A Romanian version of the UCLA Scleroderma Clinical Trial Consortium Gastrointestinal Tract Instrument

M. Gorga1, C. Mihai1,2, A.-M. Soare1,2, R. Dobrotă1,2, A.-M. Gherghe1,2, V. Stoica1,2

Carol Davila University of Medicine and Pharmacy Bucharest, Romania;
Department of Internal Medicine and Rheumatology, Dr I. Cantacuzino Clinical Hospital, Bucharest, Romania.

Marilena Gorga, MD
Carina Mihai, MD, PhD
Alina-Mihaela Soare, MD
Rucsandra Dobrotă, MD*
Ana-Maria Gherghe, MD*
Victor Stoica, MD, PhD, Prof.
*These authors made an equal contribution to this work.

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Abstract

Objective. UCLA Scleroderma Clinical Trial Consortium Gastrointestinal Tract (UCLA SCTC GIT 2.0) Instrument is a comprehensive, self-administered survey for the assessment of gastrointestinal involvement in scleroderma patients, developed and validated in English. Our objective was to translate and validate a Romanian version of UCLA SCTC GIT 2.0.

Methods. Translation from English into Romanian has been made using the forward-backward method. Sixty-four patients, attending a referral centre as part of an extensively studied cohort, were approached in a consecutive manner over a period of two years for administration of the questionnaire. We evaluated the reproducibility, internal consistency, construct validity and discriminative capacity of the translation (Romanian GIT).

Results. Fifty-four patients returned completed questionnaires. Internal consistency was demonstrated by Cronbach’s alpha coefficient (0.931). Construct validity is supported by moderate, but significant correlations of Romanian GIT total score with the Mental Component Summary (MCS) of SF-36 (r=0.541, Spearman correlation) and among subscales, by significant correlations with SHAQ total score (r=0.559, Spearman correlation) and by strong correlations with gastrointestinal subscale of SHAQ (SHAQ GI) (r=0.726, Spearman correlation).

Reproducibility was also good. Divergent validity was supported by significant differences between patients with or without a clinical diagnosis of gastrointestinal disease. Other differences in the Romanian GIT total score were tested among subgroups of patients.

Conclusion. The Romanian GIT has acceptable reliability and validity. This questionnaire can be used for the assessment of gastrointestinal involvement in scleroderma patients.

Introduction

Systemic sclerosis or scleroderma is a connective tissue disease, affecting the skin and visceral organs, with significant mortality and a high impact on quality of life (1-3). The disease is characterised by a unique combination of immunological abnormalities, vascular disease and fibrosis (4), while smooth muscle atrophy and replacement fibrosis are the main pathological features in the gastrointestinal tract (5, 6). These pathological changes correlate with a decrease in motility, most frequently noted in the oesophagus (7), and are responsible for a variety of symptoms, depending on the affected segment (8, 9).

The involvement of the digestive tract in scleroderma is of great interest, since its presence can be detected in nearly all scleroderma patients. Before the introduction of proton pump inhibitors (PPIs), clinically significant gastrointestinal involvement was estimated to occur in approximately 50% of cases (10). Investigations using sensitive methods, especially classical manometry, demonstrated the presence of abnormalities in up to 90% of cases (8, 9), thus indicating a lack of symptoms in some patients or a more subtle disease. A systematic application of a symptom questionnaire in a large hospital cohort recently suggested that gastrointestinal symptoms are very frequent in scleroderma, with only 10% of patients reporting daily symptoms, but just 3% having no symptoms at all (11).

Khanna et al. developed the UCLA Scleroderma Clinical Trial Consortium Gastrointestinal Tract Instrument (UCLA SCTC GIT 2.0), a comprehensive self-administered survey, translated and validated in the recent years in English (12, 13), French (14) and Dutch (15). Our objectives were to translate and validate the UCLA SCTC GIT 2.0 instrument in Romanian lan-
gauge, as a potential useful tool in the clinical evaluation of gastrointestinal symptoms in scleroderma patients.

