Ischemic Digital Ulcers Affect Hand Disability and Pain in Systemic Sclerosis

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ABSTRACT. ***Objective.*** Ischemic digital ulcers (DU) are frequent and severe complications of systemic sclerosis (SSc). The purpose of our study was to assess the effect of DU on hand disability and pain in patients with SSc.

Methods. The Evaluation of the Impact of Recurrent Ischemic DU on Hand Disability in Patients with SSc (ECLIPSE) is a prospective, multicenter, noninterventional study with a 2-year followup. Patients with SSc who experienced at least 1 DU in the previous year and received bosentan therapy were included between October 2009 and March 2011. This cohort is described at the time of inclusion.

Results. There were 190 patients (132 females) from 53 centers. Mean age ± SD was 43 ± 15 years at SSc diagnosis and 53 ± 15 years at inclusion. In 105 patients (56.2%), DU were the first non-Raynaud symptoms of SSc. The mean time interval between the occurrence of Raynaud phenomenon and the first DU episode was 6.6 ± 9.1 years. The mean numbers of active DU and fingers affected per patient for both hands were 2.3 ± 1.8 and 2.2 ± 1.6, respectively. Presence of active DU at inclusion was significantly associated with pain and impaired hand function: Visual Analog Scale for pain (0 to 10) was 6.2 ± 2.6 versus 2.5 ± 2.4 ($p < 0.0001$) and Cochin Hand Function Scale for hand disability (0 to 90) was 38 ± 20 versus 25 ± 19 ($p < 0.0001$), respectively.

Conclusion. DU represent a major sign of SSc, often affecting multiple fingers and both hands. They are significantly associated with pain and hand disability. (First Release June 15 2014; J Rheumatol 2014;41:1317–23; doi:10.3899/jrheum.130900)

Key Indexing Terms:
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Systemic sclerosis (SSc) is a connective tissue disease characterized by vascular damage, fibrosis of skin and internal organs, and production of autoantibodies[1]. Digital vasculopathy, which is responsible for Raynaud phenomenon (RP) and for the occurrence of ischemic digital ulcers (DU), is a hallmark of SSc[2]. Thus, a history of DU is reported in 44–60% of patients with SSc[3,4,5,6,7] and DU have been associated with severe pain, disability, and impaired quality of life (QoL)[3,6,8].

In patients with SSc, hand function can be evaluated using the Cochin Hand Function Scale (CHFS), a self-assessment questionnaire that has been set up for patients with rheumatoid arthritis[9] and validated in patients with SSc[10,11]. We recently reported that SSc patients with active (i.e., unhealed) DU have reduced wrist and hand mobility, increased global and hand disabilities, and altered health-related QoL compared to those without active DU[8].

Patient education is key in DU prevention, with recommendation for reducing cold exposure, avoiding use of tobacco and vasoconstrictive agents, and preventing hand injury and repeated microtrauma. Treatment options for SSc-related digital vasculopathy are based on aggressive vasodilation, with the objective to improve blood flow to ischemic areas. These options include longterm treatment with calcium channel blockers to reduce the frequency and/or severity of RP attacks, intravenous prostanoids to treat severe RP and active DU, and the dual endothelin receptor antagonist bosentan to prevent the occurrence of DU in patients with ongoing DU disease[12]. Indeed, in patients with SSc, the preventive effect of bosentan on the occurrence of new DU was demonstrated in 2 prospective randomized studies[13,14]. Sildenafil, a phosphodiesterase type 5 inhibitor, reduces RP, and according to pilot studies[15], may be effective in promoting healing of DU.

To assess the effect of recurrent ischemic DU on hand disability in patients with SSc, we have set up a prospective, multicenter, longitudinal, noninterventional study in patients with ongoing ischemic DU disease. To focus on a homogeneous study population, ongoing ischemic DU disease was defined as a recent history of DU (≥ 1 ischemic DU during the preceding year) and patients had to be eligible for bosentan therapy. We herein present the patients' characteristics at the time of inclusion and assess the effect of the presence of active ischemic DU on hand functionality, pain, and QoL.

MATERIALS AND METHODS

Study design. ECLIPSE (Evaluation of the Impact of Recurrent Ischemic DU on Hand Disability in Patients with SSc) is a prospective, longitudinal, noninterventional, multicenter study with a 2-year followup (primary endpoint at 1 year; AC-052-517). A total of 201 patients were planned to be recruited in 70 French centers from October 2009 to March 2011. Few categories of physicians are allowed to prescribe bosentan in France and study investigators were restricted to hospital-based internal and vascular medicine specialists, dermatologists, and rheumatologists.

