
A three-year follow-up study of the development of joint contractures in 131 patients with systemic sclerosis

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ABSTRACT

Objective. To analyse the correlation between the number of joint-contractions and other major clinical findings in a follow-up study of 131 patients with systemic sclerosis (SSc).

Methods. The range of motion of joints (ROM), HAQ-DI, and the major clinical characteristics were assessed.

Results. A high frequency of contractures (ROM<75% of the normal) were present at baseline in small joints of the hand (82%), wrists (75%), and shoulders (50%). ROM of the dominant side hand was significantly more decreased compared to the non-dominant side. The number of the upper extremity contractures correlated positively with ESR ($p<0.01$), CRP ($p<0.01$), HAQ-DI ($p<0.01$), and negatively with forced vital capacity (FVC) ($p<0.05$). The number of contractures was not significantly different in cases with early (≤ 4 years) and late disease duration in both the limited and diffuse subgroups. During the three-year follow-up period, an increase in the number of joint contractures (ROM<75%) was associated with an increase of ESR, modified Rodnan's skin score, and the European Scleroderma Study Group Activity Index by multiple linear regression analysis.

Univariate analysis over a six-year period demonstrated poor outcome in patients with more than ten contractures, or more than four contractures of unilateral hand-joints.

Conclusion. Contractures predominantly develop during the early years following disease onset in both SSc subgroups. Inflammation and skin-involvement are significant contributing factors for the development of contractures. The dominant hand may be more pronouncedly impaired compared to the non-dominant side. A high number of joint-contractions might be an unfavourable prognostic factor in SSc.

Introduction

Systemic sclerosis (SSc) is a connective tissue disease characterised by fibrosis of the skin, musculoskeletal system and internal organs associated with vasculopathy and late stage tissue atrophy (1, 2). Musculoskeletal manifestations are a major cause of morbidity and disability, including arthralgia/arthritis, tendon friction rubs, joint contractures, digital tuft resorption, subcutaneous calcinosis, and muscle weakness. Joint contractures have been reported to occur in up to 31% to 97% of SSc patients (1, 3-6). Hands are commonly affected, leading to significant disability in both the limited cutaneous (lcSSc) and diffuse cutaneous (dcSSc) subsets of SSc (4-9).

SSc generally starts with Raynaud's phenomenon. Polyarthralgia and joint stiffness are also usual early complaints in 36–80% of patients (3-7). Local skin thickening, involvements of tendons, tendon sheaths/retinacula as well as mild arthritis lead to the development of early contractures. Based on sonographic investigations, the increased thickness of retinacula of the wrists or ankles is in close relations with the sign of tendon friction rubs (10). Histological evidence of synovitis has been found in up to 66% of synovial biopsies from patients with late stage SSc (2, 3). Hand-digital and/or wrist arthritis were found in 46–57% by ultrasonography (5, 9-13), or detected in 47–100% by magnetic resonance imaging (MRI) (5, 6, 9, 13-15) in recent studies. Typical contractures and deformities of the joints of the hand consist of decreased flexion of the metacarpophalangeal (MCP) joint, impaired extension of the proximal and distal interphalangeal (PIP and DIP) joint, and decreased abduction of the thumb (6-9).

Little is known about the development and changes of joint involvement in SSc. Although there is some evidence for the

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efficacy of rehabilitation techniques for musculoskeletal impairments (16–19), useful preventive measures and optimal therapeutic modalities for joint contractures are not yet known, with only few observational studies, with a duration longer than one year, available on joint function (16, 17, 20, 21).

With regard to the outcome of SSc, previous findings have shown that besides the diffuse skin involvement (22–32), anti-DNA-topoisomerase I autoantibody positivity (22, 23, 28) and internal organ involvement including pulmonary (22–28), heart (22–25, 27, 29), renal (22, 24, 26, 29, 32) or gastrointestinal (25, 27), as musculoskeletal abnormality, the appearance of large joint contractures (22, 29) are associated with poor outcome of disease. Laboratory findings indicating inflammation increased ESR (22, 24, 30, 32) is also known to be unfavourable prognostic signs.

The aim of this study was to perform a three-year longitudinal study to observe the developments and changes of joint contractures, and assess their association with disease outcome. Furthermore, this particular study was extended up to 6 years to better evaluate the impact of joint contracture on the outcome of SSc over a longer period.

