Hands and feet radiologic involvements in systemic sclerosis

Fatemeh Badiee1, Alireza Fatemi2, Reza Zahedpasha1, Mohammad Hadi Gharib3,4, Mohammadhassan Jokar1, Somayeh Livani4,5, Mehrdad Aghaie1 and Nafiseh Abdolahi1*

Abstract

Aim Systemic sclerosis (SSc) is a rare autoimmune disorder characterized by vascular and fibrosing involvement of the skin and internal organs. In this study, we determined the prevalence and characteristics of radiological hands and feet involvements in Iranian SSc patients to identify the associations between clinical features and radiologic findings.

Methods 43 SSc patients (41 women and 2 men), with a median age of 44.8 years (ranges 26–70 years) and a mean disease duration of 11.8 years (ranges 2–28 years) were studied in this cross-sectional study.

Results 42 patients had radiological changes both in their hands and feet. Only one patient had alteration just in hand. The most frequent changes that we found in hand were Juxta-articular Osteoporosis (93%), Acro-osteolysis (58.2%), and Joint Space Narrowing (55.8%). The prevalence of joint space narrowing or acro-osteolysis was higher in subjects with active skin involvement [modified Rodnan skin score (mRSS) > 14] (16/21 vs. 4/16 for patients with inactive skin involvement (mRSS < 14); \( p = 0.002 \)). The most frequent changes that we found in the foot were Juxta-articular Osteoporosis (93%), Acro-osteolysis (46.5%), Joint Space Narrowing (58.1%), and subluxation (44.2%). The presence of anti-ccp antibody was detected in 4 (9.3%), while positive rheumatoid factor was found in 13 (30.2%) of SSc patients.

Conclusion This study corroborates that arthropathy is common in SSc patients. The introduction of the specific radiological involvements of SSc needs to be confirmed by further studies, in order to define the appropriate prognosis and treatment of patients.

Keywords Systemic Sclerosis, Arthropathy, Acro-osteolysis, Hand Stiffness, Joint space narrowing, Juxta-articular osteoporosis

Introduction

Systemic sclerosis (SSc) is a rare autoimmune disorder characterized by a vascular and fibrosing involvement of the skin and internal organs [1]. Hand stiffness and articular pain are two of the highest rated symptoms in terms of frequency and moderate to severe impacting the quality of life of patients with SSc [2]. To date many distinct radiographic abnormalities of hand and foot have been recognized. Different proposals of radiographic classification patterns have been published [3, 4]. But there is not any specific pattern of radiological involvement recognized in SSc. There is a critical need for the
development and validation of some uniform system for identification of joint involvements in SSc (ie, as Sharp as findings known for rheumatoid arthritis). While the frequency of some findings such as foot subluxation in past studies were close and ranging from 13.1% [3] to 16% [5]; there were findings like hand joint space narrowing with controversial reported frequencies, ranging from 17.9% [6] to 75.3% [7]. Most reports on the prevalence of radiological involvements in SSc were on hand and from Western countries (Europe [3–5, 7–17], Canada [18], United States [19, 20] and Africa [21] with only four previous reports from Asia [6, 22–24]. Few studies evaluated radiographic changes in the feet and they were from Europe [3, 5, 25], Africa [21] and only one old from Asia [26]. Increasing our understanding of hand and foot involvements may make it possible to improve therapeutic approaches. Keeping in mind these findings, this study was undertaken first to determine the prevalence and characteristics of radiological hand and foot involvements in Iranian SSc patients and second, to identify disease–phenotype associations. To better investigation of radiological findings, we included only patients with disease duration (measured from the onset of the first symptom) ≥ 2 years and excluded those with rheumatoid arthritis-systemic sclerosis overlap syndromes or other overlap syndromes.

