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Original Article

Common Causes of Pain in Systemic Sclerosis: Frequency, Severity, and Relationship to Disease Status, Depression, and Quality of Life

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ABSTRACT

Background: In routine clinical practice, healthcare professionals draw little attention to pain in patients with systemic sclerosis (SSc). Pain has adverse effects on functional ability, social and emotional wellbeing.
Aims: This study aims to assess the frequency and severity of different types of pain in patients with SSc, and the relationship of pain with disease status, depression and quality of life.
Design: Consecutive patients with SSc were included in this cross-sectional study. Patients with previously diagnosed painful diseases or conditions (other rheumatic diseases, angina pectoris, neurological disorders, etc.) were excluded.
Settings: Patients, who visited our rheumatology outpatient clinic from February to November 2016, participated in this study.
Participants/Subjects: 42 consecutive patients with SSc (38 women and 4 men), mean age 56.5 years, mean disease duration 9.5 years, were included.
Methods: All patients filled in a questionnaire, to indicate the presence or absence of some predefined pain syndromes. Disease status was assessed using the Scleroderma Assessment Questionnaire (SAQ), symptoms of depression by the Beck's Depression Inventory (BDI), whilst the quality of life was evaluated using the EuroQol questionnaire.
Results: It was found that 92.9% of SSc patients suffer from different types of pain, and 45.2% of patients have pain every day. Joint pain was the most common type of pain, present in 78.6% of patients, followed by pain associated with Raynaud's phenomenon (69%), back pain (47.6%), headache (31%), chest pain (23.8%), odynophagia (21.4%) and painful digital ulcers (19%). Symptoms of neuropathic pain were noticed in 26.2% of patients. Severe joint pain, everyday pain and symptoms of neuropathic pain in SSc were associated with more severe disease and poorer quality of life. Pain related to Raynaud's phenomenon, digital ulcers, odynophagia and joint pain were associated with significant symptoms of depression.
Conclusion: The majority of patients with SSc suffer from different types of pain. Pain is associated with more severe disease, depression and poor quality of life.

Patients with rheumatic diseases attach great importance to the treatment of pain and prioritize improvement of pain management (Heiberg & Kvien, 2002). However, pain in systemic sclerosis (SSc) has received relatively little attention from researchers and is less often assessed and treated compared with other rheumatic diseases.

SSc is a chronic connective tissue disease characterized by overproduction and deposition of collagen into the skin and internal organs (gastrointestinal tract, lungs, heart, and kidneys). Prevalence of SSc varies between 88 per million in England and 276

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per million in the United States (Chifflot et al., 2008). Immunologic and vascular changes precede fibrosis. It is believed that endothelial damage is the first link in the pathogenesis of SSc (Altorok, Wang, & Kahaleh, 2014). Endothelial dysfunction results in vasoconstriction, wall thickening of arterial blood vessels, and tissue ischemia. Moreover, damage of endothelial cells causes activation of T lymphocytes, mast cells, and macrophages, which secrete different cytokines, known as growth factors—transforming growth factor−β, vascular endothelial growth factor, platelet-derived growth factor, responsible for activation of fibroblasts (Cantatore, Maruotti, Corrado, & Ribatti, 2017; Solanilla et al., 2009). Fibroblasts in turn produce extracellular matrix compounds, including collagen, glycosaminoglycans, and fibronectin, leading to fibrosis of the skin and visceral organs (Usategui, del Rey, & Pablos, 2011). Symptoms and signs of microvascular damage usually precede other clinical manifestations for months or even years (Seibold, 1997). In many patients, Raynaud's phenomenon, characterized by episodic vasospasms, followed by color changes in the fingers and toes (pallor or cyanosis) in response to cold or emotional excitement, is the only clinical manifestation in the early stage of SSc. Necrotic changes (digital ulcers and gangrene) may be a result of reduced blood flow in peripheral blood vessels (Ostojic & Damjanov, 2006a; Ostojic, Damjanov, Pavlov-Dolijanovic, & Radunovic, 2004). Gastrointestinal involvement is the most common visceral manifestation of the disease. It includes esophageal and intestinal dysmotility, gastroesophageal reflux, heartburn, maldigestion, and malabsorption. The two major features of lung involvement are interstitial lung disease and pulmonary arterial hypertension (Ostojic, Matucci Cerinic, Silver, Highland, & Damjanov, 2007). Myocardial involvement by patchy fibrosis is associated with repeated myocardial ischemia as a result of microvascular damage. This leads to chronic heart failure, arrhythmia, and conduction disturbances. Many patients with SSc have reduced renal blood flow and decreased glomerular filtration rate (Ostojic & Stojanovski, 2017).