We found that joint contractures, range of motion (ROM) less than 75% of the normal, developed early in the first four years of the disease, with inflammation and a greater skin-involvement as outstanding contributing factors. It could also be shown that more than ten contractures in the limbs, or more than four contractures in the joints of one hand, might be unfavourable prognostic factors.

Patients and methods

One hundred and thirty-one consecutive Caucasian patients, 119 females and 12 males, 41 with dcSSc, 90 with lcSSc were included in the study. Every patient fulfilled the criteria proposed by LeRoy *et al.* (33). At baseline, their mean age was 55.9 ± 11.6 years (\pm SD), with a mean disease duration of 8.1 ± 7.2 years from the first non-Raynaud's symptom. The mean follow-up time was 4.43 ± 3.34 years. Nine deaths caused by SSc were recorded during the

investigated three-year period. Six patients were lost to follow-up, one died for reasons other than SSc. The major clinical characteristics of the patients were recorded as described earlier (34). For each patient electrocardiogram and echocardiography were performed. Cardiac catheterisation was initiated in the presence of signs of right ventricular involvement on echocardiography: (i) tricuspidal insufficiency diagnosed by flow velocity over 3m/s or consistently at a rate of 2.5–3m/s in the presence of unexplained dyspnea; (ii) signs of right ventricular hypertrophy/dilatation, or right ventricular D sign. Right heart catheterisation was performed according to the actual clinical guidelines to verify the diagnosis of PAH. The measurements were done at rest as well as during physical load (a 3-min bench-fly physical stress test with 1 kg dumbbells) (33). Diagnosis was established based on the mean pulmonary artery pressure values (mPAP) using the modified Venice criteria (mPAP over 25 mmHg at rest or over 30 mmHg on exertion in the absence of rise in the pulmonary capillary wedge pressure (less than 15 mmHg) (35).

Each early diffuse SSc case and patients having forced vital capacity (FVC) <80% of predicted value underwent high resolution computed tomography (HRCT) of the lungs aiming to assess interstitial lung disease.

The joint function of patients was evaluated at baseline, and at the end of the first and third years. Investigations of joint movements included the assessment of ROM and contractures of the MCPs and PIPs II, III, the wrists, the elbows, the shoulders, the hips, the knees and the ankles which were evaluated by three experienced physical therapists (ZB, HF and KH). After a practicing period the intra-class correlation coefficient (ICC) showed a good agreement (>88%) in measurements of ROM of the above mentioned joints in ten patients between the three physiotherapists in repeated evaluations.

Limitation in ROM greater than 25% of the normal range was considered a 'contracture'. The normal ROM of the wrist was considered 150 degrees in flexion-extension, less than 75% of

ROM was calculated as <115 degrees, less than 50% of ROM was <75 degrees. The average normal ROM of the wrist in radial-ulnar abduction was considered 50 degrees, in MCP II, III flexion-extension 125, in PIP II, III flexion-extension 100, in shoulder retroflexion- flexion-extension 240, in shoulder abduction-adduction 225, in shoulder external-internal rotation 180, in elbow flexion-extension 145, in hip flexion-extension 100, in hip abduction-adduction 50 and hip external-internal rotation 40, in knee flexion-extension 135, in ankle flexion-extension and in ankle inversion-eversion 70 degrees (36).

Modified Rodnan's skin score (MRSS) (37), European Scleroderma Study Group Activity Index (EScSG Activity Index) (38), Health Assessment Questionnaire Disability Index (HAQ-DI) (39, 40), Disabilities of the Arm, Shoulder, and Hand (DASH) (34), and Hand Anatomic Index (HAI) (41) were also calculated. HAI was measured as distance of open hand span minus closed hand span divided by the maximum lateral height of the hand.

Antinuclear antibody (ANA), anti-centromere antibody (ACA), anti-DNA-topoisomerase I, anti-cyclic citrullinated peptide autoantibodies (anti-CCP) and rheumatoid factor (RF) were detected using commercial ELISA-kits.

At baseline, the patients underwent a five-day training programme consisting of ROM improvement, muscle strengthening and stretching exercises for hands, mouth and all large joints. During the practical training, each patient enrolled in the study received verbal and written instructions about the exercises they should do at home. The patients were also educated about minimising Raynaud's attacks during daily living tasks, and protecting their skin and joints. The education and clinical treatment programmes were repeated every 6–12 months over the three years of the study.