Methods

All SSc patients, fulfilling the American College of Rheumatology classification criteria for SSc [27], referred to Sayyad Shirazi Medical Education Center and rheumatologists’ offices in Gorgan (Golestan, Iran), were invited by telephone call. SSc patients with disease duration < 2 years or overlap syndromes were excluded. A total of 43 patients were evaluated in this cross-sectional study. All patients gave informed consent for all procedures and underwent skin examination. Active skin involvement was determined on the basis of modified Rodnan skin score (mRSS > 14) [28]. The following laboratory tests; fasting blood glucose (FBS), Hemoglobin A1c (HbA1c), rheumatoid factor (RF) and anti-cyclic citrullinated peptide (Anti-CCP) antibody were carried out. Radiographic examination, obtained at the moment of evaluation and clinical data collection. Standard anteroposterior views of both hands and feet were obtained for all patients. All radiographs were evaluated by a radiologist using a predefined set of radiographic findings according to the previous studies [3, 7]. Radiographs were examined directly on computer, and the two radiologists was blinded to serological data and severity of the SSc patients’ disease. Each finding was separately scored [0 (normal), 1 (mild), 2 (moderate), or 3 (severe)]. For the classification of extent of degenerative changes in X-ray, there is a well-known classification system called Kellgren Lawrence classification, which is a 4-class category. Class 2, 3 and 4 are assumed as mild, moderate and severe degenerative changes, respectively [29]. The clinical data of age, sex, cutaneous subtype as defined by Leroy et al. [30], disease duration (measured from the onset of the first symptom) and heart involvement; were collected from patients’ records. Occurrence of pericarditis, left ventricular ejection fraction (LEVF) < 55%, pericardial effusion, valve regurgitation, chamber hypertrophy, and primary pulmonary arterial pressure (PAP) on echocardiography were considered signs of scleroderma heart involvement. Pulmonary involvement was assessed by a new chest radiograph, reduced forced vital capacity (FVC) in pulmonary function tests (PFT), and fibrosis in high-resolution computed tomography (HRCT) of patients’ records. Pulmonary arterial hypertension (PAH) was defined as PAP higher than 25 mmHg on echocardiography. Gastrointestinal involvement was defined from the simultaneous study of these patients; based on the questionnaire about gastrointestinal symptoms [University of California at Los Angeles Scleroderma Clinical Trial Consortium (UCLA SCTS) 2.0] [31] and the abnormal findings of barium swallow and computed tomography (CT) enterography. Statistical analysis was undertaken using statistical packages for social sciences (16th version). Percentage, mean and standard deviation were used to describe the data, and Chi-square test was used to examine the relationship between variables. Also, P values less than 0.05 were considered statistically significant.

Results

We studied 43 SSc patients (41 women and 2 men), with a median age of 44.8 years (ranges 26–70 years) and a mean disease duration of 11.8 years (ranges 2–28 years). 23 patients had ISSc and 18 patients had dSSc (Two patients’ disease type was unspecified). Other detailed clinical and laboratory data are provided in Tables 1 and 4. 2 patients had radiological changes both in their hands and feet. Only one patient had modifications just in hand. She was middle-aged and had a long disease duration, diffuse subset, inactive skin involvement, and GI involvement. In particular, severe radiographic findings were less prevalent in the feet than in the hands (18.6% vs. 39.5%; P value < 0.05). The most frequent changes that we found in hand were Juxta-articular Osteoporosis (93%), Acro-osteolysis (58.2%), and Joint Space Narrowing (55.8%). Table 2 shows in detail the prevalence and distribution of each radiological change observed in hand. Figure 1A. The most frequent changes that we found in the foot were Juxta-articular Osteoporosis (93%), Acro-osteolysis (46.5%), Joint Space Narrowing (58.1%), and subluxation...
Foot radiological findings of patients with SSc are detailed in Table 3 and Fig. 1B. Eight patients had at least one severe radiographic change in the hand or foot. All of them were negative for anti-ccp antibody and except one whose skin type was unspecified; others had active skin involvement.

The presence of anti-ccp antibody was detected in 4 (9.3%), while positive RF was found in 13 (30.2%) of SSc patients. 12 was the lowest value accepted as a positive anti-ccp antibody. 25% of them had cardiac involvement and 75% had lung involvement. Except for one whose GI involvement was unspecified, all the others had GI involvement. All of them had hand joint space narrowing and hand and foot juxta-articular osteoporosis. Other clinical, laboratory and radiological characteristics of patients with SSc and positive anti-ccp antibodies are shown in Table 4.

Association between radiologic findings and features

Hand

The prevalence of joint space narrowing and acro-osteolysis were higher in subjects with active skin involvement (mRSS > 14) [16/21 vs. 4/16 for patients with inactive skin involvement (mRSS < 14); P value = 0.002]. Marginal erosion was significantly associated with GI involvement (13/25 vs. 0/13 for patients without GI involvement, P value = 0.001). Subluxation or flexion deformity tended to be associated with active skin involvement (mRSS > 14) [5/21 vs. 0/16 in patients with inactive skin involvement (mRSS < 14); P value = 0.05]. We found no significant difference between patients with and without other radiological changes in terms of clinical features, autoantibody profile, or organ involvement.

