Malnutrition Is Common in Systemic Sclerosis: Results from the Canadian Scleroderma Research Group Database

MURRAY BARON, MARIE HUDSON, and RUSSELL STEELE, Canadian Scleroderma Research Group

ABSTRACT. ***Objective.*** Systemic sclerosis (SSc) is a multisystem disease associated with significant morbidity and increased mortality. Little is known about nutritional status in SSc. We investigated the prevalence and demographic and clinical correlates of nutritional status in a large cohort of patients with SSc.

Methods. This was a cross-sectional multicenter study of patients (n = 586) from the Canadian Scleroderma Research Group Registry. Patients were assessed with detailed clinical histories, medical examinations, and self-administered questionnaires. The primary outcome was risk for malnutrition using the "malnutrition universal screening tool" (MUST). Multiple logistic regression was used to assess the relationship between selected demographic and clinical variables and MUST categories.

Results. Of the 586 patients in the study, MUST scores revealed that almost 18% were at high risk for malnutrition. The significant correlates of high malnutrition risk included the number of gastrointestinal (GI) complaints, disease duration, diffuse disease, physician global assessment of disease severity, hemoglobin, oral aperture, abdominal distension on physical examination, and physician-assessed possible malabsorption. Among 14 GI symptoms, only poor appetite and lack of a history of abdominal swelling and bloating predict MUST. These factors accounted for 24% of the variance in MUST scores.

Conclusion. The risk for malnutrition in SSc is moderate and is associated with shorter disease duration, markers of GI involvement, and disease severity. Patients with SSc should be screened for malnutrition, and potential underlying causes assessed and treated when possible. (J Rheumatol First Release Oct 15 2009; doi:10.3899/jrheum.090694)

Key Indexing Terms:
MALNUTRITION SYSTEMIC SCLEROSIS RISK FACTORS

Gastrointestinal (GI) involvement in patients with systemic sclerosis (SSc) is common, and diffuse bowel involvement may result in bacterial overgrowth and malabsorption[1-5]. Prokinetic agents, antibiotics, and parenteral nutrition may be required[6-11], but although malnutrition might be an expected consequence of these features, a systematic approach to assessment of nutritional status in patients with SSc has been undertaken infrequently, and then only in small numbers of patients[12,13].

Malnutrition has been defined as "a state of nutrition in which a deficiency, excess or imbalance of energy, protein, and other nutrients causes measurable adverse effects on tissue/body form (body shape, size, composition) and function and clinical outcome"[14], but assessment of nutritional status is difficult and controversial. Various screening tools for malnutrition have been developed including the "malnutrition universal screening tool" (MUST) for adults, which was produced for the British Association for Parenteral and Enteral Nutrition[15]. In Great Britain the MUST has been adopted by the British Dietetic Association, the Royal College of Nursing, the Registered Nursing Homes Association, and the British Association for Parenteral and Enteral Nutrition. The extent and associated features of malnutrition have never been assessed in a standardized fashion in a large number of patients with SSc; we undertook this study to determine, with the MUST screening tool, the prevalence and predictors of protein-energy malnutrition in a cohort of patients with SSc followed by the Canadian Scleroderma Research Group (CSRG).

MATERIALS AND METHODS

Design. A cross-sectional study of a national cohort of patients with SSc.

Study subjects. The subjects consisted of those enrolled in the CSRG

From the SMBD-Jewish General Hospital and McGill University, Montreal, Quebec, Canada.

Supported by the Canadian Institutes of Health Research, the Scleroderma Society of Canada, and educational grants from Actelion Pharmaceuticals and Pfizer Inc. Dr. Hudson is supported by a New Investigator Award from the Canadian Institutes of Health Research.

M. Baron, MD; M. Hudson, MD, MPH; R. Steele, PhD, SMBD-Jewish General Hospital and McGill University.

Address correspondence to Dr. M. Baron, SMBD-Jewish General Hospital, Room A216, 3755 Cote Ste Catherine Road, Montreal, Quebec H3T 1E2. E-mail mbaron@rhu.jgh.mcgill.ca

Accepted for publication July 27, 2009.

