Clinical and Experimental Rheumatology 2007; 25: 878-880.

Prevalence of systemic sclerosis in Valtrompia in northern Italy. A collaborative study of rheumatologists and general practitioners

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Received on December 29, 2006; accepted in revised form on May 7, 2007.

Key words: Systemic sclerosis, prevalence, Italy.

Competing interests: none declared.

ABSTRACT

Objective. *To evaluate the prevalence of patients with Systemic Sclerosis (SSc) in Valtrompia in northern Italy.*

Methods. *Patients were recruited from the records of 28 general practitioners (GPs) whose practices covered 38,348 individuals aged over 14 years, and from a public Hospital database covering all patients evaluated in community clinics, day-hospitals and inpatient units of the area. Crossing data from the two sources revealed a 100% concordance. Rheumatological re-evaluation confirmed a diagnosis of SSc in 13 patients (11 female, 2 male; 2 diffuse SSc, 11 limited SSc), fulfilling ACR criteria in 10 cases and Le-Roy-Medsger 2001 criteria in 3 further cases.*

Results. *Prevalence of SSc was estimated at 33.9 cases among 100,000 adults aged over 14 years (95% confidence intervals: 15.5-52.3).*

Conclusion. *This rather high prevalence reflects both changes in the diagnostic criteria for SSc including milder forms of disease, and recruitment of these mild cases due to active collaboration between GPs and specialists.*

Introduction

Assessing the prevalence of rheumatic diseases has important value for clinical practice and health care provision strategy (1). Therefore, several surveys have recently tried to define the prevalence of systemic sclerosis (SSc), a connective tissue disease carrying considerable morbidity and mortality. Prevalence of SSc appears to be greater in the USA, where it has been estimated at 24.2 per 100,000 (2), than in Europe, where recent studies in Iceland, England, France and Greece have estimated rates ranging from 7.1 to 15.8 per 100,000 (3-6). These results have been attributed to differences in the methodologies used to retrieve patients or in case definitions, but also to real geographical variations, due to environmental or genetic factors (5, 7, 8). There are no data available in Medline-censed medical literature concerning the prevalence of SSc in Italy.

We have therefore evaluated the prevalence of patients with a known diagnosis of SSc in Valtrompia in northern Italy, taking advantage of the geographic characteristic of the area, the efficient organization of rheumatological services in this district, and the close collaboration between rheumatologists and general practitioners (GPs).

Methods

Valtrompia is a 40 km-long prealpine valley, north-to-south oriented. The only easy access to the valley is from Brescia, the main town of the province, which is located just in proximity to the southern end of the valley, while the northern end is a cul-de-sac, without comfortably practicable passes. Public rheumatology health care is provided by the tertiary referral center of Spedali Civili/University of Brescia, (the only public Hospital in the area), with a Day-Hospital Unit of Rheumatology and Clinical Immunology, and a specialized Unit of Internal Medicine (Systemic Autoimmune Diseases), and by secondary community clinics in Gardone Valtrompia, the most important town in the valley, and in Brescia. Rheumatology consultants in the community clinics are members of the Rheumatology Unit (hereafter, indicated as Spedali Civili team). Active collaboration between specialists and GPs was sought through training courses on the relevance of early diagnosis of connective tissue diseases.

Patients with a known diagnosis of SSc were captured from two sources, using a variation of the capture/recapture method (9).

1) Twenty-eight out of 70 GPs working in Valtrompia volunteered to take party in this study. Their practices were distributed throughout the entire valley and covered a total of 38,348 individuals (female: 19,677; male: 18,671) aged over 14 years, *i.e.* almost half of the entire population of the valley. During the year 2004, they identified through their records patients with a known diagnosis of SSc, and, having obtained an informed written consent, fulfilled a semi-anonymous form including information on the disease (initials of patient name, birth date, sex, year of diagnosis, comorbidity, and name of the hospital where they were followed or other specialist consulted).

At the end of the year, they collected data concerning the year of observation (number of visits at the GPs, and at physician specialists, admissions to the hospital). Fourteen patients with a diagnosis of SSc were traced: 13 of them were regularly followed by the Spedali Civili team, while one was cared for in a private practice.

2) The database of the Rheumatology Unit of Spedali Civili includes all patients with a known diagnosis of SSc evaluated since 1989 in secondary clinics in Brescia and Gardone Valtrompia, or in the Spedali Civili. Among the information included in the database, there is the name of the GP of the patients. Fourteen patients with a diagnosis of SSc followed by GPs collaborating in the study were traced: 13 of them were still regularly followed by the Spedali Civili team.

Crossing data from the two sources revealed a 100% concordance, *i.e*. the same patients were identified by both sources.

All the patients (including the one followed by a private practitioner), after written informed consent, were re-evaluated by rheumatologists of the Spedali Civili team according to standard procedures, as recommended by a consensus conference (10). To confirm the diagnosis, the 1980 American College of Rheumatology (ACR) criteria (11), and the 2001 LeRoy and Medsger criteria (12) were used.

Ethical Committee approval was not sought since the patients were evaluated by usual clinical practice and provided their consent for data treatment.

Confidence intervals for prevalence were calculated using the normal approximation to the binomial distribution.

Results

On the basis of a previously formulated diagnosis of SSc, 14 individuals were retrieved from two sources, with a 100% concordance. After re-evaluation, one patient was reclassified as suffering from undifferentiated connective tissue disease, because of the presence of Raynaud's phenomenon, puffy hands, and anti U1-Rnp antibodies. Three patients did not fulfil ACR criteria, but were classified as having limited cutaneous SSc according to the LeRoy-Medsger criteria, due to the presence of Raynaud's phenomenon, sclerodactily, anticentromere antibodies, scleroderma pattern at nailfold capillaroscopy and, in two out of three, of sclerodema oesophagopathy at manometry. Ten patients fulfilled both ACR and LeRoy-Medsger criteria.