Feet

In our study, subluxation was found to be strongly associated with the young age group (< 44 years) (13/21 vs. 6/22 for patients in the middle age group, P value = 0.02). Tarsal degenerative pattern showed...
significant association with long disease duration (>10 years) [7/19 vs. 2/24 for patients with short disease duration (<10 years); \( P \) value = 0.03]. Diffuse osteopenia was associated with non-cardiac involvement (0/15 vs. 4/12 for patients with cardiac-involvement; \( P \) value = 0.02). It means that from 27 patients for whom cardiac-involvement had been evaluated; only four patients had diffuse osteopenia and none of them had cardiac involvement. Acro-osteolysis tended to be associated with the absence of rheumatoid factor (17/30 patients vs. 3/13 for patients with the presence of rheumatoid factor; \( P \) value = 0.05). The frequency of digital ulcers in our study population was less than 20% which may explain this lower-level difference. We found no significant difference between patients with and without other radiological changes in terms of clinical features, autoantibody profile, or organ involvement.

**Discussion**

Our results highlight the striking level of hand and foot involvement in SSc, as evaluated by X-ray. The severity and frequency of these findings are demonstrated in Tables 2 and 3.

Hand acro-osteolysis was seen in 58.2% of patients. It is nearly in agreement with the prevalence of other reports (9%–55%) [4–7, 12, 13, 17, 23, 32]. The distribution of hand acro-osteolysis severity in our patients was 65.1% (normal or mild) and 34.9% (moderate or severe). They were nearly in agreement with the prevalence of a study in England [10] and higher than another research in Iran [24]. We have found a higher frequency of foot acro-osteolysis (46.5%) than La Montagna's findings (8%) [5].

Prevalence of hand calcinosis in our series (6.9%) is lower than that reported in previous studies (10%–37.8%) [3–7, 9, 12, 13, 16, 17, 23, 24, 33]. But it is nearly in

---

**Fig. 1** A Hands radiographic images. B Foot radiographic images. A 46-year-old woman with SSc presented with joint pain. Hands and foot radiographic images show the following abnormality (arrows) on the left and right: 1-Bone erosion representing Juxta-articular Osteoporosis 2-Joint Space Narrowing with an abnormal distance between bones.
agreement with the recent study of Sakata and coworkers (10%) from Japan in 2019. Due to previous reports, Calcinosis was significantly associated with and most often seen in patients with digital ulcers. Digital ulcers were identified as independent predictors of the radiographic progression of calcinosis [4, 15].

We have found hand marginal erosion in 34.9% of patients, whereas was reported (6.7–17.1%) [7, 11, 16]. For a careful distinction between osteoarthritis- and inflammatory-related erosions Koutaissoff and coworkers [7] introduce marginal erosion. Marginal erosions are typical of arthritis while surface erosions are mostly observed in spondyloarthopathy or Calcium pyrophosphate dihydrate crystal deposition (CPPD) disease. We think this difference is because they grouped normal (score 0) and doubtful lesions (score 1) together (the corresponding areas were considered as “normal”), and evident (score 2) and severe lesions (score 3) together (the corresponding areas were considered as “abnormal”). But we grouped normal (score 0) and abnormal (score 1, 2, 3). Foot erosion was seen in 16.3% of our study group and is nearly in agreement with the prevalence of other reports (2.6%–13%) [3, 5, 21, 26].

The frequency of hand juxta-articular osteoporosis in SSc had been estimated at 12%–22.6% in previous studies [3, 7, 9, 11] and was 93% in our series. The frequency of foot juxta-articular osteoporosis in SSc had been estimated at 6.6% in previous studies [3] and was 93% in our series. Due to Koutaissoff and coworkers’ findings in their case–control study of 167 patients and 168 of age- and gender-matched controls; juxta-articular osteoporosis had never been observed in controls [7]. In Thietart et al. [34] case–control cohort study; they found that SSc may be a risk factor for low bone mineral density (BMD), with no significant association with the usual osteoporosis risk factors. Unless previous studies which the mean age was 52 and most of their patients were post-menopausal women, the mean age of our patients was 44.79 and only 35% were females around the age of 50. Overall, we could rule out the possibility of such an arthropathy, unrelated to SSc, occurring in our patients and we think it may represent a specific arthropathy in scleroderma.