Patients. The study enrolled patients aged ≥ 18 years, with limited cutaneous (lcSSc) or diffuse cutaneous SSc (dcSSc) according to American College of Rheumatology[16] or Leroy and Medsger[17] criteria. Eligible patients had to have experienced ≥ 1 predominantly ischemic DU during the previous year, regardless of whether they presented active DU at inclusion. A predominantly ischemic DU was defined as an ulcer located on the pulpar face of the fingers, distal to the proximal interphalangeal joints, and not facing a calcinosis or bone profile (otherwise they were considered mechanical DU)[13]. All DU described herein refer to "predominantly ischemic DU" unless otherwise specified. Moreover, patients should be eligible for bosentan therapy according to the approved indication by the European Medicines Agency[18].

Variables of assessment at inclusion. The following SSc/DU disease characteristics were collected from the patient's history: disease form (lcSSc or dcSSc); modified Rodnan Skin Score[19]; history of ischemic ulcerative disease; characteristics of current DU, if any (ischemic as well as nonischemic); number of previous DU episodes (a DU episode being defined as a time period when at least 1 active DU is present); sequelae resulting from DU history; and presence of other complications of SSc (esophageal, gastrointestinal, hand joint and muscle involvement; left ventricular involvement; interstitial lung disease; pulmonary arterial hypertension; and renal crisis). Clinical examination looked for potential mechanical causes of hand disability such as ankylosis of the distal and proximal interphalangeal joints, of the metacarpophalangeal (MCP) joints, presence of a nonulcerative calcinosis, tendinous retractions in the fingers, presence of a mechanical DU, loss of substance, autoamputation, surgical amputation, arthrodesis, and sympathectomy. Factors likely to influence the severity of digital vasculopathy were collected, such as smoking status, exposure to cold, and intake of vasoconstrictive agents. Immunological data recorded anticentromere and antitopoisomerase I (Scl-70) antibodies at enrollment. Systemic therapies prescribed for treatment of DU and/or SSc in addition to bosentan were collected, with special focus on calcium channel blockers. Finally, uses of supportive measures (such as physiotherapy, orthesis) were also collected.

Global disability was assessed with the self-administered Health Assessment Questionnaire-Disability Index (HAQ-DI)[19], the scale ranging from 0 (no disability) to 3 (maximal disability). The HAQ-DI comprises 20 items divided into 8 domains and has been validated in French[20].

Hand disability was evaluated by use of the self-administered CHFS[9], with 18 items concerning daily activities, each question scored on a scale of 0 (performed without difficulty) to 5 (impossible to do). The total score is obtained by adding the scores of all items (range 0-90). This questionnaire has been validated in French in patients with SSc[10,11].

The French version of the Medical Outcomes Study Short Form-36 health survey (SF-36) was used to assess QoL[21]. This self-administered questionnaire covers 8 areas: Physical Function, Physical Role, Bodily Pain, General Health, Vitality, Social Functions, Emotional Role, and Mental Health. For each area, the score ranges from 0 (poorest) to 100 (best). Scores can also be summarized in 2 global scores: the Physical Component Summary (PCS) and Mental Component Summary (MCS)[22]. Pain was rated by patients on a 10-point visual analog scale (VAS).

Ethical considerations. Our study was conducted in compliance with the Good Clinical Practices protocol and Declaration of Helsinki principles. According to French law, formal approval from an ethics committee is not required for observational studies. Patients gave their oral consent to participate.

Statistical analysis. For the cross-sectional analysis of the ECLIPSE cohort at the time of inclusion, presented here, descriptive statistics were used to summarize patient data and disease characteristics. Only the SF-36 physical and mental components were normally distributed. Two sample t-tests were performed to compare outcome variables between different patient groups. To identify potential confounding factors influencing the CHFS in addition to the presence of active DU, univariate regression analyses were performed including the following variables: presence of nonulcerative calcinosis, tendinous retractions, ankylosis of the distal and proximal inter-

phalangeal joints, ankylosis of the MCP joints, DU located on the dorsal surface of the fingers, DU complicating calcinosis, DU located on bone profile, loss of substance, autoamputation, surgical amputation, arthrodesis, and sympathectomy. A multivariate regression analysis was then conducted to identify independent risk factors for increased CHFS.

