Minimally Important Differences of the UCLA Scleroderma Clinical Trial Consortium Gastrointestinal Tract Instrument

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ABSTRACT. ***Objective.*** To provide minimally important difference (MID) estimates for the UCLA Scleroderma Clinical Trial Consortium Gastrointestinal Tract 2.0 (UCLA SCTC GIT 2.0) in a longitudinal observational cohort.

Methods. We administered the UCLA SCTC GIT 2.0 to 115 patients with systemic sclerosis (SSc) at 2 timepoints 6 months apart. The UCLA SCTC GIT 2.0 has 7 multi-item scales: Reflux, Distension/Bloating, Diarrhea, Fecal Soilage, Constipation, Emotional Well-being, and Social Functioning and a total GIT score. All scales are scored from 0 [better health-related quality of life (HRQOL)] to 3 (worse HRQOL) except the diarrhea and constipation scales (ranges 0–2 and 0–2.5, respectively). Patients also rated their overall and upper and lower GIT involvement during the second visit using a response scale with options "much better; somewhat better; almost the same; somewhat worse; or much worse." The minimally changed group was defined by those reporting they were somewhat better or somewhat worse compared to first visit.

Results. Study participants were 84% female and 81% white with a mean disease duration of 6.9 years. The MID estimates for improvement ranged from 0.07 for the Social Functioning scale to 0.36 for the Emotional Well-being scale. For worsening, the MID estimates ranged from 0.06 for the Fecal Soilage scale to 0.21 for the Social Functioning scale.

Conclusion. We provide MID estimates for the UCLA SCTC GIT 2.0 scales. This information can aid in interpreting scale scores in future randomized controlled trials and observational studies. (First Release July 1 2011; J Rheumatol 2011;38:1920–4; doi:10.3899/jrheum.110225)

Key Indexing Terms:

GASTROINTESTINAL
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Gastrointestinal tract (GIT) involvement occurs in approximately 90% of patients with systemic sclerosis (SSc)[1,2] and has a negative influence on health-related quality of life (HRQOL)[3,4]. The UCLA Scleroderma Clinical Trial Consortium GIT 2.0 (UCLA SCTC 2.0)[5] includes 34 items and 7 multi-item scales (Reflux, Distension/Bloating, Diarrhea, Fecal Soilage, Constipation, Emotional Well-being, and Social Functioning) and a total GIT score to assess HRQOL and GIT symptom severity in SSc. All scales are scored from 0 (better HRQOL) to 3 (worse HRQOL) except the Diarrhea and Constipation items (ranges 0–2 and 0–2.5, respectively). The GIT 2.0 takes 6–8 minutes to complete and was found to have acceptable feasibility, reliability (test-retest and internal consistency), and validity in a large observational study. This study estimates minimally important differences (MID) — the smallest change in score that patients perceive as beneficial — for the GIT 2.0 scales[6]. MID estimates provide a benchmark for the future design of gout clinical tri-

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als by helping researchers and clinicians determine whether HRQOL score differences between 2 treatment groups or if changes within one group over time are meaningful[7].

MID estimates were obtained using an anchor-based approach. An "anchor" is a clinically relevant indicator of change that is used to evaluate change on a patient-reported outcome measure. Anchors include clinical indicators of response to treatment (disease severity) and subjective patient or physician reports.

MATERIALS AND METHODS

Patient characteristics and study methods have been published[5,8]. In brief, patients with SSc and GIT involvement were invited to participate at the following 3 scleroderma centers in the United States: UCLA, Los Angeles, CA; University of Michigan, Ann Arbor, MI; and University of Texas at Houston, Houston, TX. The protocol was approved by the institutional review board at each institution (UCLA approval no. 07-08-004-04), and each subject signed a consent form prior to completing the questionnaires. In addition to completing the paper-and-pencil UCLA SCTC 2.0 questionnaire[9], patients reported their age, sex, race/ethnicity, and level of education. Each physician did a physical examination to determine the type of SSc (limited or diffuse cutaneous) and provide their GIT diagnoses.