The frequency of hand flexion deformity was 14% and agrees with previous studies (7%–55%) [3–6, 9, 16, 23]. It is close to Sakata and coworkers [23] published data (7%) from Japan in 2019. They said that flexion contracture was more prevalent in SSc patients with digital tip ulcers or digital pitting scars.

Hand subluxation was seen in 11.6% of our patients and agrees with the prevalence of other reports (4.8%–23%) [3, 5, 9, 23, 32]. Frequency of foot subluxation in our study group was higher (44.2%) than in previous studies (13.1%–16%) [3, 5]. Weight-bearing could be a risk factor but interestingly we have found a significant association between foot subluxation and the young age group (P value = 0.02). This is a new relation; So, we hypothesized that this may be due to specific arthropathy in SSc patients.

Prevalence of hand joint space narrowing was 55.8% and agrees with the prevalence of other reports (4.8%–75.3%) [4–7, 9, 15, 17, 21, 23, 32]. We have found foot joint space narrowing in 58.1% of patients but previous reports do not support this finding (5%–40%) [5, 21]. Foot para-articular calcification was rare in our series of

| Table 3 Foot Radiological Findings in patients with systemic sclerosis compared with other studies |
|----------------------------------|------------------|------------------|
| **Our study**                   | **Other studies**|
| Acro-osteolysis                 |                  |
| Mild                            | 8%               |
| Moderate                        | 6 (14%)          |
| Severe                          | 2 (4.7%)         |
| Hallux valgus                   |                  |
| Mild                            | 10 (23.3%)       |
| Moderate                        | 3 (7%)           |
| Severe                          | 7 (16.3%)        |
| Joint space narrowing           |                  |
| Mild                            | 25 (58.1%)       |
| Moderate                        | 16 (37.2%)       |
| Severe                          | 1 (2.3%)         |
| Erosions                        |                  |
| Mild                            | 7 (16.3%)        |
| Moderate                        | 4 (9.3%)         |
| Severe                          | 1 (2.3%)         |
| Para articular calcifications   |                  |
| Mild                            | 1 (2.3%)         |
| Moderate                        | 10 (40%)         |
| Severe                          | 6 (24.2%)        |
| Juxta-articular osteoporosis    |                  |
| Mild                            | 40 (93%)         |
| Moderate                        | 15 (34.9%)       |
| Severe                          | 24 (55.8%)       |
| Subluxation                     |                  |
| Mild                            | 19 (44.2%)       |
| Moderate                        | 12 (27.9%)       |
| Severe                          | 6 (14%)          |
| Diffuse osteopenia              |                  |
| Mild                            | 11 (25.6%)       |
| Moderate                        | 3 (7%)           |
| Severe                          | 8 (18.6%)        |
| Pencil-in-cup deformity         |                  |
| Mild                            | 3 (7%)           |
| Moderate                        | 2 (4.7%)         |
| Tarsal degenerative pattern     |                  |
| Mild                            | 9 (20.9%)        |
| Moderate                        | 7 (16.3%)        |
| Severe                          | 1 (2.3%)         |

To present a specific arthropathy in scleroderma.
Table 4  Clinical features of 4 female patients with systemic sclerosis and positive anti-ccp antibody

| Patient | Age (year) | Disease duration (year) | SSc subset | RF Anti-CCP antibody titre positive ≥6 | Organ involvement | Radiographic abnormalities | Foot |
|---------|------------|-------------------------|------------|----------------------------------------|-------------------|--------------------------|------|
|         |            |                         |            |                                        |                   |                          |      |
|         |            |                         |            |                                        | Heart             | Subluxation              |      |
|         |            |                         |            |                                        | Skin              | Juxta-articular           |      |
|         |            |                         |            |                                        | GI                | Subluxation              |      |
|         |            |                         |            |                                        | Lung              | Hallux valgus             |      |
|         |            |                         |            |                                        |                   | Periarticular calcification |      |
| 1       | 32         | 8                       | dSSc       | + 67.8                                 | Active            | +                        |      |
| 2       | 50         | 25                      | lSSc       | - 12.7                                 | Active            | +                        |      |
| 3       | 66         | 20                      | lSSc       | + 241                                  | Inactive          | -                        |      |
| 4       | 42         | 2                       | dSSc       | - 23                                   | Active            | -                        |      |