RESULTS

Between October 2009 and March 2011, 194 patients were recruited at 53 centers. The number of patients enrolled by internists, dermatologists, vascular medicine specialists and rheumatologists was 92, 65, 26, and 11, respectively. More patients were recruited during January–March (75) and October–December (85) than during April–June (16) and July–September (14).

Four patients had no history of hand DU within the preceding year and were excluded from the analysis. Thus, 190 patients could be analyzed. Demographics, clinical characteristics, immunological data, and the history of DU are shown in Tables 1 and 2. The population included a majority of middle-aged female patients with an almost balanced distribution of lcSSc and dcSSc, with frequent gastrointestinal and pulmonary complications. Duration of the DU was 7.6 ± 8.2 years. In our cohort, the time from first RP to DU tended to be shorter in patients with dcSSc compared to those with lcSSc (5.7 ± 8.3 vs 7.3 ± 9.6 yrs, p = 0.24).

History of DU in the overall population. DU was the first non-RP manifestation in 105 patients (56.2%; Table 2). One hundred eight patients (56.8%) had over 5 DU episodes since their first DU. Many patients had sequelae from previous DU including loss of substance (63.2%), autoamputation (6.8%), and/or surgical amputation (10.0%). Up to 15.3% patients had an aggravating factor, including smoking, cold exposure, and/or vasoconstrictive drug treatment. A limited number of patients were currently receiving adjunctive therapy such as physiotherapy (14.7%) or orthoses (10.0%). Patients may have received calcium channel blockers (60.9%, n = 69) or intermittent iloprost (18.5%) for the treatment of SSc and/or DU in addition to bosentan (100%).

Number of DU, and hands and fingers affected in patients with active DU at inclusion. The number of active DU per patient, per hand, and per finger is depicted in Figure 1. At inclusion, 113 patients (59.5%) had 1 or more active DU (Table 3), with a mean total number of DU of 2.3 ± 1.8 (median 2). The dominant hand of 88 patients (77.9%) was affected and 43 (38.1%) presented with DU on both hands. The mean number of DU on the right and left hands was 1.4 ± 1.1 and 0.9 ± 1.1, respectively. Similar numbers were found for the mean number of DU affecting the dominant (1.4 ± 1.2) and nondominant hand (1.0 ± 1.1). The mean number of fingers affected by DU per patient overall, of the right and left hand, respectively, amounted to 2.2 ± 1.6 (median 2), 1.3 ± 1.0 (median 1), and 0.9 ± 1.0 (median 1). Whatever the hand involved, the second (index) and third (middle) finger were most often affected (Figure 1).

Table 1. Demographics and clinical characteristics at inclusion in 190 patients with SSc. All values are n (%) unless otherwise specified.

Patient Characteristics	
Demographics	
No. patients	190 (100)
Female	132 (69.5)
Age at inclusion, yrs, mean ± SD	53 ± 15
Clinical characteristics	
Age at diagnosis of SSc, mean ± SD yrs	43 ± 15
Disease form	
Limited SSc	109 (57.4)
Diffuse SSc	81 (42.6)
Time since RP occurrence, yrs, mean ± SD (IQR)	14 ± 12 (5–20)
Time since first non-RP symptom, yrs, mean ± SD (IQR)	9.7 ± 8.4 (3–14)
Organ involvement	
Any organ involvement	160 (84.2)
Pulmonary fibrosis	86 (45.3)
Pulmonary arterial hypertension*	22 (11.6)
History of renal crisis	6 (3.2)
Esophagus involvement	140 (73.7)
Gastrointestinal involvement	52 (27.4)
Skin involvement	
Modified Rodnan Skin Score, mean ± SD	14.2 ± 8.8
≤ 14	108 (56.8)
> 14	81 (42.6)
Score not available	1 (0.5)
Factors limiting hand function	
Nonulcerative calcinosis	27 (14.2)
Tendinous retractions	81 (42.6)
Ankylosis of the distal interphalangeal joints	128 (67.4)
Ankylosis of the proximal interphalangeal joints	107 (56.3)
Ankylosis of the metacarpophalangeal joints	61 (32.1)
Immunological characteristics	
Antitopoisomerase 1 (Scl-70) antibodies	97/188 (51.6)
Anticentromere antibodies	54/181 (29.8)
Treatment for DU	
Bosentan	190/190 (100)
Calcium channel blockers	42/69 (60.9)
Iloprost	35/190 (18.4)

*Determined by either right heart catheterization with a mean pulmonary pressure > 25 mm Hg or Doppler echocardiography. DU: digital ulcer; IQR: interquartile range; RP: Raynaud phenomenon; SSc: systemic sclerosis.