Depending on the range of sclerodermatous skin changes, one can differentiate between limited cutaneous SSc (lcSSc) and diffuse forms of the disease (dcSSc). In lcSSc skin thickening is localized distal to the clavicles (face and neck), distal to the elbows (forearms and hands), and distal to the knees. In dcSSc, skin changes are extended also on the trunk, thighs, and upper arms (Le Roy et al., 1988; Subcommittee for Scleroderma Criteria of the American Rheumatism Association Diagnostic and Therapeutic Criteria Committee, 1980). It is believed that dcSSc is the more severe subset of the disease, with rapidly progressive and sometimes fatal visceral organ involvement (Giordano, Valentini, Migliaresi, Picillo, & Vatti, 1986). Almost all patients with SSc have positive total antinuclear antibody tests, but specific antinuclear antibodies associated with SSc are anticentromere antibodies (ACA) and antibodies against topoisomerase-I (ATA).

Because SSc is a complex multisystem disorder, pain may have multiple sources. Pain can be caused by stimulation of nerve endings (nociceptive pain), or by damage or illness affecting nerve fibers, that conduct impulses from nociceptors to the central nervous system (neuropathic pain). Nociceptive pain is usually present in tissue injury caused by mechanical, chemical, or thermal stimuli; infection; or inflammation. Neuropathic pain may be caused by damage of nerves, nerve roots, and central pain pathways in the spinal cord and the brain and therefore is classified as peripheral or central (Loeser & Treede, 2008). Regarding intensity, pain can be broadly categorized as mild, moderate, or severe. Depending on duration, pain may be classified as acute or chronic. Pain is usually considered to be chronic if lasts for more than 3-6 months or persists beyond the course of an acute disease or after tissue healing is complete (Merskey & Bogduk, 1994; Ready & Edwards, 1992).

Several clinical features in SSc may cause painful sensations. Patients often have joint pain (arthralgia) but seldom overt joint inflammation (arthritis). In many patients, digital pallor and cyanosis during attacks of Raynaud's phenomenon are accompanied by pain. Moreover, patients with severe vascular damage may have painful necrotic changes, like digital ulcers and gangrene. Patients may complain of chest pain as a result of myocardial ischemia or gastroesophageal reflux disease. Some patients report pain when swallowing (odynophagia) (Ostojic & Damjanov, 2006a).

This study aimed to assess the frequency and severity of different pain types in patients with SSc and the relationship of pain with disease status, depression, and quality of life.

Methods

Forty-two consecutive patients with SSc (38 women and 4 men), mean age 56.5 years, mean disease duration 9.5 years, who visited our rheumatology outpatient clinic from February to November 2016, were included in this study. All patients fulfilled the 2013 American College of Rheumatology−European League Against Rheumatism classification criteria for SSc (van den Hoogen et al., 2013). Patients with previously diagnosed painful diseases or conditions (e.g., other rheumatic diseases, angina pectoris, neurological disorders) were excluded. This study was approved by the local ethics committee. Informed consent was obtained from all individual participants included in the study. The limited form of the disease was present in 31 patients (73.8%), whereas 11 (26.2%) had dcSSc. ACA antibodies were positive in 15 (35.7%), ATA antibodies in 17 patients (40.5%). Demographic characteristics of patients are shown in Table 1.