+ 1 mild, +2 moderate
*Unspecified
SSc patients (2.3%) consistent with frequency reported in other series (2.6%) [3]. The frequency of hand diffuse osteopenia was 18.6% and agrees with the prevalence of other reports (9.7%–46%) [3, 9]. The frequency of foot diffuse osteopenia was lower (25.6%) than in La Montagna and coworkers’ study (44.7%) [3]. Hand periarticular calcification was demonstrated in 6.6%–35.7% of previously reported SSc patients [3, 7] and was 4.7% in our study population. Hand or foot pencil-in-cup deformity was seen in 7% of patients. It is nearly in agreement with the prevalence of other reports (1.3%) [3]. Foot hallux valgus was seen in 23.3% of patients. It is nearly in agreement with the prevalence of other reports (26.3%) [3]. The frequency of foot tarsal degenerative pattern in our study group was higher (20.9%) than in previous studies (3.9%) [3].

These very disparate results may be accounted for differences in the number of patients, the combination of retrospective and prospective data, characteristics of the study population, the role of longitudinal studies on the hypothesis that foot changes began later, and few studies especially on foot involvements. It is worth mentioning that most of the radiological involvements we found; had a higher prevalence than the previous studies. Foot tarsal Degenerative Pattern was found to be significantly associated with long disease duration (> 10 years) (p = 0.03). There isn’t any other study to assess this relation. We hypothesized that degenerative changes could happen over time.

Foot diffuse osteopenia was associated with non-cardiac involvement (P value = 0.02). It means that of those who had cardiac involvement, none of them had diffuse osteopenia. Up to now, there isn’t any study that has exactly assessed this relation. Ashida and coworkers reported a significantly greater prevalence of heart involvement in the patients with Contracture of phalanges [35]. Tas and coworkers in 2012 reported a correlation between heart involvement and arthritis (concomitant erosions and joint space narrowing) [6].

We have found a significant association between hand marginal erosion and GI involvement (P value = 0.001). Ashida and coworkers reported significantly greater prevalence of esophageal involvement in the patients with Contracture of phalanges [35]. Erre and coworkers found a significantly association between finger flexion deformities or bone resorptions and esophageal involvement. Something that highlights the role of the fibrotic process on disease expression [9]. Sakata and coworkers found an association between calcinosis and GI involvement and between flexion contracture and GI involvement [23]. Due to Koutaissoff and coworkers’ findings in their case–control study of 167 patients and 168 of age-and gender-matched controls; Marginal erosions had never been observed in controls [7]. Keeping in mind this definition, and the previous reported association of bone resorption and esophageal involvement is consistent with the existence of a specific arthropathy in SSc unexplained by other arthropathies.

We have found a significant association between hand joint space narrowing or hand acro-osteolysis and active skin involvement (mRSS>14) (P value = 0.002). Hand subluxation or hand flexion deformity tended to be associated with active skin involvement (mRSS>14) (P value = 0.05). Due to Koutaissoff and coworkers [7] patients with tuft calcinosis had a significantly higher Rodnan-modified total skin score. La Montagna and coworkers found a significant correlation between flexion contractures in the hands and the severity score of skin (mRSS) [3]. It cannot be excluded that cutaneous and subcutaneous sclerosis or tenderness and/or swelling of joints have a determinant role in conditioning the joint anatomy. Nevertheless, this pathological link that we have found is noticeable. Especially in the case of the fact that previous studies had investigated mean modified Rodnan skin score instead of classifying mRSS. Thus, we think it could reflect a specific arthropathy in SSc unexplained by other arthropathies.

In our survey, positive RF was found in 30.2% of patients and was the same as what was detected in previous studies (3.9%–44%) [3–6, 9, 11, 15, 16]. Arco-osteolysis tended to be associated with the absence of rheumatoid factor (P value = 0.05). This is a new association. The presence of anti-ccp antibody was in 9.3% as suggested by published studies (1%–15%) [11, 36–43], so our data support these findings. We have found both joint space narrowing and marginal erosion in 3 out of 4 patients with positive anti-ccp antibody, consistent with the existence of primary erosive arthropathy in SSc unexplained by overlap with rheumatoid arthritis, as suggested by Auvuç et al. and Cuomo et al. [4, 11, 17].

