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Abstract: Objective: To gain insight into clinical practice regarding referral, early diagnosis and other aspects of the management of patients with dcSSc in Europe and the USA. Methods: Semi-structured interviews were conducted with 84 rheumatologists (or internal medicine physicians) and 40 dermatologists in different countries (the UK, France, Germany, Italy, Spain and the USA). Physicians were asked to identify key steps in the patient pathway relating to patient presentation, diagnosis and referral, in addition to other treatment and follow-up processes. Results: The interviewed physicians reported that late presentation with dcSSc was common, with some patients presenting to primary care physicians after symptoms had persisted for up to 1 year. Awareness of dcSSc is reported to vary widely among primary care physicians. Final diagnosis, generally following guideline-based recommendations, was by rheumatologists in most cases (or internal medicine physicians in France) and they remained responsible for global patient management, with lesser involvement in diagnosis and management by dermatologists. Specialist centres were not well defined and did not exist in all countries. Conclusion: Patients and primary healthcare providers can be unaware of the symptoms of dcSSc, therefore presentation and referral to specialist care are often late. Thus, improved awareness among patients and primary care physicians is necessary to facilitate earlier referral and diagnosis. Once referred, more consistent use of the modified Rodnan skin score at diagnosis and follow-up may help to monitor disease progression. Furthermore, establishing specialist centres may help to promote such changes and improve patient care.

DOI: <https://doi.org/10.1093/rheumatology/kex504>

Posted at the Zurich Open Repository and Archive, University of Zurich

ZORA URL: <https://doi.org/10.5167/uzh-150689>

Published Version



Originally published at:

Distler, Oliver; Allanore, Yannick; Denton, Christopher P; Matucci-Cerinic, Marco; Pope, Janet E; Hinzmann, Barbara; Davies, Siobhan; de Oliveira Pena, Janethe; Khanna, Dinesh (2018). Factors influencing early referral, early diagnosis and management in patients with diffuse cutaneous systemic sclerosis. *Rheumatology*:Epub ahead of print.

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Factors influencing early referral, early diagnosis and management in patients with diffuse cutaneous systemic sclerosis

Oliver Distler¹, Yannick Allanore², Christopher P. Denton³, Marco Matucci-Cerinic⁴, Janet E. Pope⁵, Barbara Hinzmann⁶, Siobhan Davies⁷, Janethe de Oliveira Pena⁸ and Dinesh Khanna⁹

Abstract

Objective. To gain insight into clinical practice regarding referral, early diagnosis and other aspects of the management of patients with dcSSc in Europe and the USA.

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Results. The interviewed physicians reported that late presentation with dcSSc was common, with some patients presenting to primary care physicians after symptoms had persisted for up to 1 year. Awareness of dcSSc is reported to vary widely among primary care physicians. Final diagnosis, generally following guideline-based recommendations, was by rheumatologists in most cases (or internal medicine physicians in France) and they remained responsible for global patient management, with lesser involvement in diagnosis and management by dermatologists. Specialist centres were not well defined and did not exist in all countries.

Conclusion. Patients and primary healthcare providers can be unaware of the symptoms of dcSSc, therefore presentation and referral to specialist care are often late. Thus, improved awareness among patients and primary care physicians is necessary to facilitate earlier referral and diagnosis. Once referred, more consistent use of the modified Rodnan skin score at diagnosis and follow-up may help to monitor disease progression. Furthermore, establishing specialist centres may help to promote such changes and improve patient care.

Key words: systemic sclerosis, scleroderma, diagnosis, treatment, skin disease

Rheumatology key messages

- Lack of disease awareness in dcSSc patients and primary physicians can delay referral to specialists.
- Identification of specialist centres may lead to improved patient care in dcSSc.
- Consistent use of validated tools may help to monitor disease progression in dcSSc.

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Submitted 5 May 2017; revised version accepted 27 November 2017

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Introduction

SSc is a rare multi-organ autoimmune rheumatic disease with high mortality, particularly in patients with dcSSc [1–6]. Timely referral to SSc centres and early diagnosis of organ manifestations are essential to allow intervention before organ damage occurs [7]. Indeed, organ involvement is observed early in dcSSc and is often already present when patients are seen at expert centres [6]. This highlights the urgent need for an improved referral process. For example, in RA the importance of early diagnosis and referral to improve long-term morbidity and mortality is well established [8]. There is, however, little knowledge of how patients with dcSSc are managed early in their disease. Better understanding of routine management is necessary to improve the early referral process.