Over the extended 6-year follow-up period, fifteen deaths caused by SSc were recorded. Six patients were lost to follow-up, and three died for reasons other than SSc.

The local Ethics Committee authorised the trial, and all patients formally agreed to participate (No. 2720/2006).

Statistical analysis

The distribution of values was assessed using the Kolmogorov-Smirnov test. Changes of ROM degrees were analysed with the Wilcoxon signed rank test. Analysis of frequency of joint involvement in the subgroups was performed by using the Mann-Whitney U-test. Correlations were determined using the Spearman's correlation coefficient. To investigate factors influencing changes in the number of contractures, multiple linear regression with stepwise selection was used. Kaplan-Meier survival curves and log rank tests were performed. Items with significant effects on survival by univariate method, and the age/gender of the patient were entered into the Cox proportional hazards model. The minimum set of predictive variables was determined by backward stepwise selection. Statistical analyses were performed using IBM SPSS Statistics v 20.0 (IBM's Corporate, New York, USA).

Results

Demographic data and general clinical characteristics of the patients are shown in Table I. During the three-year follow-up MCP II and III joints were most commonly affected, contractures (ROM<75%) were present in 73–82% of the patients. In PIP II-III flexion-extension were impaired in 34–43%. Contractures in wrist flexion-extension were found in 69–75%, adduction-abduction in 18–22%. Impaired flexion-extension of the elbows appeared only in 1–2% of the patients. Shoulder contractures in flexion-extension were present in 49–50%, adduction-abduction in 13–15%, rotation in 9–11%. Hip contractures in rotation and flexion-extension were found in 7–8%, abduction in 1–2%, knee flexion-extension ROM was decreased in 9–11%, ankle extension-flexion in 8%.

More contractures were found in dcSSc than lcSSc, and in anti-DNA-topoisomerase I positive patients compared to patients without those particular antibodies (Table II). The presence of ACA, RF or anti-CCP antibodies was not associated with an increased number of contractures in our patients. A significant difference was present in

Table I. Demographic and clinical data of 131 patients with systemic sclerosis (SSc).

	lcSSc	dcSSc
Number of patients	90	41
Females	82	34
Mean age \pm SD (y)	57.4 \pm 10.3	52.6 \pm 13.8
Disease duration \pm SD (y)	8.6 \pm 7.5	7.0 \pm 6.3
SSc duration \leq 4 years	34	17
Interstitial lung disease	47 (52%)	29 (71%)
FVC: 50–80% ^s	38 (42%)	27 (66%)
FVC <50% ^s	0	2 (5%)
Cardiac involvement*	57 (63%)	25 (61%)
Subcutaneous calcinosis of hands by x-ray	18 (20%)	6 (13%)
Active digital ulcers	12 (13%)	8 (19%)
<i>Antibody profile:</i>		
Anti-DNA topoisomerase I	22 (24%)	30 (73%)
Anticentromere antibody	18 (20%)	1 (2%)
Rheumatoid factor	25 (17%)	5 (12%)
Anti-CCP	7 (11%)	3 (12%)

FVC: forced vital capacity of the lung. *Conduction defects, arrhythmias, pericarditis, myocardial ischaemia on ECG and/or pulmonary arterial hypertension, anti-CCP: Anti-cyclic citrullinated peptide autoantibodies.

the number of contractures between patients with interstitial lung disease (ILD) and those without lung involvement, as well as between patients with and without active digital ulcers and subcutaneous calcinosis (Table II).

Seven patients with lcSSc and three with dcSSc had elevated anti-CCP autoantibodies in their sera, among them five showed also positivity for rheumatoid factor, six patients for anti-topoisomerase, two for anticentromere antibodies and one for RNA polymerase III. All of them had hand radiographs. Five of them were normal; calcinosis was observed in one, acroosteolysis in two. Only one of them presented erosions and periarticular osteoporosis. Three patients had osteoarthritis type narrowing of articular space in their hand joints.

There was no significant difference in the number of contractures between male and female genders, cases with and without arterial pulmonary hypertension or skin hypo/hyperpigmentation, respectively (Table II).

The median of modified Rodnan's skin scores was higher ($p<0.01$) for patients with joint contractures (median /quartiles/: 4.5 /3.25–11/) than for patients without it (1.75 /1.3–5/) at baseline as well as in all of the investigations during the three years.