Our study has several limitations. It was a cross-sectional and not a longitudinal radiological study, so it prevented the evaluation of the natural history of the damage in SSc. It was a retrospective study and analyzed a small number of patients. Large studies are required to confirm our results. Other limitations were the observational character of the trial and the lack of a control group. Also, juxta-articular osteoporosis is a subjective finding and it may have caused overdiagnosis in our study.

Conclusion
In conclusion, this study confirms that arthropathy is prevalent in SSc patients. Juxta-articular osteoporosis is the most common radiological manifestation of systemic
scleroderma arthropathy. There seems to be a significant relationship between radiological hand and foot involvement and active skin involvement, which requires studies with a larger sample size. Radiological involvements necessitate conducting studies with a larger sample size and considering a healthy control group.

Abbreviations

| Abbreviation | Description                     |
|--------------|----------------------------------|
| SSC          | Systemic sclerosis               |
| FBS          | Fasting blood glucose            |
| HbA1c        | Hemoglobin A1c                   |
| RF           | Rheumatoid factor               |
| Anti-CCP     | Anti-cyclic citrullinated peptide|
| LEVF         | Left ventricular ejection fraction|
| PAP          | Pulmonary arterial pressure      |
| FVC          | Forced vital capacity            |
| PFT          | Pulmonary function tests         |
| PAH          | Pulmonary arterial hypertension  |
| UCLA SCTS    | University of California at Los Angeles scleroderma clinical trial consortium |
| CT           | Computed tomography              |
| LcSSc        | Limited cutaneous systemic sclerosis |
| DcSSc        | Diffuse cutaneous systemic sclerosis |
| CPPD         | Calcium pyrophosphate dihydrate crystal deposition |
| BMD          | Bone mineral density             |

Acknowledgements

Special thanks to all the fellow authors who contributed to this article.

Role of the funder/sponsor

The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Author contributions

FB: Design of the work and data interpretation. AF: Manuscript writing and Data entry. RZ: Manuscript writing. MHG and SL: Radiologic analysis and interpretation. MJ, MA and NA: Data interpretation and substantial manuscript revision. FB: Contribution: Patients visiting, necessary data collection. All authors read and approved the final manuscript.

Funding

The Golestan University of Medical Sciences financially supported this work.

Availability of data and materials

Data supporting the findings of this study are available from the corresponding author, but restrictions apply to the availability of these data, which were used under license for the current study, and are therefore not publicly available. However, the data is available in the form of an Excel file from the authors upon reasonable request and with the permission of Nafisseh Abdolah.

Declarations

Ethical approval and consent to participate

The study and all experimental protocols were approved by the Professional Ethics Committee of the Golestan University of Medical Sciences with the ethical code of ir.goums.rec.1396.74. The informed consent was also obtained from all patients for the implementation of this project. All methods were performed in accordance with the relevant guidelines and regulations.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