Patients were re-administered the UCLA SCTC GIT 2.0 during their second clinic visit. We used 3 different patient-reported anchors. Patients rated their overall and upper and lower GIT involvement: (1) "Compared to your LAST VISIT, how would you rate your overall gastrointestinal symptoms?"; (2) "Compared to your LAST VISIT, how would you rate your upper gastrointestinal symptoms (such as heartburn, nausea, vomiting, bloating or gas or air in the stomach)?"; and (3) "Compared to your LAST VISIT, how would you rate your lower gastrointestinal symptoms (such as diarrhea or constipation)?". Responses were provided using a categorical response scale: "Much better; somewhat better; almost the same; somewhat worse; or much worse."

For Reflux and Distension/Bloating scales, we used the overall and upper GI items as anchors to estimate the MID. For Diarrhea, Constipation, and Fecal Soilage scales, the overall and lower GI scales were used as anchors. For the Emotional Well-being and Social Functioning scales and the total GIT score, we used all 3 rating items as anchors.

The MID was estimated by examining change in scores of different GI scales (Time 2 – Time 1) in subjects who reported they were somewhat better or somewhat worse. MID have been found to range between effect sizes (ES) of 0.20 and 0.50[10]. ES is the ratio of observed change to a measure of variance[11] and was defined as (mean score for individual scale at Time 2 – mean score for individual scale at Time 1)/SD baseline. Because we had multiple anchors for each scale, we present individual MID estimates and as an average across different anchors.

To assess the usefulness of an anchor, previous research has recommended reporting the correlation between the anchor and the change score; for example, a correlation of zero will make the anchor useless and a correlation of at least 0.30–0.35 has been suggested[10,12]. We assessed the association between the anchors and the change scores for scales using the Spearman rank-order correlations to account for the ordinal level of measurement of the anchors.

All analyses were performed using Stata software version 10.2 (Stata Corp., College Station, TX, USA).

RESULTS

Study population. The participants had a mean age of 51 years, 84% were female, and 81% were white; 55% had diffuse SSc with a disease duration of 6.9 (SD 7.4) years[5,8]. The majority of patients had a diagnosis of gastroesophageal reflux disease (91%) followed by small intestinal bowel bacterial overgrowth, gastroparesis, and diarrhea (11% each). Of 152 patients, 115 patients returned for their second visit a mean of 6 (SD 3) months later. Of these, 10 patients were started on proton-pump inhibitor (PPI) or dose was increased, 8 were started on pro-motility agents or dose was increased, and 1 each was started on antibiotics and laxatives during the 2 visits.

Spearman correlation coefficients for 3 anchors versus 7 scales ranged from 0.04 for the Constipation scale with the upper GI anchor to 0.41 for the Reflux scale with the upper GI anchor (Table 1). Only the Constipation scale had nonsignificant correlations with its anchors (overall and lower GI). The other correlations were statistically significant (Table 1).

There were no significant changes in the mean scores of GIT scales and total GI score from baseline to second visit (Table 2). In 8 patients who started or increased their dose of PPI, the mean change score was 0.09 (SD 0.46) compared to 0.05 (SD 0.39) in patients with no change in their PPI ($p = 0.7$). In 8 patients who were started on pro-motility agents, the mean change score was –0.61 (SD 0.78) compared to +0.01 (SD 0.69) in patients in whom pro-motility agents were not started ($p = 0.03$).

The mean MID estimates for improvement ranged from 0.07 for the Social Functioning scale to 0.36 for the Emotional Well-being scale (Tables 3 and 4). Except for the Distension/Bloating and Social Functioning scales, ES for MID estimates ranged from 0.20 to 0.58. For the Distension/Bloating scales, MID estimates for improvement were 0.04 (ES 0.05) for overall GI anchor and 0.24 (ES 0.26) for upper GI anchor. For the Social Functioning scale, the MID estimates ranged from 0.04 (ES 0.10) to 0.11 (ES 0.33) for all 3 anchors.

For worsening, the mean MID estimates ranged from 0.06 for the Fecal Soilage scale to 0.21 for the Social Functioning scale. ES were generally smaller for the worsening than for the improvement group and ranged from 0.00 to 0.43. All MID estimates for improvement and worsening were larger than for the "no change" group.

Table 1. Spearman correlation coefficients between the UCLA SCTC GIT 2.0 scales and ratings of overall gastrointestinal (GI), upper GI, and lower GI involvement. Scores are calculated as the difference between Time 1 and Time 2 and anchors were administered at Time 2.