All patients filled in a questionnaire to indicate the presence or absence of some predefined scleroderma-related pain syndromes (pain associated with Raynaud's phenomenon, pain caused by digital ulcers, odynophagia, and joint pain), as well as other types of pain, which may not be necessarily related to SSc (headache, chest pain, and back pain). If the presence of a particular type of pain was confirmed, the patient was asked to answer how often the pain occurs (rare [once weekly or less], common [more than once a week], or everyday pain). The patient was also asked to assess the intensity of particular pain type on a 0-10 Numeric Rating Scale, which was used to evaluate average pain intensity (median). Moreover, pain intensity was interpreted as 0 (no pain), 1-4 (mild pain), 5-7 (moderate pain), 8-10 (severe pain), to get a better insight into the distribution of patients according to pain intensity. Presence of neuropathic pain symptoms was assessed using the PainDetect screening questionnaire (Freynhagen, Baron, Gockel, & Tölle, 2006). This self-assessment questionnaire, specifically developed to identify the likelihood of a neuropathic pain component in adult patients, consists of seven questions. The final score ranges between −1 and 38. A score of ≤12 indicates that pain is unlikely to have a

Table 1
Demographic Characteristics of Patients (n = 42)

Gender	
Female	38/42 (90.5%)
Male	4/42 (9.5%)
Age: mean (min-max) years	56.5 (26-69)
Disease duration: mean (min-max) years	9.5 (0.3-35)
Disease subtype	
lcSSc	31/42 (73.8%)
dcSSc	11/42 (26.2%)
SSc-specific antibodies	
ACA	15/42 (35.7%)
ATA	17/42 (40.5%)

Max = maximum; min = minimum; lcSSc = limited cutaneous SSc; dcSSc = diffuse cutaneous SSc; SSc = systemic sclerosis; ACA = anticentromere antibodies; ATA = antibodies against topoisomerase-I.

Table 2
Frequency and Intensity of Different Pain Types

Type of Pain	n (%)	Pain Intensity			
		Median (Min-Max)	Mild	Moderate	Severe
Pain during attacks of RP	29/42 (69.0%)	6.0 (2-10)	7/29 (24.1%)	13/29 (44.9%)	9/29 (31.0%)
Pain caused by ischemic ulcers	8/42 (19.0%)	8.5 (4-10)	1/8 (12.5%)	2/8 (25.0%)	5/8 (62.5%)
Pain when swallowing	9/42 (21.4%)	5.0 (1-10)	3/9 (33.3%)	5/9 (55.6%)	1/9 (11.1%)
Joint pain	33/42 (78.6%)	6.0 (1-10)	7/33 (21.2%)	15/33 (45.5%)	11/33 (33.3%)
Headache	13/42 (31.0%)	7.0 (4-10)	1/13 (7.6%)	6/13 (46.2%)	6/13 (46.2%)
Chest pain	10/42 (23.8%)	6.0 (2-8)	1/10 (10.0%)	7/10 (70.0%)	2/10 (20.0%)
Back pain	20/42 (47.6%)	5.0 (2-9)	4/20 (20.0%)	12/20 (60.0%)	4/20 (20.0%)

RP = Raynaud's phenomenon.

neuropathic component, whereas a score of ≥19 suggests that neuropathic pain is likely. A score between these values indicates that the result is uncertain, and a more detailed examination is required to ensure a proper diagnosis (Freynhagen et al., 2006).