In 23 patients (20.4% of patients with active DU), the DU diameter was ≥ 1 cm.

Of the 113 patients with active DU, 28 (24.8%) also presented with nonischemic DU in addition to ischemic DU at inclusion (Table 3). Complications included osteitis (1.8%), cutaneous infection (9.7%), and gangrene (4.4%).

Hand disability, pain, and QoL according to presence of ischemic active DU at inclusion. Outcome measure scores at inclusion for the total population, for patients with and without active DU at entry, are displayed in Table 4. The Global Disability Index of the HAQ was not different in patients with and without active DU at baseline. Conversely, the mean baseline scores of the CHFS and VAS were 38 ± 20 and 6.2 ± 2.6 in patients with active DU versus 25 ± 19

Table 2. History of digital ulcers (DU) at inclusion and sequelae from previous DU in 190 patients with SSc. All values are number of patients, shown as n (%), except as otherwise specified.

History and Sequelae of DU	
Occurrence of DU	
DU first sign other than RP	105 (56.2)
> 5 DU episodes* since first DU	108/188 (57.4)
DU episodes* during last year, mean ± SD (median)	1.95 ± 2.0 (1)
Time intervals, yrs, mean ± SD (IQR)	
RP-first DU, n = 187	6.6 ± 9.1 (1–9)
RP-first DU in patients with limited SSc, n = 108	7.3 ± 9.6 (0–7)
RP-first DU in patients with diffuse SSc, n = 79	5.7 ± 8.3 (1–10)
First non-RP sign-first DU, n = 187	2.2 ± 4.5 (0–2)
First DU-study enrollment, n = 187	7.6 ± 8.2 (2–10)
Sequelae from previous DU**	
Loss of substance	120 (63.2)/106
Autoamputation	13 (6.8)/12
Surgical amputation	19 (10)/13
Arthrodesis	6 (3.2)/3
Sympathectomy	3 (1.6)/3
Aggravating factors	
Current smoking	29 (15.3)
Cold exposure	22 (11.6)
Vasoconstrictive treatment	5 (2.6)

*A DU episode is defined as a time period when at least 1 active DU is present. ** On at least 1 hand/on dominant hand. IQR: interquartile range; DU: digital ulcer; RP: Raynaud phenomenon; SSc: systemic sclerosis.

Table 3. Characteristics of digital ulcers (DU) in 113 patients with at least 1 active ischemic DU at inclusion. All values are no. patients (%).

Characteristics of DU	
No. DU	
Patients having at least 1 DU	113 (100)
≥ 2 DU	64 (56.6)
≥ 4 DU	18 (15.9)
Pathogenesis of DU	
Ischemic DU	113 (100)
At least 1 other concomitant DU on the dorsal surface of the fingers	21 (18.6)
At least 1 other concomitant DU complicating calcinosis	2 (1.8)
At least 1 other concomitant DU on bone profile	15 (13.3)
At least 1 other concomitant DU related to nonischemic mechanism	28 (24.8)
Sequelae of previous DU	
Loss of substance	69 (61.1)
Autoamputation	7 (6.2)
Surgical amputation	13 (11.5)
Arthrodesis	3 (2.7)
Sympathectomy	5 (4.4)
Complications of active DU at inclusion	
Osteitis	2 (1.8)
Cutaneous infection	11 (9.7)
Gangrene	5 (4.4)