Registry. Patients in the Registry are recruited from 15 centers across Canada. They must have a diagnosis of SSc made by the referring rheumatologist, be ≥ 18 years of age, and be fluent in English or French. Patients are seen yearly. Patients included in this study were those whose baseline visit was between September 2004 and April 2008 and whose complete data for the outcomes and predictors of interest were entered into the database as of April 2008. Only data from the baseline visit were used. The presence of lung involvement was defined as a severity score ≥ 1 for lung as defined by the criteria of Medsger, *et al*[16]. Heart involvement was defined as a severity score ≥ 1 for heart as defined by the criteria of Medsger, *et al*[16]. Designations of limited and diffuse disease were assigned according to LeRoy, *et al*[17].

Ethics committee approval for this study was obtained at each site, and each patient provided informed written consent to participate.

Malnutrition screening instrument. The MUST assigns the following scores to body mass index (BMI): > 20.0 = 0, 18.5–20.1 = 1, < 18.5 = 2[14]. A weight loss score (unplanned weight loss in the past 3–6 mo) is assigned as follows: < 5% = 0, 5%–10% = 1, > 10% = 2. The MUST also adds a score of 2 if there has been or is likely to be no nutritional intake for the next 5 days or more. As all the participants were outpatients, their nutritional intake was ongoing and hence they were scored as zero for this issue. The scores for BMI and weight loss are summed for the total score, which is interpreted as follows: risks for malnutrition are low for MUST score of 0, medium for MUST score = 1, and high for MUST score ≥ 2. Measurements of height and weight are performed by the Registry nurse at the time of the CSRG visit using standard equipment available at the sites. There is no particular standardization of this equipment. Weight loss is based on recall by the patient and refers to the previous year rather than the previous 3–6 months.

Predictor variables. Patients recruited into the Registry underwent an extensive standardized evaluation including a history, physical evaluation, and laboratory investigations. Disease duration is calculated from the first non-Raynaud's manifestation, as in other studies[18-23]. Physician global assessments of disease severity are made using 11-point numerical rating scales ranging from 0 to 10[24,25]. The physician was asked to assess the presence of possible malabsorption [physician answers "yes" to the following question: "Does the patient either answer yes to: "Do you pass stools that are difficult to flush, particularly foul smelling or associated with a ring of grease in the toilet bowl?" and/or does the patient have low ferritin with no blood loss, elevated International Normalized Ratio (INR), low serum vitamin B12 level and not pernicious anemia, low serum carotene, or low Mg or Ca level otherwise unexplained?"]. The skin score was calculated according to the modified Rodnan skin score method (mRSS)[26].

To assess GI involvement patients answer yes/no to a series of 14 questions concerning appetite loss, difficulty swallowing, regurgitation of acid, nocturnal choking, heartburn, early satiety, abdominal bloating, nausea and vomiting, constipation, diarrhea, need for antibiotics for diarrhea, greasy stools, fecal incontinence, and the need for parenteral nutrition. We obtained this information by reviewing protocols from 7 major scleroderma centers in North America and compiled a list of the GI symptoms included in those protocols. The patients were also asked about the presence of dryness of the mouth ("I have had a feeling of dry mouth on a daily basis for more than 3 months"). There was no formal assessment by any criteria for the presence of Sjögren's syndrome. The physical examination by the physician is recorded and includes a yes/no response for the presence of abdominal distension. The oral aperture is the distance measured between the incisors to the nearest millimeter measured with a tape measure with the mouth fully open.

Statistical analysis. Descriptive statistics were used to summarize the baseline characteristics of the patients. Bivariate analyses were performed to identify clinical associations of factors with MUST score using bivariate ordinal logistic regression. The predictors of MUST score were analyzed by multivariate ordinal logistic regression using number of GI complaints, age, sex, disease duration, diffuse disease, physician assessment of disease severity, oral aperture, hemoglobin, abdominal distension, dry mouth, and malabsorption with standardized continuous variables. The specific GI symptoms associated with the MUST scores were investigated by regressing all 14 symptoms instead of number of GI symptoms in the model. All statistical analyses were performed with SAS v9.1 and with the MUST scores categorized into 3 categories (0, 1, ≥ 2) for all regression analyses.