Furthermore, the relationship among different types of pain with disease status, symptoms of depression and quality of life was evaluated. Disease status was estimated by the Index of Disease Status (IDS), which was calculated using the Scleroderma Assessment Questionnaire (Ostojic & Damjanov, 2006b, 2008). It comprises 23 items divided into 4 subgroups: 4 items related to vascular dysfunction, 6 items to respiratory, 5 items to gastrointestinal, and 8 items to musculoskeletal dysfunction. There is a multiple choice of four answers to each question. The answers are assessed on a 0-3 scale. The IDS is obtained by dividing the total score for the entire questionnaire by the number of questions. The IDS value ranges from 0 to 3. Higher IDS value indicates more severe disease. The occurrence of depressive symptoms was assessed by the Beck's Depression Inventory (BDI [Beck, Ward, Mendelson, Mock, & Erbauch, 1961]), which was used to calculate the BDI score. The highest possible total for the BDI is 63; the lowest possible score is 0. BDI score ≥10 indicates the presence of significant symptoms of depression, whereas values between 0 and 9 are considered as normal mood variations. Quality of life was evaluated using the EuroQol EQ-5D-5L self-completed questionnaire, which measures health using five levels of severity (no problems, slight problems, moderate problems, severe problems, and extreme problems) in five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression).

The χ^2 and Fisher's exact tests were used to assess differences in the frequency of particular pain types, and Student's *t* and Mann-Whitney *U* tests were used to compare pain intensity among patients with lcSSc and dcSSc with different antibody profiles. Spearman's test was used to correlate the intensity of particular pain types with IDS, BDI, and EQ-5D-5L index.

Results

In this cross-sectional study, 39 out of 42 of SSc patients (92.9%) reported the presence of at least one type of pain, and 19 out of 42 (45.2%) suffer from pain every day. Frequency and intensity of different types of pain are shown in Table 2. Joint pain was the most common type of pain, whereas pain caused by digital ulcers was reported as most severe.

All types of pain were equally frequent and severe in patients with lcSSc and dcSSc, except joint pain, which was more intense in patients with the diffuse form of the disease (7.6 vs. 5.5, $p = .02$).

Table 3
Frequency and Intensity of Pain in SSc Patients with Different Subtypes of the Disease and Antibodies

Type of Pain	lcSSc (n = 31)	dcSSc (n = 11)	*p*	ACA (n = 15)	ATA (n = 17)	*p*
Pain during attacks of RP						
Frequency	21 (67.7%)	8 (72.7%)	1.00*	13 (86.7%)	12 (70.6%)	.40*
Intensity	6.2 ± 2.3	6.3 ± 1.8	.82†	7.4 ± 1.8	5.4 ± 2.0	.14‡
Painful ischemic ulcers						
Frequency	4 (12.9%)	4 (36.4%)	.17*	3 (20.0%)	4 (23.5%)	1.00*
Intensity	7.8 ± 2.2	8.0 ± 2.8	.78†	8.7 ± 1.5	8.0 ± 2.8	.76‡
Pain when swallowing						
Frequency	5 (16.1%)	4 (36.4%)	.21*	5 (33.3%)	4 (23.5%)	.70*
Intensity	4.6 ± 3.5	5.3 ± 1.7	.41†	4.6 ± 3.5	5.3 ± 1.7	.34†
Joint pain						
Frequency	24 (77.4%)	9 (81.8%)	1.00*	14 (77.4%)	12 (70.6%)	.18*
Intensity	5.5 ± 2.4	7.6 ± 1.5	.02†	6.3 ± 2.2	6.7 ± 2.4	.79†
Headache						
Frequency	10 (32.3%)	3 (27.3%)	.49*	7 (46.7%)	5 (29.4%)	.47§
Intensity	6.7 ± 1.6	7.7 ± 2.5	.21‡	6.7 ± 1.8	7.0 ± 2.0	.66‡
Chest pain						
Frequency	7 (22.6%)	3 (27.3%)	1.00*	6 (40.0%)	3 (17.6%)	.24*
Intensity	6.0 ± 1.2	5.7 ± 3.2	.54†	2.0 ± 1.2	5.7 ± 3.2	.11†
Back pain						
Frequency	15 (48.4%)	5 (45.5%)	.87§	12 (80.0%)	7 (41.2%)	.35*
Intensity	5.9 ± 1.8	4.8 ± 2.2	.48†	6.3 ± 1.4	5.3 ± 2.1	.43†

SSc = systemic sclerosis; lcSSc = limited cutaneous SSc; dcSSc = diffuse cutaneous SSc; ACA = anticentromere antibodies; ATA = antibodies against topoisomerase-I; RP = Raynaud's phenomenon.
* Fisher's exact test.
† Mann-Whitney *U* test.
‡ Student's *t* test.
§ χ^2 Test.