The main demographic and clinical data of the 13 patients with a confirmed diagnosis of SSc are reported in Table I. One of these 13 patients was diagnosed during the year of observation 2004.

Table II summarizes the prevalence estimates for SSc according to disease subset.

Table I. Demographic and clinical characteristics of the 13 patients with SSc.

Sex	F: 11; M: 2
Median age (range), years	60 (47-80)
Ethnic background	Caucasian: 13 (100%)
Median disease duration (range), years	9 (0-34)
Disease subset	
lcSSc:	11 (84%)
dcSSc:	2 (16%)
Autoantibodies	
ANA	13 (100%)
Anticentromere	7 (54%)
Anti-Scl70	3 (23%)

Table II. Estimates of the prevalence of SSc in Valtrompia. Data are expressed as cases per 100,000 adults aged over14 years.

Parameter	Prevalence	95% CI
SSc among total population	33.9	15.5-52.3
SSc among females	55.9	22.9-88.9
SSc among males	14.8	0.1-25.1
SSc fulfilling ACR criteria	26.1	10.0-42.2
dcSSc among total population	5.2	0.1-12.4
lcSSc among total population	28.7	11.8-45.6

Discussion

This study provides information about the prevalence of SSc in an Italian population, suggesting that it may be higher than reported by recent studies in other European countries (3-6), although lower confidence intervals of our data overlap with some of them (5, 6).

The main sources of discrepancies among studies of SSc prevalence are case definition and retrieval of patients. Case definition in our study was not based only on the 1980 ACR criteria for definite SSc. These were designed for classification, and not for diagnostic purpose, and to be specific rather than sensitive (11). Nailfold capillaroscopy and autoantibodies, which were later proven to be reliable predictors of SSc, were not considered. Many clinicians nowadays agree that the spectrum of patients suffering from SSc is wider than that included in the ACR definition (13). For these reasons, in 2001, LeRoy and Medsger proposed new criteria for the early diagnosis and classification of SSc (12). Although not yet validated, these criteria provided clear and largely shareable definitions, allowing the classification of several patients with Raynaud's phenomenon and minor signs or symptoms belonging to the clinical spectrum of SSc. In some recent prevalence studies, these criteria (5), or similar (4), have been used for the definition of SSc, but others have recorded only patients according to the ACR definition (3, 6). The proportion of patients fulfilling LeRoy-Medsger, but not ACR criteria, was reported to account for around 20% of the overall prevalence estimate (5), similar to that observed in the present study (3 patients out of 13: 23%). This figure should therefore be

taken into consideration, when comparing prevalence estimates from studies using different disease definitions.

The other crucial issue in prevalence studies is the identification of cases, which should be as complete as possible. This objective was probably achieved by our study, as far as cases with a known diagnosis of SSc are concerned, as suggested by the concordance from the two sources (GPs and specialists records),

Based on these considerations, we suggest that results of our study reflect both changes in the diagnostic criteria for SSc, including milder forms of disease, and recruitment of these mild cases due to active collaboration between GPs and specialists. In accordance, we found a high proportion of lcSSc to dcSSc, compatible with recent studies, in which the highest prevalence figures have also shown the highest proportion of lcSSc (4).

We cannot exclude that individuals with even milder forms of SSc were undiagnosed. It is of note that even a higher prevalence was reported by studies based on the screening of patients with Raynaud's phenomenon (RP), and the multiplication of the observed percentage of patients with SSc among those with RP by that of RP within the general population (14, 15). However, these studies were based on the active identification of a very small number of SSc cases, and their results might have been positively biased by an increased tendency of individuals suffering from SSc to participate in these investigations (5). Moreover, we cannot exclude the potential source of missed SSc patients, such as the practices of dermatologists or other specialists, but the organization of health care in Valtrompia makes this possibility unlikely, and such cases were not identified by GPs' forms.

However, although we cannot exclude that the prevalence of SSc is even higher than that which we calculated, it is most likely that patients who sought medical advice were identified. Since offering someone a diagnosis of SSc is not appropriate if the patient has no active problems (4), we think that our study offers a reasonable estimate of the prevalence of clinically relevant SSc in northern Italy.

Since case definition and completeness of case retrieval were most probably similar to ours in studies performed in England and northern France (4, 5) which recorded a lower prevalence, our data may confirm the suggestion of Greek authors (6) that the prevalence of SSc in southern Europe is higher than in northern Europe, indicating the need for other studies in order to confirm this suspicion.

Finally, this study underlines the usefulness of an active rheumatological network on the territory and of an active collaboration between GPs and rheumatologists for early diagnosing, regularly following up and regularly treating SSc patients.

Acknowledgements

The GPs of the Valtrompia District, ASL 02 who collaborated in the study (Antonini I, Belleri E, Belleri R, Beltrami G, Benzoni V, Bolognini F, Casilli E, Cossina B, Cucchi C, D'Argenio A, Di Mauro G, Gatta G, Jeannin A, Lena MA, Magliolo L, Minelli F, Mombelloni B, Nicoli R, Pagani C, Paterlini P, Pelliccioli G, Platto B, Remedio A, Romano M, Rossini G, Venturoli F, Zadra A) are gratefully acknowledged.

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