There was no difference in the number of contractures (ROM<75%) between cases of \leq 4 year disease duration

compared to those of >4 year disease duration. The median number of contractures in cases ($n=52$) with short disease duration (\leq 4 years) was 8 (6–11; 25–75% quartiles), which was the same in patients with longer disease duration (median contractures 8, range 6–13; 25–75% quartiles). Similar findings were obtained if we separately analysed the lcSSc and dcSSc subsets (data not shown).

At baseline, the number of 'severe contractures' (ROM<50%) of the upper extremities correlated positively with erythrocyte sedimentation rate (ESR) (ρ : 0.249, $p<0.01$), serum level of C-reactive protein (CRP) (ρ : 0.319, $p<0.01$), HAQ-DI (ρ : 0.386, $p<0.01$) and DASH (ρ : 0.341, $p<0.001$). Conversely, a negative correlation was found between 'severe contractures' of the upper extremity and forced vital capacity (FVC) (ρ : -0.251, $p<0.05$). Similar correlations were detected also at the first and third-year investigation (data not shown). The large joints in lower extremities were less frequently affected (13%), and did not show significant associations with inflammatory parameters, nor cardiac or pulmonary involvements.

Both the overall number of joint contractures and the number of 'severe contractures' in all four limbs, showed a strong correlation ($p<0.001$) with the number of contractures in either of the

Table II. Median number of joint-contractures* (ROM<75%) in different subgroups of 131 patients with systemic sclerosis (SSc) at baseline.

Subsets (n)	Symptom manifestations		<i>p</i> [§]
	present	absent	
	no. of contractures*		
Diffuse SSc skin involvement (41)	10 (8; 14)	7 (4; 10)	<0.001
Skin hypo/hyperpigmentation (33)	8 (6; 12)	8 (6; 12)	0.304
Active digital ulcers (20)	11 (7; 17)	8 (6; 11)	0.050
Subcutaneous calcinosis (24)	9 (7; 12)	7 (6; 11)	0.042
Detected fibrosis on HRCT (76)	9 (7; 13)	7 (5; 11)	0.002
Pulmonary arterial hypertension (10)	8 (6; 12)	8 (6; 12)	0.859
Anticentromere antibodies (19)	8 (6; 12)	8 (6; 11)	0.624
Anti-DNA-topoisomerase I (52)	10 (7; 13)	7 (5; 11)	0.016
Rheumatoid factor (30)	8 (5; 14)	8 (6; 12)	0.072
Anti-CCP (10)	11 (7; 14)	8 (6; 12)	0.060

*Median (quartiles) number of contractures; the metacarpophalangeal joints (MCP) II and III, the proximal interphalangeal joints (PIP) II and III, wrists, elbows, shoulders, hips, knees, ankles were evaluated in both side (30 different joint movements together). ROM: Range of motion, §*p*-values using Mann-Whitney U-test, HRCT: High Resolution Computed Tomography anti-CCP: Anti-cyclic citrullinated peptide autoantibodies.

upper extremities (rho: 0,953–0,957 and 0,939–0,950 respectively).

Regarding the effect of therapy, in the early SSc group (duration ≤4 years) a greater increase (*p*<0.05) in the number of contractures was observed in the subgroup receiving cytostatic therapy (n=58), than in the group not undergoing cytostatic treatment (n=73). In patients with longer disease duration (>4 years) no difference was found in the number of contractures between patients treated with cytostatic agents

and those who were not treated. The same result was found when the lcSSc and dcSSc cases were separately evaluated. Similar results were obtained in the group undergoing cyclophosphamide (CPH) therapy (n=39), and in the group with cytostatic agents different from CPH therapy (n=19; methotrexate, azathioprine, or leflunomide). Cases treated with cytostatics had significantly more contractures (*p*<0.05), lower FVC and diffusing capacity of the lung for carbon monoxide (DLCO)

(*p*<0.05), as well as a higher skin score (*p*<0.01) compared to the rest of the investigated patients.

Twenty-one patients with lcSSc and 27 with dcSSc were treated with methylprednisolone at the usual dosage of six milligram. No significant difference could be found in changes in the number of contractures between the groups treated or not with steroids during the follow-up both in early and late duration groups.