Patients and methods

Patients

We approached 64 patients with a confirmed diagnosis of scleroderma, attending a referral centre over a period of two years, from November 2011 to November 2013, in a consecutive manner. The patients were part of a hospital cohort of scleroderma cases, each consented in writing before taking part in this cohort and with responsible ethics committee approval in place for this research. Patients in the cohort regularly attended the hospital, at least for a yearly evaluation, which included a detailed clinical assessment, annual pulmonary function tests (PFTs), annual echocardiography for pulmonary hypertension screening and additional tests, depending on clinical status of each patient. All patients fulfilled ACR classification criteria (16) or LeRoy classification criteria for early or limited systemic sclerosis (17). All patients also fulfilled the 2013 classification criteria applied in retrospect (18). All questionnaires were filled in by patients during a visit in the hospital. Socio-demographic and clinical data were systematically collected, including but not limited to patient general characteristics (age, sex, education level, work capacity), disease subtype, disease duration (defined as duration since appearance of first non-Raynaud symptom), body mass index, weight loss, lab results, autoantibodies status, physical and mental health assessments, functional tests, clinical diagnoses, comorbidities, current and previous treatments. One patient has been excluded due to history of extensive gastric resection for duodenal ulcer. Gastrointestinal (GI) diagnoses by clinician were documented at each visit and included: gastro-esophageal reflux disease, gastritis, diarrhea, fecal incontinence and constipation. There was no case of pseudo-obstruction noted in this cohort. Gastrointestinal tests performed at each visit were retrieved from patient’s files and consisted in oesophagogastroduodenoscopy, X-ray studies including barium transit studies and colonoscopy.

Translation and field-testing

UCLA SCTC GIT 2.0 questionnaire is a validated 34-items questionnaire with 7 subscales, assessing reflux (8 questions), distension/bloating (4 questions), diarrhea (2 questions), social functioning (6 questions), emotional well-being (9 questions) and constipation (4 questions) (12). Each item scores the frequency of symptoms over a recall period of 7 days, on a 0 to 3 possible range, where 0 indicates better health and 3 indicates worse health, with the exception of questions 15 (diarrhea subscale) and 31 (constipation subscale), scored on 0 (better health) to 1 (worse health). The average of items in each subscale can be calculated as a separate subscale score (for reflux, distention/bloating, fecal soilage, diarrhea, constipation, social functioning, emotional well-being), with scores ranging from 0 to 3, except diarrhea and constipation, with ranges 0–2 and 0–2.5, respectively. A combined score of 6 subscales (excluding constipation) is calculated as a total score, to capture the overall burden of disease (possible scores from 0 to 2.83). The English version of UCLA SCTC GIT 2.0 is available at http://uclasclerodema-researchcore.org/ and it was used in this study with kind permission from the author (Dr D. Khanna). The UCLA SCTC GIT 2.0 was translated from English into Romanian by an independent translator and a rheumatologist (MG), then agreement on the draft translation was reached among the two. The back-translation of the draft was performed by another rheumatologist (CM) and a second independent translator (See Appendix). Adjustments were made by consensus among all translators. To assess the time needed for completion and the choice of some terms, the questionnaire was preliminarily administered and discussed with five patients attending the hospital.

Statistical methods

The questionnaires were excluded in cases of more than 50% missing answers for a scale or more than 10% overall missing answers. All statistical analyses were carried in SPSS 20.0 software and a few missing values were imputed by using the overall sample median (except for constipation scale, which does not contribute to the total score). Reproducibility was assessed by retesting the questionnaire over a period varying from 8 to 14 days in a group of 16 patients, with correlations r > 0.7, considered as acceptable. Internal consistency as a measure of reliability was evaluated by applying Cronbach’s alpha method for the seven subscales and the total score of the Romanian GIT questionnaire. For a good correlation, the minimum Cronbach’s alpha coefficient should be 0.7. The proportion of patients scoring the worst possible score (the maximum possible value of the instrument) was defined as floor effect. The proportion of patients scoring the best possible score of the instrument (absence of symptoms) was defined as ceiling effect (19). These proportions were calculated for each scale and an effect was considered present if more than 15% of patients gave maximum or minimum scores, respectively. Construct validity: convergent validity was tested by examination of Spearman correlation coefficients 1) between Romanian GIT scores and Short Form (36) Health Survey (SF-36) and 2) between Romanian GIT scores and Scleroderma Health Assessment Questionnaire (SHAQ). Correlations Φ 0.29 were considered to be small, 0.30 to 0.49 moderate, and 0.50 strong. The Short Form (36) Health Survey (SF-36) is a generic health survey, widely used for estimating disease burden. The instrument provides an 8-scale profile of functional health and well-being, as well as two summaries, physical and mental component scores (PCS and MCS). The Physical Functioning, Physical Role functioning and Bodily Pain scales contribute mostly to the scoring of Physical Component Summary (PCS), while Mental Health, Emotional Role functioning and Social Functioning scales contribute mostly to the Mental Component Summary (MCS). Vitality and General Health perceptions scales each contribute to
both PCS and MCS. Norm-based scoring transforms all scales to have the same average score (50) and the same standard deviation (10 points) (20, 21).