Methods

The objective of this research was to gain insights into the real-world referral, diagnosis, treatment and follow-up of patients with dcSSc in Europe and the USA. This was achieved through semi-structured interviews of treating physicians from the UK, France, Germany, Italy, Spain and the USA.

To be eligible, rheumatologists and internal medicine (IM) physicians needed a caseload of 15 patients or more with SSc and 4 or more with dcSSc; dermatologists were required to have 10 patients or more and 3 patients or more, respectively. Only one physician from each centre could participate in the study. To ensure representation of different practice settings, physicians were recruited from specialist centres (defined as those who were participating in SSc trials or members of associated networks) as well as other hospital or office-based settings. Each physician participated in a 30-min (dermatologists) or 60-min (rheumatologists and internists) interview that followed a discussion outline (see [supplementary data](#), available at *Rheumatology* online). Physicians were asked to identify key steps in the patient pathway, that is, typical patient presentation to the primary healthcare provider (HCP), specialist referral, the diagnostic process, approaches to treatment and disease evaluation. Physicians were also asked who was responsible for implementing each step.

All research materials (see [supplementary data](#), available at *Rheumatology* online) were designed by a team (led by S.D.) with extensive experience in qualitative and quantitative research in specialist medical indications. All analyses and the interpretation were conducted by the same team. One member of the team read the transcripts for each country, and a five-step analysis process adapted from Ereaut [9] was adopted (see [supplementary data](#), available at *Rheumatology* online).

Participants

The sample of rheumatologists (including IM physicians in France) was designed to provide a small-scale, qualitative overview to determine the appropriate sample composition for an anticipated larger survey. The target sample was 15 physicians per country. When structured to ensure

responses from a range of different practice settings, this would provide a sufficient breadth of perspective and a reasonable expectation that key features and issues in SSc referral, diagnosis and management would emerge.

As skin changes are an early manifestation of SSc, dermatologists often play a role in patient identification, diagnosis and referral. Furthermore, a minority of centres in each country are based in dermatology clinics. Therefore, we sampled seven dermatologists per country to allow sufficient representation of those who work in SSc centres and those who do not.

Results

Eighty-four 60-min interviews were conducted with rheumatologists in the UK, France, Germany, Italy, Spain and the USA, and IM physicians in France ([Table 1](#)). Forty 30-min interviews were conducted with dermatologists ([Table 1](#)).

Primary care: presentation and referral

Late presentation was commonly reported; patients with dcSSc generally presented to their primary HCP after symptoms had persisted for up to 1 year, depending on severity. Patients with severe symptoms, such as digital ulcers, breathing problems or renal issues, presented immediately, while patients with RP typically presented after 3–9 months. Physicians stated that patients often considered early symptoms (e.g. gastrointestinal reflux, cold fingers, mild skin thickening and fatigue) not to be serious enough to justify medical attention, and patients initially made lifestyle modifications to accommodate them. The symptoms most commonly prompting patients to visit a primary HCP were skin and vascular complications, such as RP, skin thickening and puffy fingers ([Fig. 1](#)). Further information on physician perceptions of dcSSc awareness among primary HCPs is included as [supplementary data](#), available at *Rheumatology* online.

Physicians reported that awareness of dcSSc among primary HCPs varied widely, and that primary HCPs may not immediately associate common symptoms, such as RP, with dcSSc, resulting in slow or inappropriate referrals and delayed diagnosis. This was more commonly noted by rheumatologists (25/84; 30%) than dermatologists (5/40; 13%), who more frequently noted that primary HCPs will refer patients to them with skin problems such as RP, but are unlikely to suspect dcSSc. It was also noted by 8/84 rheumatologists (10%) that when a combination of symptoms is apparent, primary HCPs are more likely to consider a systemic condition and request antibody testing, which leads to a correct referral. In all countries, at least one rheumatologist noted that patients experienced delayed referral as a result of waiting lists to see a specialist.