Table 4
Correlation of Pain with Disease Severity, Depression, and Quality of Life

Type of Pain	IDS		EQ-5D-5L		BDI	
	Spearman's Test	*p*	Spearman's Test	*p*	Spearman's Test	*p*
Pain during attacks of RP	0.30	.23	−0.33	.32	0.69	.003
Painful ischemic ulcers	0.44	.13	0.31	.29	0.81	.001
Pain when swallowing	0.53	.09	−0.37	.42	0.73	.002
Joint pain	0.66	.0003	0.52	.004	0.60	.003
Headache	0.30	.31	0.22	.67	0.50	.25
Chest pain	0.49	.11	−0.33	.41	0.49	.31
Back pain	0.39	.21	0.05	.88	0.21	.49

IDS = Index of Disease Status; BDI = Beck Depression Inventory; RP = Raynaud's phenomenon.

Frequency and intensity of any type of pain did not differ significantly among patients with positive ACA or ATA (Table 3).

In contrast to other pain types, the intensity of joint pain correlated with the IDS ($p = .0003$), as well as with the EQ-5D-5L index ($p = .004$). A significant positive correlation was found between the BDI index and intensity of pain associated with Raynaud's phenomenon ($p = .003$), digital ulcers ($p = .001$), odynophagia ($p = .002$), and joint pain ($p = .003$). These data are shown in Table 4.

We found that 11 out of 42 patients (26.2%) had symptoms of neuropathic pain. These patients had a higher mean value of the IDS index compared with patients without neuropathic pain (1.28 vs. 0.66, $p < .001$), as well as a higher mean value of the BDI index (18.3 vs. 9.9, $p = .003$) and a lower value of the EQ-5D-5L index (0.39 vs. 0.79, $p < .001$). These data are shown in Table 5.

Compared with patients with intermittent pain, patients suffering from everyday pain had a significantly higher mean value of the IDS (1.21 vs. 0.53, $p < .001$) and lower mean value of the EQ-5D-5L index (0.52 vs. 0.79, $p < .001$) (Table 6).

Discussion

The majority of patients (92.9%) in the present study suffered from pain. Pain in SSc has been assessed in other studies (Richards, Herrick, Griffin et al, 2003; Schrier et al., 2010; Suarez-Almazor, Kallen, Roundtree, & Mayes, 2007), and all concluded that pain was common, occurring in 60%-83% of patients. Severity of pain in SSc patients was found to be comparable with that in rheumatoid arthritis (Schrier et al., 2010).

In the present study, joint pain was the most common type of pain in SSc, occurring in 78.6% of patients. Most of the patients who reported joint pain rated the intensity of their pain as moderate or severe. In other studies the frequency of joint pain was found to be between 48% and 61%. The authors noticed that all joints may be involved, although the fingers, wrists, and ankles predominate (Avouac, Clements, Khanna, Furst, & Allanore, 2012). According to the results from the European League Against Rheumatism Scleroderma Trial and Research Group database (Avouac et al., 2010), clinically overt joint inflammation is present in only 15% of SSc patients. However, subclinical arthritis with joint effusion, synovial proliferation, and positive power Doppler signal, may be found in up to 49% of SSc patients (Cuomo et al., 2009). Other possible causes of musculoskeletal pain include bursitis (which may be associated with regional arthritis) and tendon abnormalities.

The majority of patients included in our study (69%) reported pain associated with Raynaud's phenomenon. Most of the patients rated intensity of this type of pain as moderate or severe (44.9% and 31%, respectively). Raynaud's phenomenon, defined as recurrent vasospasms related to cold exposure or stress, is present in more than 95% of patients with SSc (Wigley & Flavahan, 2016). Attacks of Raynaud's phenomenon may be painful or cause numbness as a result of a lack of oxygenated blood, with changes in pH and other metabolites that activate nociceptive nerves in the fingers and toes.

