severity including skin score, internal organ involvement scores, or laboratory data were not significantly correlated with BDI or RAI (data not shown). Also, as shown in Table 4, there was little difference in the SSc severity score of each organ system between patients showing high BDI scores and those showing low BDI scores.

The mean score for SOC was 67.7 ± 13.4. There was a strong negative correlation between SOC scores and BDI scores and between SOC and RAI, but there were no significant relationships between SOC, mHAQ, and pain.

The mean visual analog scale score for pain was 34.0 ± 27.4 mm, and the pain scale also showed a positive correlation with working abilities and overlap with another rheumatic disease (data not shown).

Multiple regression analysis. Step-wise multiple regression analysis was performed to elucidate the factors closely related to depressive symptoms. The following independent variables that showed significant univariate correlations with the BDI scores were entered into the analysis: RAI, SOC, pain, working abilities, and social function. Variables were entered into the model when $p < 0.05$, and were removed from the model when $p > 0.10$.

As shown in Table 5, high levels of RAI and low levels of SOC were found to be closely associated with high BDI scores. This model finally accounted for 37.2% of the variance of BDI scores.

DISCUSSION

SSc injures not only skin but also the musculoskeketal system and various internal organs in various degrees during a long disease course, resulting in decreased physical function and psychosocial problems in some patients, thus causing decreased patients' QOL. However, there have been only a few reports on the psychosocial problems in SSc patients[4], particularly on depression or a depressive state that is frequently a serious problem in patients with rheumatic diseases. We examined the frequency of depressive symptoms in SSc patients and also investigated the factors closely associated with their development.

It is thought that the patients who have high BDI score (≥ 17) need to see a psychiatrist and to be evaluated to

Table 3. Factors significantly correlated with depressive symptoms (BDI scores) in patients with SSc. Numbers are correlation coefficients. Cognitive-affective symptoms (items 1–13 of BDI) analyzed separately shown in parentheses.

Variables	BDI	RAI	SOC	Pain	Social Function	Working Ability
BDI	1.000					
RAI	0.491** (0.441**)	1.000				
SOC	–0.543** (–0.641**)	–0.351*	1.000			
Pain	0.338* (0.270)	0.362**	0.061	1.000		
Social function (AIMS2)	0.295* (0.208)	0.354*	–0.081	0.241	1.000	
Working ability (AIMS2)	0.374** (0.266)	0.380**	–0.193	0.322*	0.102	1.000

BDI: Beck Depression Inventory; RAI: Rheumatology Attitude Index; SOC: Sense of Coherence.

Table 4. Comparison of SSc severity scores between patients with high BDI scores and those with low BDI scores. Differences in severity scores between high BDI group and low BDI group were statistically evaluated by Fisher's exact probability method.

	Mean SSc Severity Score (range)		
	BDI < 17 (n = 40)	BDI ≥ 17 (n = 10)	p
General	0.38 (0–3)	0.2 (0–1)	NS
Peripheral vascular	1.73 (0–4)	1.8 (0–3)	NS
Skin	1.23 (0–2)	1.5 (0–3)	NS
Joint/tendon	0.35 (0–4)	0.3 (0–2)	NS
Muscle	0.28 (0–2)	0.5 (0–1)	NS
Gastrointestinal tract	0.5 (0–2)	0.7 (0–1)	NS
Lung	0.7 (0–4)	1 (0–2)	NS
Heart	0.4 (0–2)	0.3 (0–1)	NS
Kidney	0.03 (0–1)	0.1 (0–1)	NS

Table 5. Multiple regression analysis for BDI scores.

Variables	ß	Adjusted R^2	p
Sense of coherence scale	–0.368	0.280	0.002
Rheumatology attitude index	0.350	0.372	0.003

determine whether the patient is truly depressed[9]. BDI is a widely used indicator for assessing the depressive state, and because our purpose was to classify the patients having depressive symptoms for a further statistical analysis, not to diagnose the patients as clinically depressed, this measurement was used for the assessment of depressive state in this study.

Since some somatic symptoms of depression assessed in BDI might be similar to the physical symptoms directly related to SSc itself, patients who are physically sick might be misdiagnosed with depression. However, in our study, physical symptoms were mild in most of the patients, and none of the severity scores showed significant association with BDI scores. In addition, when only cognitive affective symptoms (13 items) of the total 21 BDI items were analyzed after subtracting scores for somatic symptoms (8 items), the results obtained were not contradictory to those when total BDI scores were used. Therefore, the possibility that patients physically sick due to SSc might be misdiagnosed with depression would be small.

In patients with RA, depression was reported to be commonly seen (31%), and their mean BDI score was 7.2[18]. According to Roca, *et al*, who also used BDI for the estimation of depression, almost two-thirds of SSc patients showed some depressive symptoms[4]. In our study, depressive symptoms including the mild form were seen in 46% of SSc patients, and their mean BDI score was 11.8 ± 7.3. In addition, 20% of the patients had a high score (≥ 17), implying

that they would need to have a clinical evaluation by a psychiatrist. These figures were higher than those of RA patients[18], indicating that a depressive state seems to be more frequent and somewhat more severe in SSc than in RA. Since depression or a depressive state is closely correlated with individual QOL, the possible presence of more frequent and severe depression in SSc patients should be recognized and considered seriously.

Most of the patients in this study had a long disease duration (> 5 years), so if this study had been undertaken early in the disease course, the results might have been different. The patients in the early disease stage might have had unfamiliar, more severe, and complex symptoms, possibly resulting in more frequent depression, which might be related to disease severity. However, a previous study showed that there was no relationship between depressive symptoms and disease duration[4]. To clarify this, further study is necessary.

Roca, *et al* reported that depressive symptoms in SSc patients were more strongly related to personality, self-rated disability (HAQ), and adequacy of emotional support than to objective medical indices of illness severity[4,19]. Our results showed that depressive symptoms in SSc patients were significantly correlated with low SOC, helplessness, low working ability, pain, and low social function, and not correlated with any other demographic or medical variables, being almost consistent with previous results[4]. When the cognitive-affective symptoms that were relatively more specific for depression were analyzed separately from total BDI, the results showed that helplessness (RAI) and low SOC were the only significant variables related to true depressive symptoms. Multiple regression analysis also revealed that 2 factors, low SOC and helplessness, were the most significant correlates of depressive symptoms in SSc patients.

To our knowledge, this is the first study to show a significant relationship between SOC and depressive symptoms in SSc patients. In RA patients, depression has been correlated with low SOC and high self-rated pain levels[11,22]. Also in RA, a negative correlation between SOC and learned helplessness was reported[11,22]. Both these findings in RA were shown in SSc patients in this study.

Those having high SOC scores are likely to perceive stressors as predictable and explicable, have confidence in their capacity to overcome stressors, and judge it worthwhile to rise to the challenges they face. Low SOC measures the relative absence of these beliefs. Low SOC superficially resembles some of the cognitive features of depression. However, several lines of evidence have shown that SOC and depression are fundamentally different, and also that SOC is not simply a measure of depression. Although, as noted above, low SOC and depression appear to be related, and high SOC represents more than the absence of depression[19,20].

We have shown that the psychological or internal factors such as low SOC and helplessness are the significant correlates of depressive symptoms in SSc patients. SSc patients having some of these factors may be vulnerable to depression, and psychological interventions including counseling with special psychotherapists and even antidepressant medication may prevent the development of depression in such patients. Further studies are needed to confirm our findings in a prospective manner if possible, and also to determine whether depression is an important prognostic indicator for QOL in SSc.

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