Specialist care

Specialist centres

There are no formal definitions or accreditations for specialist SSc centres in most countries. However, the physicians interviewed identified what they considered to be specialist centres based on high patient caseloads, multidisciplinary

TABLE 1 Characteristics of physicians interviewed for the study

Characteristics of physicians	UK	France	Germany	Italy	Spain	USA	Total
Rheumatologists/IM physicians, n	11/0	7/8	15/0	15/0	13/0	15/0	76/8
SSc patient caseload, mean (s.d.)	140 (134)	84 (119)	86 (68)	65 (72)	39 (33)	214 (229)	104 (137)
LcSSc	89 (95)	52 (82)	40 (41)	33 (49)	25 (27)	124 (144)	60 (88)
DcSSc	50 (48)	32 (48)	45 (36)	32 (32)	15 (8)	89 (94)	44 (56)
Duration of specialization, mean (s.d.), years	14 (6)	17 (7)	12 (6)	10 (4)	18 (6)	19 (9)	15 (7)
Dermatologists, n	7	7	7	7	5	7	40
SSc patient caseload, mean (s.d.)	34 (31)	18 (8)	44 (41)	11 (2)	11 (2)	24 (18)	24 (25)
LcSSc	19 (16)	12 (6)	27 (25)	7 (2)	5 (3)	16 (17)	15 (16)
DcSSc	16 (16)	7 (3)	17 (17)	5 (2)	6 (5)	7 (5)	10 (11)
Duration of specialization, mean (s.d.), years	11 (5)	19 (5)	9 (3)	8 (2)	16 (7)	11 (6)	12 (6)

team management, trial involvement and the presence of individual physicians with a known interest in SSc.

Diagnosis

Final diagnosis was made by rheumatologists (and IM physicians in France) in most cases. In Germany, France and Italy, dermatologists also provided the diagnosis (Fig. S1, available as [supplementary data](#) at *Rheumatology* online). In all countries, dermatologists' caseloads were 11–51% greater than those of rheumatologists or IM physicians (Table 1). The dcSSc diagnosis was less frequently made by pulmonologists, followed by angiologists (Germany/France) or primary HCPs (who referred patients with a highly suspected diagnosis).

Diagnosis was based on signs and symptoms (e.g. skin thickening on proximal extremities and trunk, and skin tightening around the mouth), and was confirmed with investigations such as autoantibody tests and nail-fold capillaroscopy. Physicians were confident that in many cases a rapid and accurate diagnosis could be made in this way without further evaluation. Supplementary tests (e.g. digital skin perfusion, skin biopsy, angiography or hand/foot X-ray) were used when other assessments were inconclusive.

Although classification guidelines were not followed rigidly, physicians reported routine diagnostic processes (Fig. S2, available as [supplementary data](#) at *Rheumatology* online) that reflected the ACR/EULAR classification of SSc [10].

Fig. S3, available as [supplementary data](#) at *Rheumatology* online, shows the most commonly reported complications. Physicians were highly vigilant for organ complications at diagnosis and at follow-up.

Treatment

Rheumatologists (and IM physicians in France) reported being the central co-ordinator of ongoing care for most patients, responsible for global management throughout the patient's disease course, with support from relevant specialists for organ-specific complications.

The main treatment goals reported were to limit organ involvement and/or progression, limit skin progression, and relieve symptoms or improve patients' quality of life. Treatment choices tended to be tailored to the presenting

complications. For example, where interstitial lung disease is present, the systemic therapy of choice for skin complications is likely to be MMF.

Most physicians were unsatisfied with current treatment options. Primary concerns were related to limiting organ complications, with skin complications—a priority for patients—recognized as being particularly poorly managed. Treatments for skin complications were also a priority for dermatologists. The [supplementary data](#), available at *Rheumatology* online, gives further details of physician responses regarding treatment.

Follow-up

Patients with stable disease generally received follow-up assessments by rheumatologists every 3–6 months unless rapid progression dictated more frequent intervention (50/59 rheumatologists; 85%), with 8/59 rheumatologists (14%) stating that they followed up more regularly. Physicians said they relied on regular screening to identify organ involvement, in addition to asking about new symptoms during routine visits.