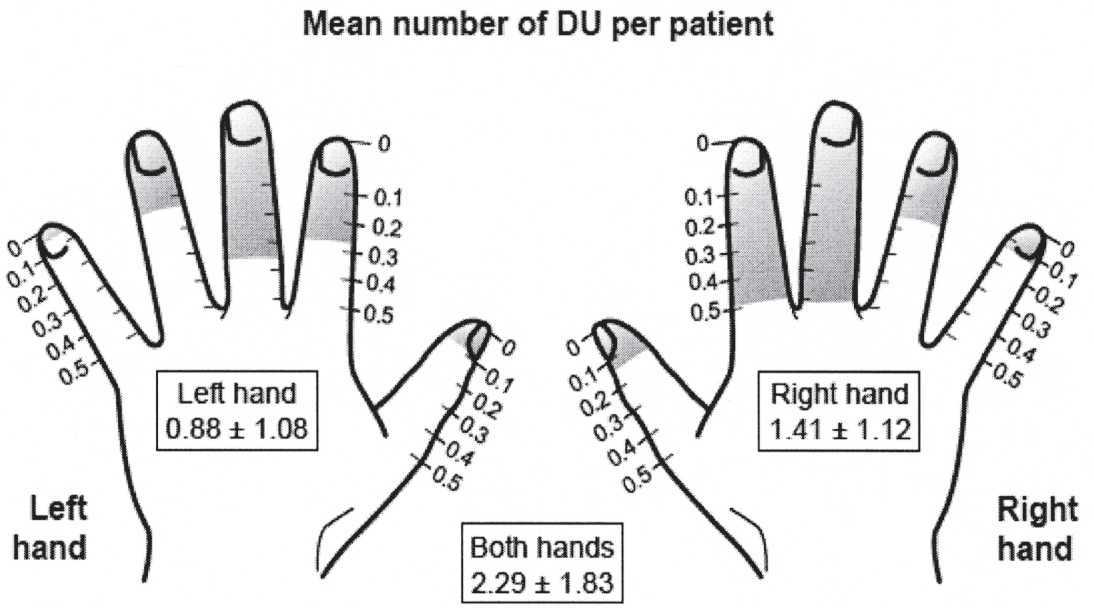

Figure 1. Digital ulcers (DU) in patients with DU at inclusion. Data are presented for 113 patients with at least 1 active DU at inclusion. Shaded areas represent the mean number of DU per finger of each hand; numbers of DU per finger, per hand, and total number of DU are mean ± SD.

Table 4. Outcome measure scores at baseline in 190 patients with SSc. All values shown as mean ± SD.

	Whole Group, n = 190	With DU at Entry, n = 113	Without DU at Entry, n = 77	p
HAQ-DI, range 0–3	1.0 ± 0.7, n = 189	1.1 ± 0.7, n = 113	0.9 ± 0.7, n = 76	0.15
CHFS, range 0–90	32 ± 21, n = 174	38 ± 20, n = 99	25 ± 19, n = 75	< 0.0001
VAS, range 0–10	4.6 ± 3.1, n = 178	6.2 ± 2.6, n = 104	2.5 ± 2.4, n = 74	< 0.0001
SF-36 PCS	38 ± 9, n = 182	37 ± 9, n = 110	39 ± 9, n = 72	0.29
Physical Functioning	53 ± 28	52 ± 29	54 ± 27	0.63
Role-Physical	47 ± 29	45 ± 28	49 ± 31	0.37
Bodily Pain	43 ± 24	39 ± 22	48 ± 25	0.01
General Health	39 ± 20	38 ± 20	42 ± 19	0.19
SF-36 MCS	38 ± 12, n = 182	37 ± 12, n = 110	40 ± 11, n = 72	0.12
Vitality	39 ± 19	38 ± 20	40 ± 18	0.46
Social Functioning	58 ± 27	56 ± 27	62 ± 26	0.11
Role-Emotional	56 ± 30	54 ± 30	59 ± 30	0.24
Mental Health	51 ± 21	48 ± 22	55 ± 19	0.04

CHFS: Cochin Hand Function Scale; DU: digital ulcer; HAQ-DI: Health Assessment Questionnaire–Disability Index; MCS: Mental Component Summary; PCS: Physical Component Summary; SF-36: Medical Outcomes Study Short Form-36 health survey; SSc: systemic sclerosis; VAS: visual analog scale.

and 2.5 ± 2.4 in patients without active DU, respectively ($p < 0.0001$). Only 5 patients without DU (6.7%) showed a CHFS score over 50, compared with 29 patients with DU (29.3%). Similarly, 10 patients without DU (13.5%) showed a VAS score over 5, compared with 63 patients with DU (60.6%; Figure 2). Patients with active DU at inclusion had a significantly poorer QoL than patients without active DU with regard to the Bodily Pain and the Mental Health subscale of the SF-36.