Scales	Overall GI Involvement	Upper GI Involvement	Lower GI Involvement
Reflux	0.40	0.41	0.28
Distension/Bloating	0.25	0.24	0.21
Diarrhea	0.27	0.25	0.23
Constipation	0.05*	0.04*	0.11*
Fecal soilage	0.20	0.09*	0.17
Emotional well-being	0.34	0.31	0.36
Social functioning	0.31	0.37	0.28
Total GIT score	0.48	0.52	0.40

* $p \geq 0.05$.

Table 2. Baseline and followup gastrointestinal scores for 115 patients who completed the UCLA SCTC GIT 2.0 instrument at 2 timepoints.

Scales	Baseline			Followup Period			p
	Mean Score	SD	Range	Mean Score	SD	Range	
Reflux	0.71	0.54	0, 2.63	0.66	0.53	0, 2.75	0.6
Distension/Bloating	1.09	0.83	0, 3.00	1.09	0.83	0, 3.00	0.8
Diarrhea	0.57	0.68	0, 2.00	0.47	0.56	0, 2.00	0.1
Fecal soilage	0.3	0.67	0, 3.00	0.28	0.61	0, 3.00	0.9
Constipation	0.44	0.50	0, 2.25	0.42	0.47	0, 2.00	0.5
Emotional well-being	0.49	0.65	0, 2.78	0.41	0.60	0, 2.78	0.6
Social functioning	0.26	0.51	0, 3.00	0.24	0.46	0, 2.5	0.8
Total score*	0.67	0.47	0, 2.18	0.62	0.47	0, 2.01	0.5

* Sum of 6 of 7 scales (excludes Constipation scale).

DISCUSSION

MID estimates provide a benchmark for interpretation of results by helping researchers and clinicians understand whether HRQOL score differences between 2 treatment groups are meaningful, or if changes within one group over time are meaningful[7]. For example, an average change of 0.15 points (on a 0–3 scale) for a patient-reported measure may be statistically significant in a clinical trial, but may not be perceived as beneficial by the subjects. It is also important to note that MID estimates are applicable at the group level and not at the individual level. Other statistical tests have been recommended to assess statistical significance at an individual level[13,14].

The UCLA SCTC GIT 2.0 was developed to assess severity of SSc-related GIT symptoms and effects of GIT symptoms on emotional well-being and social functioning[5,8]. In this study, we present MID estimates for improvement and worsening that are applicable for interpretation of scores in clinical trials and observational studies. Our study is in alignment with other studies that have shown that an effect size of 0.20 to 0.50 corresponds to the MID for patient-reported outcome measures[14,15,16]. Also, the MID estimates were larger than those for the "no change" group, providing confidence in our estimates.

Previous reports have shown that the MID estimates may differ for worsening compared to improvement groups[14,17,18]. Therefore, we decided to present the MID estimates separately for improvement and worsening groups. Our results are in agreement with the published data. On average, our MID estimates for the improved group were larger than those for the worsened group. The only exception was the Social Functioning scale, where MID estimates were 0.07 for the improved group and 0.21 for the worsened group.

Although we show that an improvement of 0.26 points (on a 0–3 scale) in the Reflux scale is the MID estimate, it should not be interpreted that a change of less than 0.26 points is not clinically important, as there is an inherent uncertainty around MID estimates. Previous studies have reported this uncertainty around the MID estimates[19,20], hence experts recommend using several anchors. In addition, they suggest gathering data from both observational and clinical trials to support confidence in MID estimates[10], as it is unlikely that a single MID estimate is applicable to all patient populations. Despite this uncertainty, these data can be used to interpret clinical trial data and observational studies.

Our study has several strengths. Our MID estimates are based on a large sample size in patients at 3 US scleroderma centers. Second, we prospectively incorporated anchors in order to estimate the MID.

Our study also has limitations. As reported[5], we used only patient-reported anchors to estimate MID. We did not include radiological test measures such as the gastroesophageal endoscopy and breath test in this study. Future studies should corroborate our estimates using these tests and different anchors. Second, our study population generally had mild to moderate GIT disease (self-rated), with only 9% of patients stating severe to very severe GIT disease. The estimates may differ by severity of illness[10]. In addition, as previously seen[14,21], the majority of patients in our study considered themselves about the same between the 2 timepoints. Therefore, these data should be considered preliminary and should be confirmed with larger cohorts and/or clinical trials.