Dominant versus non-dominant side

Comparison of the ROM of the joints in dominant and non-dominant sides of the body is shown in Table III. Concerning the hand joints' ROM (Table III), as well as, the number of contractures of all investigated joints (*p*<0.01) (data not shown), the dominant side was significantly more impaired, while no such a difference was observed in the large joints. In addition the median value of HAI was significantly less (worse) in the dominant side compared to the non-dominant side in all investigations during the three years (Table III).

Changes in the number of joint contractures

Over the three-year follow-up only the MCP joints of digits II and III,

Table III. Results of three-year longitudinal evaluations of range of motions (ROM) and functional tests of dominant *versus* non-dominant sides in 131 patients with systemic sclerosis.

	Baseline n=131		1-st year n=123		3-rd year n=115		<i>p</i> ¹ Baseline/ 1st y	<i>p</i> ² Baseline/ 3rd y
	Median range of motions in degrees (IQR)							
	Non-dominant	Dominant	Non-dominant	Dominant	Non-dominant	Dominant		
MCP II extension-flexion	82 (28)**	78 (30)	100 (26)**	91 (27)	98 (25)**	81 (31)	0.000	0.000
MCP III extension-flexion	80 (28)	80 (30)	98 (31)**	92 (28)	96 (25)**	91 (29)	0.000	0.000
PIP II extension-flexion	82 (29)*	80 (26)	86 (27)*	84 (26)	83 (26)	81 (28)	0.129	0.509
PIP III extension-flexion	86 (24)*	80 (24)	90 (20)*	87 (24)	88 (21)**	83 (23)	0.024	0.442
Wrist extension-flexion	98 (48)**	90 (45)	104 (41)**	102 (33)	103 (36)**	96 (38)	0.005	0.460
abduction-adduction	58 (30)	55 (27)	53 (19)	54 (17)	54 (19)*	52 (24)	0.021	0.000
Knee extension-flexion	122 (48)	122 (45)	128 (41)*	126 (33)	120 (36)	121 (38)	0.001	0.800
<i>Median scores of the tests (IQR)</i>								
HAI	2.5 (1.5)**	2.16 (1.6)	2.7 (1.3)**	2.17 (1.2)	2.4 (1.2)**	2.09 (1.2)	0.963	0.139
HAQ-DI	1 (1.25)		1.125 (1.25)		0.875 (1.25)		0.940	0.780
DASH	31.0 (34)		33.6 (34)		35.3 (31)		0.125	0.079

IQR: interquartile range; MCP: metacarpophalangeal joints; PIP: proximal interphalangeal joints; lcSSc: limited cutaneous SSc; dcSSc: diffuse cutaneous SSc; HAQ-DI: Health Assessment Questionnaire Disability Index (35); DASH: Disabilities of the Arm, Shoulder, and Hand (32); HAI: Hand Anatomic Index (37).

p*<0.05; *p*<0.001 Differences between results ROMs of joint in dominant and non-dominant sides (Wilcoxon signed rank test).

*p*¹: comparative results of ROM degrees at baseline to 1st year investigation; *p*²: comparative results of ROM degrees at baseline to 3rd year investigation (Wilcoxon signed rank test).

and extension-flexion of the shoulders showed some significant improvement (Table III). These particular findings were similar in both the dcSSc and lcSSc subset (data not shown). However, the other large joints did not show any significant change.

The values of the functional indices (HAQ-DI and DASH) did not show any significant changes during the three years, except for the dcSSc group ($n=17$) with a disease duration ≤ 4 years, where HAQ-DI showed some improvement ($p<0.05$) at the end of the first year. However, the HAQ-DI of this particular dcSSc group became worse by the end of the third year. Neither DASH nor HAI changed significantly in this particular subgroup of dcSSc cases (Table III). The increase in the overall number of contractures (ROM $<75\%$) was independently associated with the increase of MRSS, ESR and EScSG Activity Index ($p<0.05$) during the one-year follow-up by multiple linear regression with stepwise selection.

Survival analysis

Univariate analysis demonstrated that male gender, presence of diffuse SSc, elevated ESR ($>30\text{mm/h}$), decreased body mass index (BMI <18.5), left ventricular ejection fraction less than 50% (LVEF $<50\%$), resting heart pulse rate $> 85/\text{min}$), DLCO $<50\%$, gastric antral vascular ectasia (GAVE) and presence of pericardial fluid at baseline caused a poor prognosis. An unfavourable disease outcome was also demonstrated when the overall number of contractures (ROM $<75\%$) was more than ten ($n=43$) ($p=0.047$), as well as in the presence of more than four contractures appearing in one hand joints ($n=59$) ($p=0.038$) (Fig. 1).