Confounding factors on hand function. Results from univariate regression analyses are presented in Table 5. In multivariate analysis, only presence of active DU was associated with hand function limitation measured by increased CHFS ($p < 0.0001$). The CHFS was linearly correlated with the number of DU (on both hands, on right and left hand, on dominant and nondominant hand) in the overall population ($p = 0.0002$, $p = 0.0004$, $p = 0.003$, $p = 0.0009$, and $p = 0.002$, respectively), but significance was lost in the group of patients with at least 1 DU at inclusion, suggesting that hand function is altered as soon as 1 DU is present.

DISCUSSION

We describe the history and extent of DU at the time of inclusion in a large cohort of 190 French patients with SSc and ongoing DU disease, and analyze consequences for hand disability, pain, and QoL. To the best of our knowledge, this is the first prospective nationwide multicenter and multidisciplinary prospective study specifically dedicated to evaluate the functional effect of SSc-related DU.

Our study indicates that DU are a frequent complication of SSc that often present with multiple recurrences and leave sequelae such as loss of substance. Often, multiple

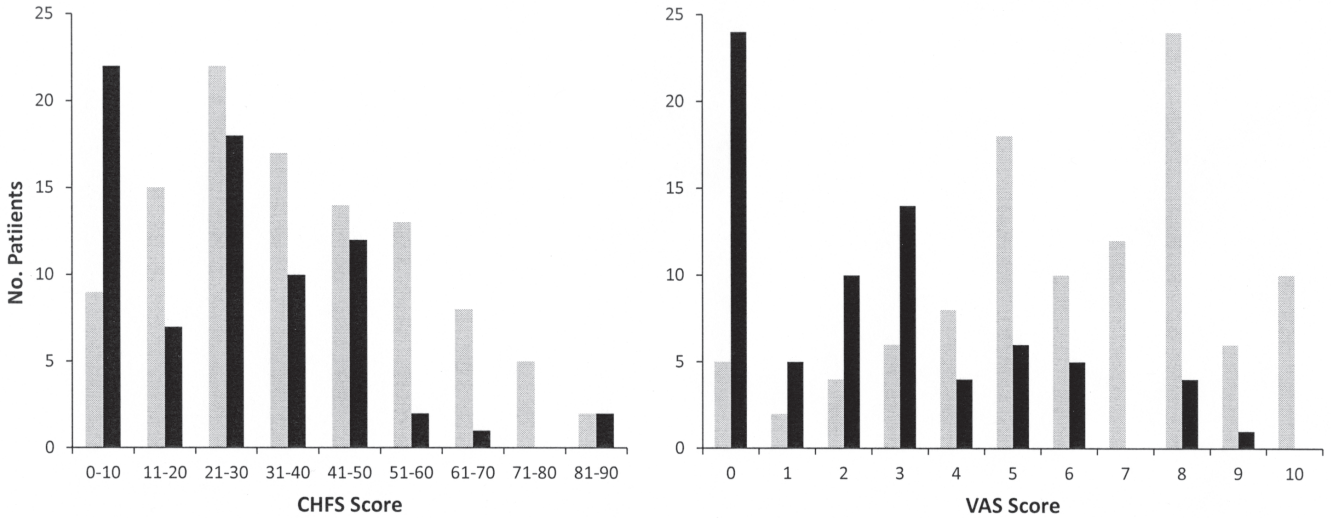

Figure 2. Effect of digital ulcers (DU) on the Cochin Hand Function Scale (CHFS) score (left panel) and on the visual analog scale (VAS) for pain score (right panel). Black bars depict patients without active DU at inclusion (n = 75/77 in left panel; n = 74/77 in right panel); grey bars depict patients with at least 1 active DU at inclusion (n = 99/113 in left panel; n = 104/113 in right panel).

Table 5. Effect of mechanical factors limiting hand function on the CHFS — results from univariate regression analyses.

Mechanical Factors Limiting Hand Function	p
Tendinous retractions	0.02
Ankylosis of the distal interphalangeal joints	0.002
Ankylosis of the proximal interphalangeal joints	< 0.0001
Ankylosis of the metacarpophalangeal joints	0.0008
DU located on bone profile	0.02
Autoamputation	0.04
Surgical amputation	0.09
Arthrodesis	0.03

CHFS: Cochin Hand Function Scale; DU: digital ulcers.

concomitant DU affect several fingers of the dominant hand, and both hands in one-third of cases. Patients with active DU present with significant impairment of hand function, increased pain, and altered QoL. Among the multifactorial complications of SSc that may affect hand function, DU play a major role.