We provide MID estimates for the UCLA SCTC GIT 2.0 scales. This information can aid in interpreting scale scores in future randomized controlled trials and observational studies.

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Table 3. Minimally important differences for UCLA SCTC GIT 2.0 scales and total gastrointestinal tract score. A negative sign indicates improvement in the scale scores.

UCLA SCTC GIT 2.0 Scale	Patient-rated*	Overall GI Anchor Mean Change (95% CI)	Overall GI Anchor Effect Size	Upper GI Anchor Mean Change (95% CI)	Upper GI Anchor Effect Size	Lower GI Anchor Mean Change (95% CI)	Lower GI Anchor Effect Size	Overall Mean Change†
Reflux	Much better (n = 11–12)	–0.35 (–0.69, 0)	–0.68	–0.26 (–0.54, 0.02)	–0.52			–0.3
	Somewhat better (n = 15–18)	–0.26 (0.44, –0.07)	–0.58	–0.27 (–0.56, 0.03)	–0.58			–0.26
	About the same (n = 66–71)	0.02 (–0.06, 0.1)	0.03	–0.02 (–0.01, 0.05)	–0.04			–0.001
	Somewhat worse (n = 15–19)	0.15 (0, 0.29)	0.29	0.22 (0.05, 0.39)	0.32			0.19
	Much worse (n = 0–1)	NA	NA	0.41	–0.52			NA
Distension/ Bloating	Much better (n = 11–15)	–0.71 (–1.15, 0.27)	–0.74	–0.41 (–0.74, 0.08)	-0.52			–0.56
	Somewhat better (n = 15–18)	–0.04 (–0.44, 0.37)	–0.05	–0.24 (–0.75, 0.26)	-0.34			–0.14
	About the same (n = 66–71)	0.11 (–0.05, 0.26)	0.14	0.04 (–0.11, 0.2)	0.06			0.08
	Somewhat worse (n = 13–19)	–0.03 (–0.29, 0.23)	–0.03	0.27 (0.05, 0.49)	0.34			0.12
	Much worse (n = 0–1)	NA		0	NA			NA
Diarrhea	Much better (n = 11–15)	–0.41 (–0.74, –0.08)	–0.61			–0.43 (–0.76, –0.1)	–0.64	–0.42
	Somewhat better (n = 16–18)	–0.22 (–0.72, 0.28)	–0.29			–0.16(–0.7, 0.38)	–0.19	–0.19
	About the same (n = 66–69)	–0.1 (–0.25, 0.05)	–0.16			–0.03 (–0.16, 0.1)	–0.05	–0.06
	Somewhat worse (n = 12–18)	0.14 (–0.15, 0.43)	0.21			0 (–0.56, 0.56)	0	0.07
	Much worse (n = 0)					NA	NA	NA
Constipation	Much better (n = 11–15)	–0.11 (–0.55, 0.32)	–0.22			–0.11 (–0.43, 0.21)	–0.24	–0.11
	Somewhat better (n = 16–18)	–0.15 (–0.47, 0.16)	–0.28			–0.19 (–0.53, 0.15)	–0.34	–0.17
	About the same (n = 66–69)	–0.01 (–0.11, 0.1)	–0.02			–0.05 (–0.13, 0.03)	–0.11	–0.03
	Somewhat worse (n = 13-19)	0.03 (–0.14, 0.21)	0.08			0.23 (–0.14, 0.6)	0.37	0.13
	Much worse (n = 0)	0.41				NA	NA	NA
Fecal soilage	Much better (n = 11–15)	–0.36 (–0.82, 0.09)	–0.56			–0.2 (–0.57, 0.17)	–0.35	–0.28
	Somewhat better (n = 15–17)	–0.18 (–0.55, 0.2)	–0.21			–0.2 (–0.57, 0.17)	–0.21	–0.19
	About the same (n = 64–67)	0.06 (–0.06–0.19)	0.11			0.01 (–0.1, 0.13)	0.03	0.04
	Somewhat worse (n = 13-19)	0.05 (–0.14, 0.25)	0.07			0.08 (–0.09, 0.24)	0.09	0.06
	Much worse (n = 0)	NA				NA	NA	NA
Emotional well-being	Much better (n = 11–15)	–0.28 (–0.56, –0.01)	–0.53	–0.3 (–0.57, 0.03)	–0.58	–0.27 (–0.49, –0.06)	–0.56	–0.29
	Somewhat better (n = 14–18)	–0.4 (–0.79, 0)	–0.57	–0.26 (–0.64, 0.11)	–0.36	–0.42 (–0.81, 0.02)	–0.58	–0.36
	About the same (n = 66–71)	0 (–0.09, 0.08)	0	–0.05 (–0.16, 0.06)	–0.08	0 (–0.09, 0.1)	0.01	–0.02
	Somewhat worse (n = 13–19)	0.14 (–0.07, 0.35)	0.23	0.15 (–0.1, 0.4)	0.19	0.2 (–0.07, 0.46)	0.24	0.16
	Much worse (n = 0–1)	NA		0.44	NA	NA	NA	NA
Social functioning	Much better (n = 11–15)	–0.23 (–0.5, 0.05)	–0.54	–0.27 (–0.55, 0)	–0.65	–0.2 (–0.4, 0)	–0.52	–0.23
	Somewhat better (n = 14–18)	–0.04 (–0.15, 0.08)	–0.1	–0.11 (–0.22, 0)	–0.33	–0.07 (–0.18, 0.03)	–0.24	–0.07
	About the same (n = 64–69)	0.02 (–0.04, 0.07)	0.04	0.03 (–0.04, 0.1)	0.09	0.09 (0.01, 0.17)	0.31	0.05
	Somewhat worse (n = 13–19)	0.24 (–0.1, 0.57)	0.39	0.33 (–0.02, 0.68)	0.43	0.08 (–0.33, 0.48)	0.08	0.21
	Much worse (n = 0–1)	NA		–0.17	NA	NA	NA	NA
Total GIT score	Much better (n = 11–15)	–0.51 (–0.85, –0.16)	–0.86	–0.36 (–0.56–0.17)	–0.82	–0.33 (–0.48, –0.17)	–0.81	–0.40
	Somewhat better (n = 15–18)	–0.18 (–0.32, –0.03)	–0.5	–0.28 (–0.57, 0.01)	–0.56	–0.16 (–0.32, 0.01)	–0.44	–0.20
	About the same (n = 66–71)	0.02 (–0.04, 0.08)	0.04	0 (–0.07, 0.07)	0	0.01 (–0.07, 0.1)	0.03	0.01
	Somewhat worse (n = 13–19)	0.12 (–0.03, 0.27)	0.22	0.2 (0.99, 0.31)	0.36	0.05 (–0.16, 0.25)	0.07	0.12
	Much worse (n = 0–1)	NA					NA	NA