Discriminative (divergent) validity was assessed by comparing total and subscales scores of the Romanian GIT questionnaire in patients with or without a clinical GI diagnosis (Mann-Whitney U-test; \( p < 0.05 \) was considered significant).

### Results

The Romanian version of the UCLA SCTC GIT 2.0 questionnaire is reproduced in the appendix. During preliminary discussions, two patients remarked a complete avoidance of ‘acidic’ foods.
due to severe heartburn. A total of 54 patients returned completed questionnaires. Patients’ characteristics are summarised in Table I. All patients were Caucasians, 49 (90.7%) were women and 40 (74%) had the limited form of the disease (ISSc). The patients with a diffuse form (dSSc) were more frequently anti-Scl70 positive and had a lower FVC (% predicted) than those with ISSc.

The Romanian GIT questionnaire showed a good internal consistency (Table II), with Cronbach’s alpha 0.931. For all subscales Cronbach’s alpha was ≥0.7, with the exception of diarrhea subscale (alpha 0.581). The median total GIT score was 0.35. Strong corrected item-total correlations were noted for all items in the reflux subscale, with only item 6 (‘...sleeping in a raised or seated position’) showing a moderate correlation (r=0.353). Corrected item-total correlation was low for item 20 on the social functioning subscale (‘...worrying of accidentally soiling the underwear’), r=0.003, most probably due to the very low prevalence of faecal incontinence in our cohort. Except for the reflux scale and the total GIT score, there was a clear ceiling effect in all other subscales, with a maximum effect in fecal incontinence scale (89%). No floor effect was noted.

Table III presents the results of analysis of correlation between Romanian GIT with SF-36 subscales and summaries, as well as with total SHAQ score and with the gastrointestinal SHAQ subscale (SHAQ-GI). Romanian GIT total score showed significant correlations with all SF-36 subscales, but not with the physical functioning subscale (PF) or with PCS. Fecal soiling and constipation correlated significantly with PF scale. We found strong correlations of Romanian GIT total score with the MCS and between the social functioning and emotional well-being subscales of Romanian GIT with the social functioning (SF), emotional role functioning (RE), bodily pain (BP) and mental health perception (MH) subscales of SF-36, as well as with the MCS score. Instead, we found a strong correlation of Romanian GIT total score with SHAQ total score (r 0.559). Reflux, distension/bloating, social functioning and emotional well-being subscales all had moderate to strong correlations with SHAQ total score. An excellent correlation has been found between Romanian GIT total score and SHAQ-GI subscale (r=0.726). Reflux, distension/bloating, diarrhea, social functioning, emotional well-being and constipation subscales demonstrated moderate to excellent correlations with SHAQ-GI subscale.

Patients with a clinical GI diagnosis scored significantly higher on the Romanian GIT total score compared with patients with no clinical GI diagnosis; significant differences were found for all subscales, except fecal incontinence and constipation subscale (Table IV). We compared Romanian GIT scores and SHAQ total score between different subgroups of patients. ACA-positive patients tended to have significantly higher scores for reflux (p=0.016) and distension/bloating subscales (p=0.011), while anti-Scl70 positive patients tended to have a lower reflux score.
score (p=0.015). There were no significant differences in GIT scores based on disease subsets (data not shown). Interestingly, a significant difference was found in patients with or without current treatment with prokinetics, for the total GIT and distension/bloating scores, with a higher burden of disease in those patients currently on treatment. There were no significant differences in GIT scores based on other current treatments (proton-pump inhibitors, calcium-channels blockers, NSAIDs, methotrexate, azathioprine, protonoids) or agent with a reported association of decreased fibrosis in the lungs (27, 28), but the relationship between pulmonary disease and the vascular component of scleroderma. Many authors support a contribution of reflux as a perpetrator of fibrosis in the lungs (27, 28), but the relationship between pulmonary disease and dysmotility is more complex, with some reports in support of a relationship and other against it (29, 30). However, most studies relied on classical manometry. The spread of high-performance investigations may bring new data, with some recent reports in support of a relationship among GI disease and the vascular component of lung disease (31).