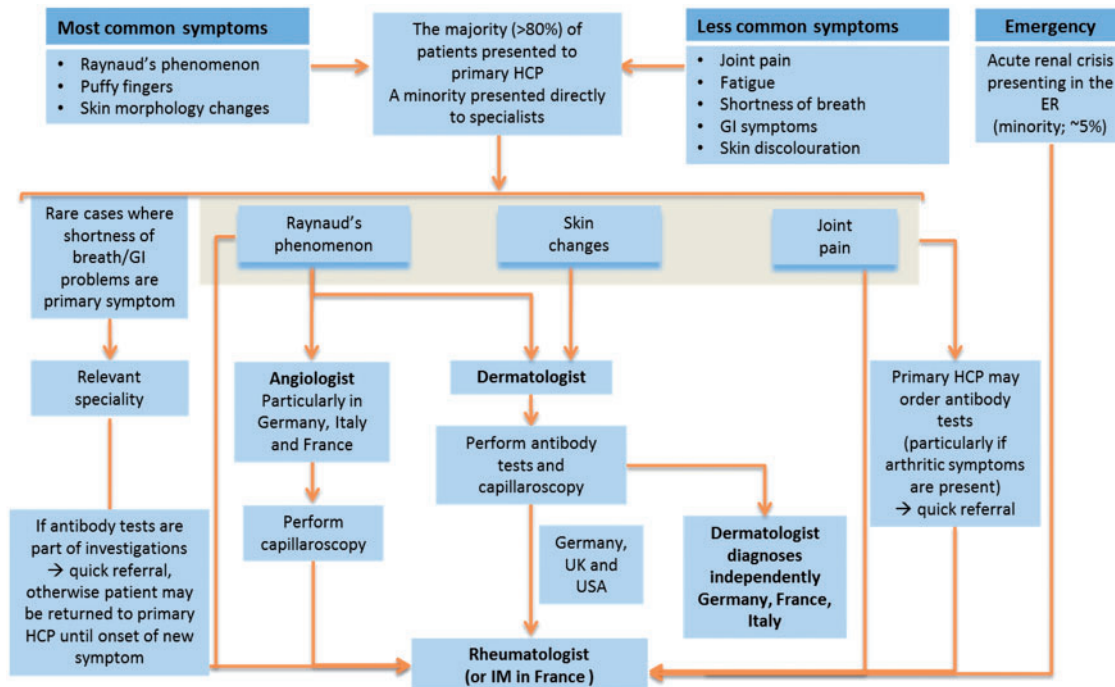
The modified Rodnan skin score (mRSS) [11] was most commonly used by rheumatologists (and IM physicians in France) (Table S1 available as [supplementary data](#) at *Rheumatology* online). Of note, 8 rheumatologists (10%) and 18 dermatologists (45%) were unaware of the mRSS. Where the mRSS was measured, physicians expected >50% of diagnosed patients would have an mRSS \geq 15. Further details of testing for organ complications, and the involvement of other specialists and general practitioners in patient follow-up, are included in the [supplementary data](#), available at *Rheumatology* online.

Physicians believed that, after diagnosis, most patients were well informed about their disease state. Patients were provided with information or support about their condition, including leaflets, website addresses, telephone helplines and support groups. However, awareness of patient associations was relatively low.

Discussion

Early detection of SSc and its complications is critical to allow early intervention and prevent progression [7]. With

Fig. 1 Initial presentation of patients with dcSSc



Causes and location of the initial presentation of patients with dcSSc and the route to patient referral, as described by the physicians interviewed. ER: emergency room; GI: gastrointestinal; IM: internal medicine physician.

novel anti-fibrotic therapies in clinical development [12], this might become even more important for avoiding irreversible tissue damage. However, in this survey of physicians, late presentation was reported to be common, with more than half of patients having an mRSS ≥ 15 . This is consistent with data from the prospective, observational Pittsburgh Scleroderma Databank [13], where mean initial mRSS was 22–25 [13]. Moreover, physicians reported that patients themselves delayed presentation due to a lack of appreciation of their symptoms. This suggests that patients are a key audience for educational initiatives highlighting the importance of symptoms, such as RP, puffy fingers and mild skin thickening, and the risk of progression to dcSSc.

The interviewed physicians considered that there was a general lack of awareness of dcSSc, including presenting symptoms, among primary HCPs. Some physicians also reported that referral was further delayed due to waiting lists. Primary HCPs are therefore also a key educational audience to improve dcSSc awareness and facilitate earlier referral to a rheumatologist or dermatologist, thereby avoiding a delay in diagnosis. There may also be scope for improved collaboration and communication between primary HCPs and specialists.