* n represents patients who are categorized into 5 different responses. n are presented as a range because the number of patients in each category is different based on their responses to the anchors. For Reflux and Distension/Bloating scales, we used overall and upper GI anchor; for Diarrhea, Constipation, and Fecal soilage, we used overall and lower GI anchors. † Overall mean change is the average of mean scores for different anchors. NA: not applicable.

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Table 4. Minimally important difference estimates for the UCLA SCTC GIT 2.0 scales. Negative score denotes improvement.

UCLA SCTC GIT 2.0	MID Estimates
Reflux	
Somewhat better	–0.26
Somewhat worse	0.19
Distension/bloating	
Somewhat better	–0.14
Somewhat worse	0.12
Diarrhea	
Somewhat better	–0.19
Somewhat worse	0.07
Constipation	
Somewhat better	–0.17
Somewhat worse	0.13
Fecal soilage	
Somewhat better	–0.19
Somewhat worse	0.06
Emotional well-being	
Somewhat better	–0.36
Somewhat worse	0.16
Social functioning	
Somewhat better	–0.07
Somewhat worse	0.21
Total GIT score	
Somewhat better	–0.20
Somewhat worse	0.12

UCLA SCTC GIT: University of California at Los Angeles Scleroderma Clinical Trial Consortium Gastrointestinal Tract; MID: minimally important difference.

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