Previous reports on UCLA SCTC GIT 2.0 conducting factor analysis suggested a primary factor dominated by diarrhoea (and related symptoms) and a secondary factor dominated by con-
stipation (and related symptoms) (12, 13). Using a preliminary version of the UCLA GIT (1.0), Thoua et al. reported an inverse relationship among diarrhoea and pulmonary fibrosis (11). A low representation of lower GI tract symptoms in our cohort might be another limitation of the study, so extension of analysis on a larger cohort is needed, as well as a longitudinal assessment.

Detailed algorithms for optimal management of digestive tract involvement in scleroderma have been recently proposed (32). For a thorough assessment of gastrointestinal disease and its impact on quality of life, the application of questionnaires might complement the objective investigations. In conclusion, the Romanian version of the UCLA SCTC GIT 2.0 has acceptable reliability and validity and might prove to be a useful tool to assess the gastrointestinal disease in patients with systemic sclerosis.

References
Appendix

**ID:** ___________________  **Data:** ___________________

Următoarea întrebare se referă la simptomele dummenoavoastră gastrointestinale (digestive) și la medii în care acesta v-a afectat viața în ultimele 7 zile. Răspunzător la fiecare întrebare selectând răspunsul din cele indicate. Dacă nu s-a întâmplat nimic care să răspundeti la o întrebare, va rugăm alegeți răspunsul cel mai bun pe care lpute de da.

### In ultima săptămână, cât de des...

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<tr>
<th>ID</th>
<th>(Alegeți Un Răspuns pentru Fecare Intrebare)</th>
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<tbody>
<tr>
<td>1.</td>
<td>săt avut dificultăți să înghiți mâncare solidă?</td>
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<td>2.</td>
<td>săt avut o senzație nepăcată de șaritorie sau arsă în piept (piroază)?</td>
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<td>3.</td>
<td>săt avut senzația de șigil în gură, amar sau acru, venind înzestrat din stomac (refluş acid)?</td>
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<td>4.</td>
<td>săt dormit o parte din consumul de alimente acide, cum ar fi râpi sau părupită?</td>
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<td>5.</td>
<td>săt dormit într-o poziție ridicată sau în șezut?</td>
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<td>6.</td>
<td>săt avut senzația de vomă sau vârsată?</td>
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<td>7.</td>
<td>săt avut vomită?</td>
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### Distrunțe

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<td>8.</td>
<td>săt simți balonat sau (senzație de gazoare sau aer în stomac)?</td>
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<td>9.</td>
<td>săt observa o balonare a abdoemului, unori reușind să vă deplasezi curăseu, pantaloni sau cămașă?</td>
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<td>10.</td>
<td>săt simți plin și după o masă redusă cantitativ?</td>
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<td>11.</td>
<td>săt eliminat gazo în exces?</td>
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### Dăiere

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<td>12.</td>
<td>săt simți pâră sau amână dăierea?</td>
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### Functionarea Socială

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<td>13.</td>
<td>săt simți dăierea sau a înalțat în timpul schimbului?</td>
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### Scoring

**Scor Total: Reflex**

- Distanță/Balonare
- Conțența fecală
- Diaree
- Funcționarea socială
- Starea emoțională

**Scor Total=** [ ] / 6 __________

**Scor Total=**

- Distanță/Balonare
- Conțența fecală
- Diaree
- Funcționarea socială
- Starea emoțională

**Scor Total=** [ ] / 6 __________

**Reținut: Scorul pentru Constație nu se incluie în calcularea scorului total.**

C= Constație; D=Dăiere; D/B=Distanță/Balonare; FS= Funcționarea socială; IM= Inconținerea fecală; RN=Refux; SE= Starea emoțională.

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