Once referred, the physicians were confident that a rapid and accurate diagnosis was made. Diagnosis of organ complications is also well established when patients are referred to specialists, further highlighting the need for educational initiatives to focus on early recognition by patients and non-specialist HCPs. Notably,

the latest EULAR treatment recommendations are aimed at different groups of physicians: rheumatologists (for most organ manifestations), dermatologists (for some milder manifestations in some countries) and pulmonologists (for pulmonary arterial hypertension) [14]. Rheumatologists generally remain responsible for the global management of patients after diagnosis, with dermatologists having lesser involvement in diagnosis and management.

Most physicians interviewed were unsatisfied with current treatment options, particularly related to limiting organ involvement and skin manifestations. There is therefore a significant need for therapies that slow disease progression. Regarding disease evaluation and monitoring, many physicians interviewed did not use the mRSS, often because of time constraints, although in some cases due to a lack of awareness. Physicians should therefore be trained in the use of such validated quantitative assessments to improve the quality of care; more consistent use of the mRSS may help to monitor disease progression. Several studies, including prospective clinical trials, have shown that the mRSS is a reliable tool for predicting disease outcome [13, 15, 16].

The lack of a clear definition of specialist centres for dcSSc should be addressed, as identification of such centres could improve patient care. Familiarity of physicians in expert centres with the latest research and guidelines ensures that the best possible care is given, and greater understanding of disease processes and treatment options is gained through experience in managing high

volumes of patients. There is also easier access to support networks from a variety of specialties.

This study was limited by the relatively small sample size; however, as a first study in a rare indication, it was designed to have qualitative validity—to provide an insight into current behaviours of referring and treating physicians across a range of practice settings. It is also important to note that our findings are based on treating physicians' perceptions of primary HCPs; no primary HCPs were interviewed for this study, and therefore these findings should be interpreted with caution. Future research may benefit from including primary HCPs in the survey cohort.

In conclusion, unawareness of dcSSc symptoms among patients and primary HCPs leads to late referral to specialist care. Specialist centres for dcSSc are not well defined, and their identification may lead to improved care. More consistent use of validated tools, such as the mRSS, at diagnosis and follow-up may help to monitor disease progression.

Acknowledgements

This study was carried out by Blueprint Partnership (Manchester, UK), supported by Bayer AG (Berlin, Germany). Editorial assistance was provided by Adelphi Communications (Bollington, UK), supported by Bayer AG. Bayer AG contributed to the study design and interpretation of data.

Funding: This work was supported by Bayer AG.

Disclosure statement: O.D. had a consultancy relationship and/or has received research funding from Actelion, Bayer, Biogen/Idexx, Boehringer Ingelheim, ChemomAb, espeRare foundation, Genentech/Roche, GlaxoSmithKline (GSK), Inventiva, Italfarmaco, Lilly, medac, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Novartis, Pfizer, Sanofi, Sinoxa and UCB in the area of potential treatments of scleroderma and its complications, and has a patent mir-29 for the treatment of systemic sclerosis licensed. Y.A. consults for Actelion, Bayer, Roche/Genentech, Inventiva, Medac, Pfizer, Sanofi, Servier and UCB, and has received research grants from Bristol-Myers Squibb (BMS), Roche/Genentech, Inventiva, Pfizer, Sanofi and Servier. C.P.D. has undertaken consultancy to Bayer, Roche, GlaxoSmithKline, Actelion, Inventiva, CSL Behring, Takeda, Merck-Serono, MedImmune and Biogen, and has received research grants from Actelion, GlaxoSmithKline, Novartis and CSL Behring. B.H. is an employee of Bayer AG, Berlin, Germany. D.K. has received investigator-initiated grants and acts as a consultant to Actelion, Boehringer Ingelheim, BMS, Bayer, Corbus, Cytari, GSK, Genentech/Roche, Sanofi and UCB, and owns stocks in Eicos Sciences, Inc. J.P. consults for and/or has research grants with Actelion, Bayer, BMS, Merck, Pfizer and Roche. S.D. is an employee of Blueprint Partnership. J.d.O.P. is an employee of Bayer. The other author has declared no conflicts of interest.

Supplementary data

Supplementary data are available at *Rheumatology* online.

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