RESULTS

There were 586 patients included in the study. Data were obtained from the baseline visit. Table 1 gives the characteristics of the patients studied and of patients for whom there were incomplete data. There were no statistical differences of clinical relevance between included and excluded patients. Eighty-seven percent of the subjects were women. The mean age (SD) of the cohort was 55.4 (12.1) years. Patients had a disease duration of 10.5 (8.6) years, and 77% fulfilled the American College of Rheumatology (ACR) criteria for SSc[27]. Diffuse cutaneous disease was present in 39%. The physician rating of disease severity was mild overall. GI symptoms were common (Table 2). The distribution of BMI results revealed a distribution slightly skewed but not dissimilar from data for the normal Canadian population (Figure 1)[28]. The mean MUST score was 0.5, but MUST scores were categorized into the 3 sets suggested by the authors of this scoring system (0, 1, and ≥ 2) as there were very few results > 2. The distribution of

Table 1. Patient characteristics.

Characteristic	Study Subjects, n = 586 Mean (SD) or %	Subjects Excluded for Missing Data, Total n = 203 Mean (SD) or % [% missing]
Age, yrs	55.4 (12.1)	55.3 (12.9) [0]
Female, %	87	84 [0]
Disease duration, yrs	10.5 (8.6)	11.0 (9.7) [12]
Meet ACR classification criteria, %	77	70.5 [4]
Diffuse cutaneous disease, %	39	46 [0]
Physician global assessment of disease severity (11-point numerical rating scale)	2.8 (2.2)	2.9 (2.2) [0]
Lung involvement, %	75	80 [27]
Heart involvement, %	27	25 [25]
No. of GI complaints, maximum = 14	4.0 (3.0)	4.6 (3.3) [7]
Oral aperture, mm	39.0 (3.0)	38.0 (9.2) [10]
Hemoglobin, g/dl	130.0 (14.5)	131.4 (16.9) [26]
Abdominal distension on physical examination, %	7	9 [1]
Dry mouth, %	45	48 [4]
Malabsorption suspected by physician, %	11	12 [1]
Body mass index	26.0 (5.7)	25.3 (6.0) [6]
MUST score	0.5 (0.9)	0.7 (1.1) [11]

MUST: malnutrition universal screening tool.

Table 2. Frequency of each of 14 gastrointestinal symptoms.

Symptom	N (%)
Poor appetite	170 (29.01)
Difficulty swallowing	316 (53.92)
Reflux symptoms	377 (64.33)
Wakes up at night and chokes	160 (27.30)
Retrosternal burning	250 (42.66)
Early satiety	235 (40.10)
Abdomen swelling or bloating	219 (37.37)
Nausea	86 (14.68)
Constipation	156 (26.62)
Diarrhea	129 (22.01)
Took antibiotics for diarrhea	41 (7.00)
Steatorrhea	113 (19.28)
Fecal incontinence	109 (18.60)
Requires parenteral nutrition	11 (1.88)

these MUST scores revealed that almost 18% were at high risk for malnutrition (Table 3).

Logistic regression assessed the relationship between predictor variables and MUST scores (Table 4). Unadjusted odds ratios indicated significant associations between MUST scores and the number of GI symptoms, diffuse disease, shorter disease duration, disease severity (physician global assessment), oral aperture, hemoglobin, abdominal distension on examination, and the physician's assessment of possible malabsorption. In addition, when we assessed each of the 14 GI questions posed to the patients, associations with MUST scores were found specifically for poor appetite, early satiety, nausea, constipation, diarrhea, and taking antibiotics for diarrhea.

