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Anal incontinence and vesico-sphincter events in systemic sclerosis: An epidemiologic bicentric cohort study

Mickaël Martin[a,*], Nadine Meaux-Ruault[a], Nadine Magy-Bertrand[a], Guillaume Beraud[b], Bernard Parratte[c], Pascal Roblot[b]

[a] Department of Internal Medicine, Besancon University Hospital, BESANCON Cédex, France
[b] Department of Internal Medicine, Infectious and Tropical Diseases, Poitiers University Hospital, Poitiers, France
[c] Department of Physiotherapy and Rehabilitation, Besancon University Hospital, BESANCON Cédex, France

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ABSTRACT

Objective: To estimate the frequency and severity of anal incontinence and vesico-sphincter events, associated factors, and impact on the quality of life of patients with systemic sclerosis.
Methods: Questionnaires assessing anal incontinence (Miller score), vesico-sphincter events (Urogenital Distress Inventory) and quality of life [Short Form Health Survey 36v2 (SF-36), and Hospital Anxiety and Depression Scale] were mailed to 139 patients with systemic sclerosis at the university hospitals of Besançon and Poitiers, France. Clinical data were collected from the medical records to identify risk factors.
Results: Among the 121 (87%) responders, severe vesico-sphincter events or severe anal incontinence occurred in 3.4% and 12.4% of cases, respectively. Frequent urination (66.3%) and anal incontinence to gas (50.4%) were the most frequent symptoms. Anal incontinence was associated positively with vesico-sphincter events, unrelated to obstetrical factors. No correlations were seen with age, sex, or systemic sclerosis characteristics. In multivariate analysis, moderate or severe vesico-sphincter events was associated with higher anxiety and depression scores and lower SF-36 scores; the same results were observed for anal incontinence, but did not reach significance.
Conclusion: Vesico-sphincter events and anal incontinence are common in systemic sclerosis, and sometimes severe, with a potential negative impact in quality of life. These results will be confirmed by a case-control study with dynamic and manometric assessment, and could legitimate a systematic screening to ensure early therapy and multidisciplinary individual management.

Introduction

Systemic sclerosis (SSc) is a systemic connective tissue disease and a source of morbidity and mortality. It preferentially affects women than men, between 45 and 64 years old [1].

Among the complications, anal incontinence (AI) has been reported in 22–38% of cases, with varying severity and symptomatology [2,3]. The prevalence of AI is often underestimated due to patients' reluctance to report symptoms or to seek care [4]. Vesico-sphincter events (VSE) in SSc have been rarely and poorly described in the literature. They can manifest as irritative symptoms [5–9], obstructions [5,6,8–10], or more rarely, as suprapubic pain [5,6], or isolated hematuria [5]. In the general population, risk factors for urinary incontinence (UI) are obesity and vaginal delivery, whereas diabetes mellitus type II and chronic diarrhea are risk factor for AI. Age above 80 years old and depression reassociated with dual incontinence (UI and AI) [11].

The impact of VSE and AI on quality of life (QoL) has rarely been studied in SSc. Only a few studies have reported that AI negatively impacts patient QoL; however, the symptoms related to AI were not reported [2,12]. One cohort study explored the impact of VSE on QoL in SSc and found that overactive bladder was associated positively with overall disability and anxiety [8].

The main objective of the current study was to estimate the frequency and the severity of VSE and AI in SSc. The secondary objectives were to assess associated symptoms, risk factors, and to estimate the impact of VSE and AI on patient's QoL.

Abbreviations: AI, anal incontinence; HADS, hospital anxiety and depression scale; QoL, quality of life; SF-36, short form health survey 36v2; SSc, systemic sclerosis; UDI-6, urogenital distress inventory; UI, urinary incontinence; VAS, visual analogic scales; VSE, vesico-sphincter events.

* Corresponding author at: Mickaël Martin, Department of Internal Medicine, Besancon University Hospital, BESANCON Cédex, France.
E-mail address: mickael.martin@chru-strasbourg.fr (M. Martin).

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Methods

Clinical records

We report here a descriptive and analytic transversal and retrospective bicentric cohort study. Patients with a SSc diagnosis according to the International Statistical Classification of Diseases and related Health Problems (ICD) from the registries of the university hospital of Besançon or Poitiers, (France), and followed in these centers between January 2010 and December 2012 were first selected. After this screening the patients only of 18 years or older, with a definite SSc diagnosis according to the criteria of LeRoy et al. [13] or LeRoy and Medsger [14] were retained. Exclusion criteria were as follows: non–French-speaking patients; localized scleroderma; and overlap syndromes (systemic lupus erythematosus (SLE) and/or rheumatoid arthritis). In fact, interstitial cystitis is reported in SLE and rheumatoid arthritis [15,16], and SLE may cause enteritis [17] and rectal ischemia [18]. Other exclusion criteria were chronic inflammatory bowel disease during treatment and/or symptomatic Crohn's disease or ulcerative colitis, that can also affect the digestive tract.