The stepwise selection of Cox model showed that an LVEF $<50\%$ ($p=0.002$), GAVE ($p=0.013$), presence of pericardial fluid ($p=0.041$), and raised ESR at baseline ($P=0.052$) were unfavourable prognostic factors. The number of joint contractures was not found to be an independent risk factor regarding outcome.

Discussion

In this observational study, we investigated the natural course of contractures

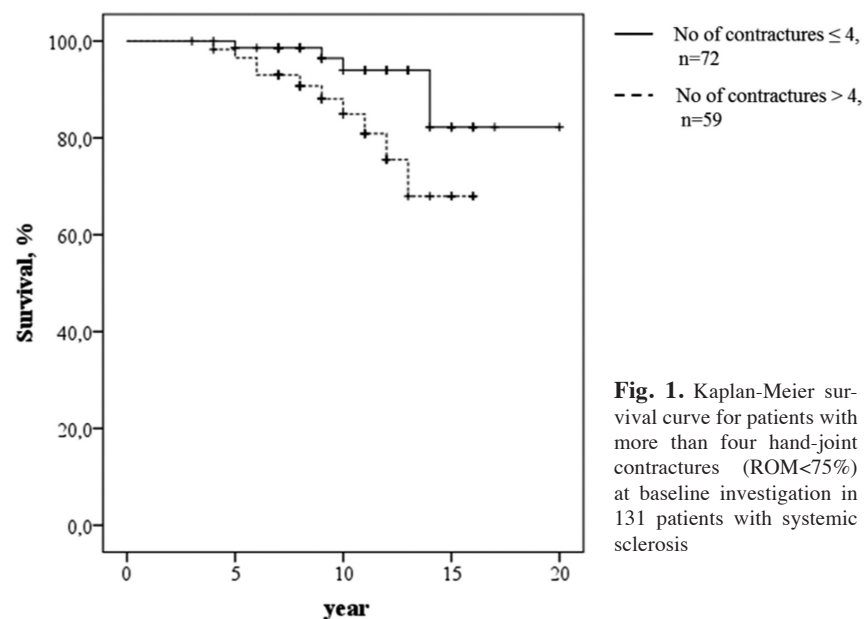


Fig. 1. Kaplan-Meier survival curve for patients with more than four hand-joint contractures (ROM $<75\%$) at baseline investigation in 131 patients with systemic sclerosis

in patients with SSc. Contractures represent one of the major causes of disability and poor quality of life in this disease. There are several contributing factors to the decrease of ROM of the joints including joint destruction, tendon inflammation, fibrosis, dermal thickening, skin ulcers, vascular injury and calcinosis (1, 2, 5-10). In recent studies (8-15, 42), ultrasonography and MRI showed synovial inflammation (47-88%), bone oedema (37-53%), erosions (41-87%), and tenosynovitis (10.5-53%) in a remarkable percent of patients. Previous studies indicated that joint contractures are more prevalent in SSc cases with pulmonary involvement, active digital ulcers or subcutaneous calcinosis (6, 7, 20, 42-45). In this study, we were able to confirm these particular clinical associations (Table II).

In accordance with previous studies (1, 2, 44, 45) we have found a high frequency of contractures in a relatively large consecutive SSc patient cohort. Contractures (defined as ROM $<75\%$ of the normal range) were most frequently present in hand joints (82%). The large joints in lower extremities were less frequently affected, and that did not show significant associations with mortality nor internal (cardiac or pulmonary) involvements.

In both dcSSc and lcSSc cases with a disease duration of four or less years, we found a similar number of contrac-

tures compared to the patients with longer disease duration (>4 years), indicating that contractures with a significant ROM limitation develop early, during the first years following the onset of SSc.

The correlation between inflammatory markers and contractures described in recent studies (1, 2, 6, 7, 22, 42) is also confirmed by our results, suggesting that persistent inflammation is probably the main contributor to the development of contractures. Similarly to rheumatoid arthritis, very early therapeutic intervention may be required to preserve joint movements (5, 6).