References

1. Denton CP, Khanna D. Systemic sclerosis. The Lancet. 2017;390(10103):1685–99.
2. Bassel M, Hudson M, Taillefer SS, Schier O, Baron M, Thomsbs BD. Frequency and impact of symptoms experienced by patients with systemic sclerosis: results from a Canadian National Survey. Rheumatology. 2010;50(4):762–7.
3. La Montagna G, Sodano A, Capurro V, Malesci D, Valentini G. The arthropathy of systemic sclerosis: a 12 month prospective clinical and imaging study. Skeletal Radiol. 2005;34(1):35–41.
4. Avouac J, Guerini H, Wipff J, Assous N, Chevrot A, Kahan A, et al. Radiological hand involvement in systemic sclerosis. Ann Rheum Dis. 2006;65(8):1088–92.
5. La Montagna G, Baruffo A, Tirri R, Buono G, Valentini G. Foot involvement in systemic sclerosis: a longitudinal study of 100 patients. Semin Arthritis Rheum. 2002;31(4):248–55. https://doi.org/10.1053/sahr.2002.29493.
6. Tas DA, Erken E, Sakalli H, Yucel AE. Evaluating hand in systemic sclerosis. Rheumatol Int. 2012;32(11):3581–6.
7. Koutaissof S, Vanthyuyen M, Smith V, De Langhe E, Depresseux G, Westhoven R, De Keyser F, Malghem J, Houssiau FA. Hand radiological damage in systemic sclerosis: comparison with a control group and clinical and functional correlations. Semin Arthritis Rheum. 2011;40(5):455–60. https://doi.org/10.1016/j.semarthrit.2010.06.008.
8. Catoggio L, Evison G, Harkness J, Maddison P. The arthropathy of systemic sclerosis (scleroderma); comparison with mixed connective tissue disease. Clin Exp Rheumatol. 1983;1(2):101–12.
9. Erre GL, Marongiu A, Fenu P, Faedda R, Masala A, Sanna M, et al. The “sclerodermic hand”: a radiological and clinical study. Joint Bone Spine. 2008;75(4):426–31.
10. Johnstone EM, Hutchinson CE, Vail A, Chevance A, Herrick AL. Acro-osteolysis in systemic sclerosis is associated with digital ischaemia and severe calcinosis. Rheumatology. 2012;51(12):2334–8.
11. Ingegnoli F, Galliati V, Zeni S, Meani L, Zahalakov L, Lubatti C, et al. Use of antibodies recognizing cyclic citrullinated peptide in the differential diagnosis of joint involvement in systemic sclerosis. Clin Rheumatol. 2007;26(4):510–4.
12. Morardet L, Avouac J, Sammour M, Baron M, Kahan A, Feydy A, et al. Late radiological changes of the hands in systemic sclerosis. Arthritis Care Res. 2012;65(8):1088–92.
13. Michalska-Jakubus M, Kowal M, Adamczyk M, Krasowska D. Antiendothelial cell antibodies do not correlate with disease activity in systemic sclerosis. Adv Dermatol Allergol. 2018;35(2):185.
14. Brun B, Serup J, Hadrup H. Radiological changes of the hands in systemic sclerosis. Acta Derm Venereol. 1982;62(3):365–73.
15. Rezza G, Colombo G, Garattini E, Tebaldi S, Vannini A, et al. Hand radiological damage in systemic sclerosis: a 10 years prospective study. Ann Rheum Dis. 2011;70(4):630–3.
16. Stamenković B, Stanković A, Dimić A, Damjanov N, Nedović J, Stojanović S, et al. The clinical significance of antibody determination to cyclic citrullinated peptides in systemic sclerosis. Srp Arh Celok Lek. 2012;140(5–6):350–4.
17. Cuomo G, Zappia M, Abignano G, Federici M, Rotondo A, Valentini G. Ultrastructural features of the hand and wrist in systemic sclerosis. Rheumatology. 2009;48(1):1414–7.
18. Baron M, Lee P, Keystone EC. The articular manifestations of progressive systemic sclerosis (scleroderma). Ann Rheum Dis. 1982;41(6):1121–6.
19. Badiee A, Tajaddini A. The arthropathy of advanced progressive systemic sclerosis. Arthritis Rheum. 1981;24(7):874–84.
20. Allali F, Tahiri L, Senjari A, Abouqal R, Hajjaj-Hassouni N. Erosive arthropathy in systemic sclerosis. BMC Public Health. 2007;7(1):260.
22. Wangkaew S, Sivasomboon C, Leungwathananan W, Kasitanon N, Louthreenoo W. Prevalence and predictors of hand involvement in Thai patients with systemic sclerosis. Int J Rheum Dis. 2018;21(1):240–8.

23. Sakata K, Kaneko Y, Yasuoka H, Takeuchi T. Association of radiographic findings in hand X-ray with clinical features and autoantibodies in patients with systemic sclerosis. Clin Rheumatol. 2019;39(1):113–8. https://doi.org/10.1007/s10067-019-04639-6.

24. Azarbari N, Javadzadeh A, Mohseni I, Jalali A, Andalib E, Poormoghim H. Association on Musculoskeletal and radiological features with clinical serological findings in systemic sclerosis: a single-center registry study. Mediter J Rheumatol. 2020;31:341.

25. Sari-Kouzel H, Hutchinson C, Middleton A, Webb F, Moore T, Griffin K, et al. Foot problems in patients with systemic sclerosis. Rheumatology. 2001;40(4):410–3.

26. Ueda H, Akahoshi T, Kashiwazaki S. Radiological changes in feet of patients with progressive systemic sclerosis. Ryumachi. 1989;29(1):25–9.