Five self-questionnaires were sent to each patient: (1) the Urogenital Distress Inventory (UDI-6) [19], testing by 6 items, each heighted from 0 to 3, (final ranging 0–18) the intensity of stress and emergency UI, as well as dysuria and pelvic pain. This scale was completed by questioning about the presence or absence of four or more urinary tract infections/year and/or macroscopic hematuria not associated with the menstrual cycle or cystitis; (2) the Miller score [20], testing AI by giving variable weights to the same frequencies according to the different type of AI: to gas (1–3), to liquid stools (4–6), or to solid stools (7–9). For each type, a total absence of AI was scored 0 (final ranging 0–18). This scale was completed by questioning about the presence or absence of clinical gastroesophageal reflux, clinical gastroparesis, frequent constipation, daily bloating, chronic diarrhea (≥ 3 months almost daily), anal seepage, urge AI, inability to distinguish gas or stool before emptying, and regular use of protective underwear; (3) the hospital anxiety and depression scale (HADS) [21] allowing distinct anxiety and depression scores, ranging from 0 (no sign) to 21 (major anxiety or depression); (4) the short form health survey 36v2 standard Canada (French) version 2.0 (SF-36) [22,23]. Each of the eight dimensions of this scale were individually scored, as well as the physical summary score (PSs) and the mental summary score (MSs), each varying from 0 (maximal QoL alteration) to 100 (no impact in QoL); and (5) visual analogue scales (VAS) exploring the impact of AI, VSE, and SSc in general, in the QoL, varying from 0 (no impact) to 10 (maximal negative impact). In order to identify potential QoL confounders, patients were also invited to indicate "yes" or "no" at the following question "Did you have any personal factors unrelated to SSc during the past 12 months that could have altered your quality of life?". The patients returned the questionnaires using an enclosed pre-paid envelope. Non-respondents were contacted by phone 1 month after the questionnaires were sent. Patients with AI and/or or VSE not previously known have been then addressed for a specific medical consultation.

On the basis of medical records, SSc patients with anticentromere antibodies were classified as limited form and those with anti-Scl70 antibodies, regardless of their skin fibrosis extension, were classified as diffuse form because of the better association of anti-Scl70 with disease severity than skin sclerosis extension [24] and the high risk of progression to diffuse cutaneous involvement and pulmonary fibrosis [25]. SSc patients without SSc-related specific auto-antibody were classified according to their skin extension and criteria of LeRoy et al. [13] or LeRoy and Medsger [14].

Patient's general data (age and sex), and SSc characteristics were collected retrospectively from medical records: SSc duration (time since the first non-Raynaud's symptom), SSc-specific autoantibodies (anti-centromere, anti-Scl70, anti-RNApolymeraseIII, and anti-PmScl), and others (rheumatoid factor and anti-SSA/SSB); current immunomodulatory/immunosuppressive drugs (corticosteroids, hydroxychloroquine, methotrexate, or others), current modified Rodnan skin score [26]. The current or past following clinical manifestations were also recorded: arthralgia and/or clinical arthritis; history of clinical digital ulcers; pulmonary arterial hypertension confirmed by right heart catheterization (mean pulmonary arterial pressure >25 mmHg and pulmonary capillary wedge pressure ≤ 15 mmHg); pulmonary fibrosis (carbon monoxide diffusing capacity $<70\%$ and typical interstitial pneumopathy on tomodensitometry); renal crisis (acute arterial hypertension with schizocytosis and proteinuria or microscopic hematuria, and acute renal insufficiency with or without renal histologic confirmation); and peripheral neuropathy supposed to be related to SSc by the practician and notified to it in the medical record. Potential confounders for VSE and AI were also collected from medical records: parity, history of UI related to postpartum, hysterectomy or bladder prolapse (operated or not), history of benign prostatic hyperplasia (treated or not), and current treatment with antidepressants and/or benzodiazepines.

This study was approved by the Besançon and Poitiers university hospital local ethical committees.

Statistical analysis

The data were entered into a computer database (Microsoft ACCESS software, PEDYN, Inc., Dallas, Fort Worth). Qualitative and ordinal variables were described using the number and frequency of each modality. Quantitative variables were expressed as the mean $\pm$ standard deviation.

The UDI-6 and Miller scores were subdivided into four categories, with 0 indicating no impairment, 1–6 slight impairment, 7–12 moderate impairment, and 13–18 severe impairment, based on the study of White et al. [27]. Groups with no or slight impairment (UDI-6 or Miller score ≤ 6) were subsequently compared to those with modest or severe impairment (UDI-6 or Miller score ≥ 6) about risk factors and quality of life.

Univariate analysis was performed to study the correlations between the various factors by comparing percentages using Fisher's exact test for qualitative variables. Quantitative variables being expressed as the mean $\pm$ standard deviation have a Gaussian distribution, so comparison were made using the parametric Student's t-test due to their wide distribution. Regarding Fisher's exact test in bilateral formulation, the 95% CI is only an approximation and may sometimes contain an odds ratio (OR) of 1 despite $p < 0.05$ [28].

The SF-36 scores were weighted by age and sex based on the scores of the U.S. population. Statistical analysis was performed with the statistical programming environment R/2.15.

Univariate analysis of the quality of life was performed and the Student's t-test was used to analyze the associations between different factors and QoL and anxiety/depression scores. Multiple linear regression analysis was then performed for each QoL and anxiety/depression score (dependent variables), adjusted for independent variables that might affect QoL, regardless of the VSE or AI, such as the presence of personal life events unrelated to SSc and antidepressants or benzodiazepines use. All significance levels are set to $p < 0.05$.

Covariate interactions with the main explanatory variable were sought, and the analysis was stratified by the interaction variable if necessary. The alpha risk was set to 5% and statistical tests were performed bilaterally.