Two separate models were performed to assess adjusted odds ratios. Model 1 assessed the number of GI symptoms as well as age, sex, diffuse disease, disease duration, physician global assessment of disease severity, hemoglobin, oral aperture, abdominal distension, history of dry mouth, and physician-assessed possible malabsorption. Model 2 replaced the number of GI complaints with each of the 14 GI symptoms. In Model 1, significant associations with MUST scores were found for the number of GI complaints, disease duration, and physician global assessment of disease severity; and borderline significance for oral aperture, hemoglobin, abdominal distension, and physician-assessed possible malabsorption. When the mRSS was entered instead of the physician assessment of disease severity, it did not perform well as an independent predictor (OR 1.2, 95% CI 0.9–1.5; data not shown). Reviewing data for the individual GI symptoms that predicted MUST scores in the adjusted model, only poor appetite and lack of a history of abdominal swelling and bloating were predictive.

DISCUSSION

Malnutrition usually refers to protein-energy malnutrition. Using the MUST screening tool we were able to determine that 10.8% of our SSc cohort were at medium risk for malnutrition and 17.4% at high risk. This compares to an 18% medium risk and 12% high risk in gastroenterology outpatients and a combined moderate and high risk of 19% to

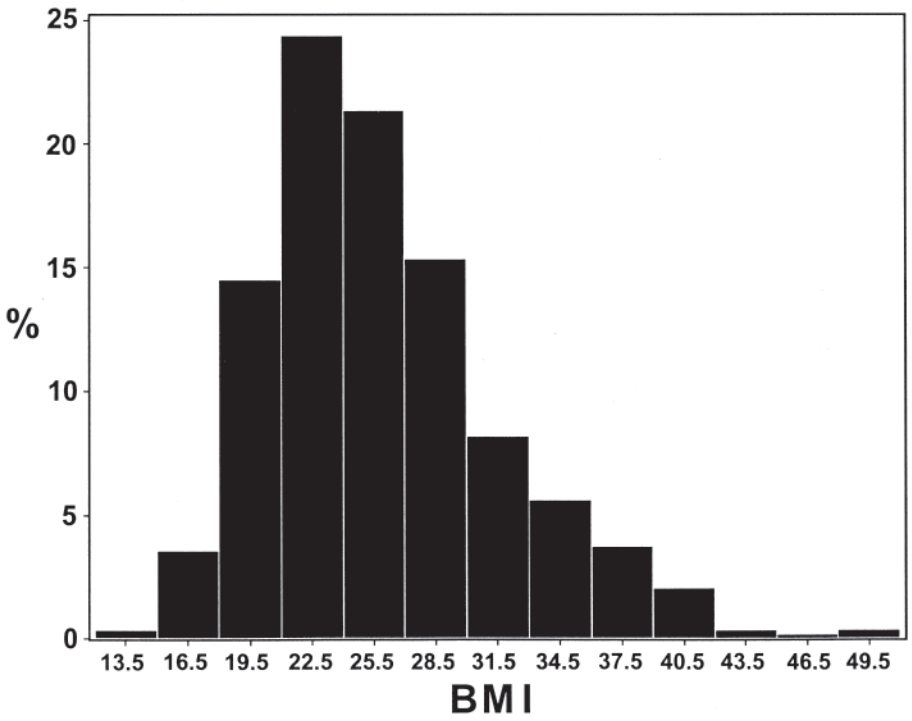

Figure 1. Distribution of BMI values in patients with systemic sclerosis.

65% in different groups of hospitalized patients[14]. In another report using the MUST, of 9336 patients screened on admission to hospital, 28% were found to be at risk of malnutrition (22% high risk, 6% medium risk), and in chronic-care homes 30% were "malnourished" (20% high risk, 10% medium risk)[29]. The findings in our patients therefore place the risk of malnutrition in SSc very near the risk observed in other understandably high-risk populations.