Severe cases with significantly more contractures and a lower rate of lung function tests were treated with cytostatic agents. This can explain the higher rate of the increase in the number of contractures in this subgroup opposite to the group without cytostatic therapy in the early cases with SSc during follow-up. In the number of contractures no significant difference could be found in the change between the groups treated or not with steroids during the follow up. Further investigations are needed to find the evidence-based therapy preventing decrease of ROM of joints. One perspective would be regular assessment of joint contractures by ultrasounds in order to better describe the lesions that account for the decrease of the range of motion in the joints.

In agreement with previous studies (6, 20, 21, 46, 47) our data did not show more contractures among anti-CCP positive SSc cases than among the anti-CCP negative patients, therefore we also confirm that the presence of anti-CCP is not a marker for functional articular impairment in SSc.

The present study indicates that extensive joint involvement could be an unfavourable prognostic factor in SSc. Similar observations were found in a drug trial study, where the presence of large joint contractures was predictive of poor outcome, and the development scleroderma renal crisis (22, 29).

Interestingly, small joints on the dominant-side hand were more pronouncedly affected based on both ROM values and number of contractures. There is little data comparing affected joints on the two sides of the body. An Italian study by Del Rosso *et al.* examining the validity of the Hand Mobility in Scleroderma (HAMIS) test (48), showed that the values of the HAMIS test were worse in the right side compared to the left side. In the original study describing the HAMIS test (49), Sandqvist and Eklund did not find any difference in the results between the two sides. In the validation study of the delta finger-to-palm measurement, Torok and her co-workers (50) have also found that the right hand of patients presented worse results compared to the left hand. In the comparative radiological analysis of right and left hand by Koutaissoff and her co-workers (42), tuft acro-osteolysis and calcinosis were found in slightly higher percentage on the right hand than on the left hand (19% vs. 17.6% and 12% vs. 9.1%, respectively), but joint space narrowing, marginal erosions, surface erosions and collapse arthropathy were no different. A larger patient population is needed for further evaluation of this phenomenon. The greater damage to the small joints on the dominant side may suggest that over-use could be detrimental for hand function in SSc.

Regular exercise could affect the natural course of development of joint contractures, but it is improbable that it would worsen hand function. Our poor ROM results of the hand joints with-

out any training could have been rather worse at the end of the follow-up.

The number of upper or lower extremity contractures strongly correlated with functional test results (HAQ-DI, DASH), demonstrating that these particular simple tests are suitable for monitoring contractures associated with decreased ROM (34, 51). The total number of contractures showed a strong correlation with the number of contractures on an upper extremity, therefore it may be sufficient to monitor contractures on a single upper extremity only. The increase in the number of contractures was independently associated with the increase of MRSS, ESR and EScSG Activity Index, indicating that very early anti-inflammatory therapy (DMARDS or biologics) may be efficient in preventing the development of severe impairment of articular movement (6).

The results of the analysis of the EUSTAR database (4) could be confirmed by our observation in a way that in both dcSSc and lcSSc cases with a disease duration of four or less years, we found a similar number of contractures compared to patients with a longer disease duration (>4 years), referring to the fact that contractures with a significant ROM limitation develop early, during the first years following the onset of SSc.

Weaknesses of our study include our inability to monitor compliance with home exercise regimens, and the relatively small number of early diffuse SSc patients involved. SSc has many subtypes based on disease duration and clinical characteristics hence, enrolling a larger number of patients of the same subtype would have been better. Other potential limitation of the study may be the lack of radiological analysis of develop and changes of contractures.

The strength of our study is the fact that we were able to follow the 131 patients for an extended period of time (3 years), with a very low drop-out rate.

In conclusion, inflammation and disease activity seem to be the main factors contributing to development of joint contractures. We underline that contractures develop already in the first years following disease onset, there-

fore early treatment of vasculopathy and the presence of inflammation, and tenosynovitis which are often subclinical, seems to be a reasonable option.

We found a strong correlation between the number of contractures and the HAQ-DI and DASH, indicating that each of these particular instruments is an appropriate tool for monitoring the development of contractures in patients with SSc.

Key messages

- Joint contractures develop during the first years of the disease course.
- Prominent use of dominant hand may contribute to its increased impairment compared to non-dominant extremity.
- The number of contractures affecting the small joints of the hand might be a useful prognostic indicator.

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