In our study, the mean number of DU on the right and left hand was 1.4 and 0.9, respectively (same findings for the dominant and the nondominant hand, respectively). This is somewhat different from published studies, where the distribution of DU was roughly equal for both hands[3]. The observation that the time from first RP to DU tended to be shorter in patients with dcSSc compared to those with lcSSc confirms a recent finding from the European Digital Ulcer Outcomes registry, where DU developed significantly earlier in patients with dcSSc than in those with lcSSc[23].

Our present study confirms in a multicenter setting the previous findings that DU severely affect hand function and QoL[3,4,5,6,7]. In a series of 213 patients with SSc that we enrolled between 2004 and 2007, 31.4% of the patients had at least 1 DU at the time of evaluation. These patients with at least 1 DU had a significantly greater HAQ-DI (1.21 ± 0.72 and 0.93 ± 0.71, p = 0.008, were reported) and CHFS (27.4 ± 20.7 vs 16.7 ± 18.2, p < 0.0001) than did patients without DU. In addition, hand and wrist mobility as well as the mental score of the SF-36 were significantly diminished[8]. In a second series of 189 patients with SSc whom we enrolled between 2008 and 2009, 59.8% of patients had a history of DU and 31.7% had at least 1 DU at the time of evaluation (20% of whom were taking bosentan). Global disability (HAQ-DI: 1.12 ± 0.79 vs 1.39 ± 0.84, p = 0.001), hand disability (CHFS: 20.2 ± 18.3 vs 27.8 ± 19.1, p < 0.0001), and anxiety (Hospital Anxiety and Depression Scale: 9.9 ± 5 vs 8.5 ± 4.2, p = 0.04) were significantly higher in patients with DU than in patients without DU[6]. However, it is difficult to compare our data with these 2 studies, which did not require a history of previous DU or treatment with bosentan. Further, only the second study categorized DU according to the possible underlying mechanism (ischemic, mechanical, associated with calcinosis).

The ECLIPSE population described here has a more severe form of digital vasculopathy than the previous populations because it was selected based on a recent history of DU and eligibility for bosentan therapy.

In our study, the mean CHFS was 38 ± 20 in patients with active DU versus 25 ± 19 in patients without active DU, which is also much higher than in the previous studies, reflecting moderate hand disability around 25 and severe hand disability over 35[6,8]. This finding suggests that the more severe the vasculopathy, the more impaired the hand function. Indeed, the effect of active DU on hand function remained statistically significant even when the comparison was adjusted on potentially confounding factors.

Hand disability in patients with SSc involves the skin, subcutaneous tissues, and the microvascular, musculoskeletal, and peripheral nervous systems[24]. These modifications lead to hand deformities and pain and are responsible for the altered hand function. In particular, synovitis, joint contractures, and tendon friction rubs, which appear to be more prevalent in the diffuse form of SSc[25], contribute to hand disability in patients with SSc[24]. Thus, a study observed that arthralgia was more frequent in patients with DU than without DU (75.0% vs 58.1%, p = 0.02)[6]. However, in our present study, the results of a multivariate analysis suggest that the greater impairment of hand function in patients with active DU at inclusion is strongly related to the presence of DU and is unlikely to be due to confounding factors. Further, hand function appears to be altered as soon as 1 DU is present.

Our study provides information of major importance in this population of patients with severe ulcerative disease: 15.3% of the patients had an aggravating factor, including smoking, cold exposure, and/or vasoconstrictive drug treatment, and only 60.9% of the 69 patients with available data received calcium channel blockers. These findings are relevant for the improvement of clinical practice and patient education.

The strength of our study is that DU description was based on the presence of an active DU at the time of inclusion, with concomitant measure of QoL and hand function. In addition, confounding factors have been taken into consideration when assessing the potential effect of DU on hand function. However, there are a number of limitations to the interpretation of the baseline results in our study: the ECLIPSE population is not representative of the whole SSc population because it is restricted to patients with an ongoing DU disease who were eligible for bosentan, and who were seen in a hospital setting.

We describe initial data from a large contemporary cohort of patients with SSc and ongoing DU disease being treated with bosentan. In our cohort, DU represent a recurrent complication of SSc and are significantly associated with pain and hand disability. Prospective followup at 2 years will provide important information on how recurrent DU episodes influence hand disability.

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APPENDIX

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