It is well known that the severe GI disease of SSc can cause malnutrition[6], in most cases because of malabsorption likely secondary to bacterial overgrowth[10]. That parenteral nutrition has often been used in patients with SSc attests to the severity of the malnutrition[8-10,30]. However, there are to our knowledge no studies of a large number of SSc patients that have established the prevalence of malnutrition in an unselected population. One of the larger studies was of 30 patients with SSc and symptoms from the GI tract compared to healthy control subjects[12]. The investigators found that the intake of energy and the distribution of nutrients did not differ between patients and control subjects, but that the intake of fiber and fruits and vegetables tended to be lower in patients. Their results suggested that either decreased nutrient absorption or increased losses, or both, were responsible for these effects, as nutritional intake was generally normal. Another report also suggested that in patients with SSc reduced blood concentrations of nutrients, particularly the water-soluble antioxidants selenium and ascorbic acid, are not due to dietary deficiency[13].

To our knowledge ours is the first study to relate possible malnutrition in SSc to particular clinical features of the disease by comparing patients with low versus high malnutrition risk. Using adjusted odds ratios we demonstrated an association of MUST scores with the number of GI complaints, shorter disease duration, diffuse cutaneous disease, physician global assessment of disease severity, hemoglobin, abdominal distension on physical examination, and physician-assessed possible malabsorption. In terms of individual GI complaints, we found an association of MUST

Table 3. Distribution of malnutrition universal screening tool (MUST) scores.

MUST Score	Frequency (%)
0	411 (70.1)
1	73 (12.5)
≥ 2	102 (17.4)

Table 4. Crude and adjusted odds ratios for the association between potential risk factors and MUST scores in SSc.

Factor	Crude OR (95% CI)	Model 1 Adjusted OR (95% CI)	Model 2 Adjusted OR (95% CI)
No. of GI complaints (maximum = 14)	1.4 (1.1–1.6)	1.3 (1.1–1.6)	
Age	0.9 (0.8–1.1)	1.0 (0.8–1.2)	1.0 (0.8–1.2)
Female	0.7 (0.4–1.1)	0.7 (0.4–1.2)	0.8 (0.4–1.4)
Diffuse vs limited disease	1.7 (1.2–2.5)	1.1 (0.7–1.7)	1.1 (0.7–1.7)
Disease duration	0.7 (0.6–0.9)	0.7 (0.6–0.9)	0.7 (0.5–0.9)
Physician global assessment of disease severity	1.6 (1.4–1.9)	1.4 (1.2–1.7)	1.3 (1–1.6)
Oral aperture	0.7 (0.6–0.8)	0.8 (0.7–1.0)	0.9 (0.7–1.1)
Hemoglobin	0.8 (0.6–0.9)	0.8 (0.7–1.0)	0.8 (0.7–1)
Physician assessment of abdominal distension	2.1 (1.1–3.8)	1.9 (1.0–3.7)	2.5 (1.2–5)
Dry mouth	1.1 (0.8–1.6)	0.9 (0.6–1.3)	0.9 (0.6–1.4)
Physical assessment of malabsorption	2.1 (1.3–3.5)	1.7 (1.0–3.0)	1.5 (0.8–2.7)
Individual gastrointestinal symptoms			
Poor appetite	4.6 (3.2–6.7)		3.4 (2.2–5.5)
Difficulty swallowing	1.3 (0.9–1.9)		1.2 (0.8–1.9)
Reflux symptoms	1.0 (0.7–1.4)		0.9 (0.5–1.4)
Wakes up at night and chokes	1.1 (0.7–1.6)		0.9 (0.6–1.5)
Retrosternal burning	1.0 (0.7–1.4)		0.7 (0.4–1.1)
Early satiety	2.1 (1.5–3)		1.3 (0.8–2.1)
Abdomen swelling or bloating	0.8 (0.6–1.2)		0.6 (0.4–0.9)
Nausea	2.4 (1.5–3.8)		1.6 (0.8–2.8)
Constipation	1.4 (1–2.1)		1.2 (0.7–1.9)
Diarrhea	1.6 (1.1–2.4)		1.4 (0.8–2.3)
Took antibiotics for diarrhea	2.0 (1.1–3.7)		1.1 (0.5–2.3)
Steatorrhea	1.2 (0.8–1.9)		1.0 (0.6–1.7)
Fecal incontinence	1.3 (0.8–2)		1.2 (0.7–2)
Required parenteral nutrition	1.9 (0.6–6.1)		1.1 (0.3–3.9)
		R^2 = 14%	R^2 = 24%

Model 1: using the number of gastrointestinal (GI) symptoms reported by patient; Model 2: omitting number of GI symptoms and replacing that with each of 14 individual symptoms.

scores with poor appetite, early satiety, nausea, constipation, and diarrhea. Each additional GI complaint confers an additional 20% risk that the patient will move to a higher MUST score.