In our study, 19% of patients reported pain caused by digital ulcers, and this type of pain was estimated as most severe compared with other pain types (median 8.5 on a 0-10 scale, rated as severe by 62.5% of patients). Structural abnormalities related to fibrotic proliferation of the vasculature contribute to reduced blood flow in patients with SSc. The consequence may be ischemic fingertip ulcers and gangrene, especially in patients with SSc-related macrovascular disease proximal to the digital artery (Frerix, Stegbauer, Dragun, Kreuter, & Weiner, 2012). Digital ulcers occur in half of patients with SSc during the disease course, and about 10% of patients have current ulcers (Hughes & Herrick, 2017).

In the present study, odynophagia (pain when swallowing) was reported by 21.4% of our patients, and most of them rated the intensity of their pain as mild (33.3%) or moderate (55.6%). To our knowledge, this is the first study to assess odynophagia as a specific type of pain in SSc. Although SSc can affect any part of the gastrointestinal tract, involvement of the esophagus predominates, occurring in up to 90% of patients (Rose, Young, & Reynolds, 1998). Hypotonia of the lower esophageal sphincter is severe in 30% of patients, leading to gastroesophageal reflux disease, esophagitis (in one third of patients), stricture formation (9%), and Barrett's metaplasia (27,2%) (Bassotti et al., 1997; Lock, Holstege, Lang, & Schölmerich, 1997). All these conditions may cause odynophagia.

A large number of our patients (47.6%) complained of back pain, and two thirds of them rated intensity of this pain syndrome as moderate. Back pain was considered to be a significant burden, although this type of pain is unlikely to be related to SSc itself. It can be a result of an underlying vertebral disease (e.g., spondylosis, spondylolisthesis, spinal disc herniation) or muscle spasm.

In our study, 31% of SSc patients reported headache, and most of them rated the intensity of this type of pain as moderate (46.2%) or severe (46.2%). Similar to our results, a systematic review of 182

Table 5
Correlates of Neuropathic Pain with Disease Severity, Depression, and Quality of Life

Type of Pain	IDS	BDI	EQ-5D-5L
With neuropathic pain	1.28 ± 0.48	18.3 ± 8.2	0.39 ± 0.13
Without neuropathic pain	0.66 ± 0.50	9.9 ± 7.8	0.79 ± 0.20
Mann-Whitney *U* test	$z = -3.63$, $p < .001$	$z = -2.86$, $p = .003$	$z = -3.13$, $p < .001$

IDS = Index of Disease Status; BDI = Beck Depression Inventory.

Table 6
Correlates of Intermittent and Everyday Pain with Disease Severity, Depression, and Quality of Life

Type of Pain	IDS	BDI	EQ-5D-5L
Intermittent pain	0.53 ± 0.31	10.4 ± 8.0	0.79 ± 0.19
Everyday pain	1.21 ± 0.58	14.6 ± 9.1	0.52 ± 0.16
Mann-Whitney *U* test	$z = -3.32$, $p < .001$	$z = -1.52$, NS	$z = -4.12$, $p < .001$

IDS = Index of Disease Status; BDI = Beck Depression Inventory; NS = nonsignificant.

case reports or studies on neurologic abnormalities in SSc, which totaled 9,506 patients, concluded that central nervous system involvement in SSc was characterized by headache in 23.7%, seizures in 13.6%, and cognitive impairment in 8.5% of patients (Amaral, Peres, Lapa, Marques-Neto, & Appenzeller, 2013). One study reported that different neurologic abnormalities were detected in 40% of SSc patients (Averbuch-Heller, Steiner, & Abramsky, 1992), and all levels of the central and peripheral nervous system were affected: muscle (22%), peripheral nerve (18%), spinal cord (8%), and brain (6%).