27. Masi AT. Preliminary criteria for the classification of systemic sclerosis (scleroderma). Arthritis Rheum. 1980;23(5):581–90.

28. Valenti G. European Scleroderma Study Group to define disease activity criteria for systemic sclerosis. IV. Assessment of skin thickening by modified Rodnan skin score. Ann Rheum Dis. 2003;62(9):904–5. https://doi.org/10.1136/ard.62.9.904.

29. Kühn MO, Sassoon AA, Fernando ND. Classifications in brief: Kellgren-Lawrence classification of osteoarthritis. Clin Orthop Relat Res. 2016;474(8):1886–93.

30. LeRoy EC. Scleroderma (systemic sclerosis): classification, subsets and pathogenesis. J Rheumatol. 1988;15:202–6.

31. Zampatti N, Garamian A, Jordan S, Dobrota R, Becker MO, Maurer B, et al. Performance of the UCLA scleroderma clinical trials consortium gastrointestinal Tract 2.0 instrument as a clinical decision aid in the routine clinical care of patients with systemic sclerosis. Arthritis Res Ther. 2021;23(1):125.

32. Sakata K, Kaneko Y, Yasuoka H, Takeuchi T. Association of radiographic findings in hand X-ray with clinical features and autoantibodies in patients with systemic sclerosis. Clin Rheumatol. 2019;39:113.

33. Muktabhant C, Thammaroj P, Chowchuen P, Foocharoen C. Prevalence and clinical association with calcinosis cutis in early systemic sclerosis. Mod Rheumatol. 2021;31(6):1113–9. https://doi.org/10.1080/14397595.2021.1886654.

34. Thietart S, Louati K, Gatfosse M, Sornay-Rendu E, Gaigneux E, Lemeunier L, et al. Overview of osteo-articular involvement in systemic sclerosis: Specific risk factors, clinico-sonographic evaluation, and comparison with healthy women from the French OFELY cohort. Best Pract Res Clin Rheumatol. 2019. https://doi.org/10.1016/j.berh.2019.01.008.

35. Ashida R, Ihn H, Mimura Y, Jinnin M, Asano Y, Kubo M, et al. Clinical features of scleroderma patients with contracture of phalanges. Clin Rheumatol. 2007;26(8):1275–7.

36. Avouac J, Gossec L, Dougados M. Diagnostic and predictive value of anti-cyclic citrullinated protein antibodies in rheumatoid arthritis: a systematic literature review. Ann Rheum Dis. 2006;65(7):845–51.

37. Morita Y, Mura Y, Sugira K, Tomita Y. Anti-cyclic citrullinated peptide antibody in systemic sclerosis. Clin Exp Rheumatol. 2008;26(4):542.

38. Marrone M, Chiala A, Tampoia M, Iannone F, Raho L, Covelli M, et al. Prevalence of anti-CCP antibodies in systemic sclerosis. Reumatismo. 2007;59(1):20–4.

39. Santiago M, Baron M, Miyachi K, Fritzler MJ, Abu-Hakima M, Leclercq S, et al. A comparison of the frequency of antibodies to cyclic citrullinated peptides using a third generation anti-CCP assay (CCP3) in systemic sclerosis, primary biliary cirrhosis and rheumatoid arthritis. Clin Rheumatol. 2008;27(1):77–83.

40. Generini S, Steiner G, Miniati I, Conforti ML, Guiducci S, Skriner K, et al. Anti-HnRNP and other autoantibodies in systemic sclerosis with joint involvement. Rheumatology. 2009;48(8):920–5.

41. Ueda-Hayakawa I, Hasegawa M, Kumada S, Tanaka C, Komura K, Hama-guchi Y, et al. Usefulness of anti-cyclic citrullinated peptide antibody and rheumatoid factor to detect rheumatoid arthritis in patients with systemic sclerosis. Rheumatology. 2010;49(11):2135–9.

42. Elsayed A, Elbaky S, El-Atiy N, Ibrahim S, Abdelzaher A, Lotfy N, et al. ABO4?3 Anti CCP and anti MCV antibodies are marker of arthritis in systemic lupus erythematosus & scleroderma. BMJ Publishing Group Ltd; 2017.

43. Rothschild BM. Distinguishing erosive osteoarthritis and calcium pyrophosphate deposition disease. World journal of orthopedics. 2013;4(2):29–31.

Publisher's Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.