Chest pain was reported by 23.8% of SSc patients in our study, and most of them (70%) rated intensity of this type of pain as moderate. This is the first study to assess the frequency of chest pain specifically in SSc. Chest pain in SSc may be a result of a coronary disease (present in 48% of patients with SSc) (D'Angelo, Fries, Masi, & Shulman, 1969), pulmonary hypertension (found in up to 12% of patients) (Condliffe et al., 2009), and pericardial disease, which has a prevalence between 5% and 16% (Gowda, Khan, Sacchi, & Vasavada, 2001).

Although dcSSc is the more severe subset of the disease, with a higher prevalence of digital ulcers, esophageal hypomotility, musculoskeletal impairment, and heart and pericardial involvement compared with patients with lcSSc in the literature (Beck et al., 1961; D'Angelo, 1969; Suarez-Almazor et al., 2007), in our study all types of pain were equally frequent in both subsets of the disease. However, joint pain was more intense in patients with dcSSc. The relationship between pain and disease subset was assessed in different studies, but findings were contradictory. Some studies found a significant correlation between the extent of sclerodermatous skin changes and pain (Furst et al., 2007; Thombs et al., 2008), whereas another reported only minimally higher pain levels in patients with dcSSc (Suarez-Almazor et al., 2007).

Joint pain was the only type of pain that significantly correlated with disease severity and poorer quality of life in patients with SSc. On the other hand, different types of pain (pain associated with Raynaud's phenomenon, digital ulcers, joint pain, and odynophagia) correlated with symptoms of depression. There is a growing body of evidence in the literature suggesting that depression often develops secondary to chronic pain (Fishbain, Cutler, Rosomoff, & Rosomoff, 1997). Pain was found to be the strongest disease-related factor associated with depression in SSc (Ostojic, Zivojinovic, Reza, & Damjanov, 2010). Unexpectedly, patients who suffered from everyday pain reported equally common symptoms of depression, compared with patients with intermittent pain. However, patients with everyday pain had a more severe disease and poorer quality of life. A previous study found that pain correlated with both physical and mental components of the Short Form 36 quality of life questionnaire (Georges et al., 2006).

Symptoms of neuropathic pain were reported by 26.2% of patients in our study. A recently published study reported a higher prevalence of neuropathic pain in SSc patients compared with controls (56.2% vs. 13.3%). Skin score was independently associated with the presence of neuropathic pain (Sousa-Neves, Cerqueira, Santos-Faria, Afonso, & Teixeira, 2018). We found that patients with symptoms of neuropathic pain have more severe disease, poorer quality of life, and more symptoms of depression than patients without neuropathic pain.

There are some limitations in our study. Only self-report instruments were used to assess disease severity, quality of life, and symptoms of depression in our patients. Therefore pain was correlated only with self-reported symptoms but not with objective parameters. However, all questionnaires used in this study were found to have criterion validity during the validation process and had significant association with clinical parameters. Another limitation is the small number of patients included in this study. Although SSc is a rare disease, results in a sample of 42 patients cannot be completely generalized to the whole population.

Conclusions

In conclusion, in our study 92.9% of SSc patients suffered from different types of pain, and 45.2% of patients had pain every day. A total of 28.6% of patients had symptoms of neuropathic pain. Joint pain was the most common type of pain. Pain caused by ischemic ulcers was less common than other types of pain but was rated as most painful by patients. Severe joint pain, everyday pain, and symptoms of neuropathic pain in SSc were associated with more severe disease and poorer quality of life. There was a positive correlation between depression and intensity of pain in patients with SSc. Besides addressing issues on involvement and dysfunction of different organs, clinicians should also consider pain, as well as other psychosocial aspects, in patients with SSc.

Clinical Implications

In routine clinical practice, health care professionals draw little attention to pain in patients with SSc. However, it has been found that the vast majority of patients suffer from different types of pain literally every day. Having in mind the adverse effects of pain on functional ability and social and emotional well-being, we recommend assessing pain in patients with SSc on a regular basis and applying adequate pharmacologic and nonpharmacologic therapy to decrease intensity of pain and improve patients' quality of life.

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