It is interesting that a shorter disease duration was associated with a higher risk for malnutrition. It has been our experience that patients who are quite ill with diffuse cutaneous disease often lose weight early in their illness and then stabilize or even regain some weight. This requires more detailed confirmation.

Although there are no validated measures of overall disease severity in SSc, a simple numerical rating scale based on physician assessment does predict malnutrition in our multivariate model. This remains true after accounting for factors such as the number of GI complaints and the physician's assessment of abdominal distension and possible malabsorption, which implies that there may be factors in the physician's assessment that do not relate to the GI tract that are still predictive of malnutrition. It could be simply that weight loss itself is a determinant of the physician's assessment of severity, or it may be that other factors such as severe pulmonary disease are associated with higher MUST scores for reasons other than decreased nutrient intake or malabsorption.

In terms of the individual GI complaints associated with higher malnutrition risk, it makes intuitive sense that poor appetite and diarrhea, possibly a symptom of malabsorption, would be independent risk factors. It is not clear, however, why subjective abdominal bloating would be protective. Also, some factors such as early satiety, nausea, constipation, and the need for antibiotics for diarrheal episodes, which were significantly associated with MUST scores only in bivariate analysis, may still be important, except that our study was underpowered to reveal independent contributions. Certainly these factors make intuitive sense as risks for malnutrition.

There are some limitations to our study. There is no validated formal definition of malnutrition. A diagnosis of malnutrition requires a formal diagnostic evaluation of each individual patient. Our goals therefore were limited to employing a screening tool. The many tools that have been developed to assess nutritional status[14,31-44] are unconfirmed for validity and reliability and vary in ease of use and acceptability. However, one must differentiate the concept of a screening tool from the actual diagnosis of malnutrition. Presumably, a screening tool such as the MUST would have good specificity and sensitivity for the presence of true malnutrition but would not likely be perfect for either. The BMI of < 20 used in the MUST will include some people who have a BMI that may be considered normal. For example, Health Canada considers only a BMI < 18.5 as underweight[28]. However, as this is a screening tool it is acceptable that its sensitivity is high, in order to include some possibly normal subjects. In inpatients, higher scores on the MUST showed moderate ability to predict greater mortality (in-hospital and post-discharge) and longer hospital stays than for patients at low risk[43]. However, if one presumes that malnourished subjects are those whose adverse prognosis could be corrected by nutritional manipulation, then to our knowledge no nutritional screening tool has been rigorously studied with regard to the validity of this endpoint. Nevertheless, the MUST has been compared to 9 other commonly used nutrition assessment tools, and demonstrates good concurrent validity in outpatients with chronic GI diseases and in elective and emergency medical inpatients with varied diagnoses[14]. The MUST is capable of predicting length of hospital stay, mortality, and discharge destination of groups of hospital patients and thus has predictive validity[45,46]. It also predicts general practitioner visits and hospital admissions in community individuals[47]. The MUST also has excellent reproducibility (k = 0.809–1.000) between users (nurses, healthcare assistants, doctors, nursing and medical students) in different healthcare settings[15,43]. We chose to use the MUST because of this validity and reliability data, because of its wide acceptance in Great Britain, and because we had available to us from our SSc Registry the information necessary to calculate the MUST scores.

All study sites used their own equipment to measure height and weight. This was not standardized and thus may have influenced the variability and reliability of the measurements. This was unlikely to have changed the overall conclusions, however, as the significant relationships that we found suggest that the study was of sufficient power despite using this nonstandardized tool. Also, as we did not have recorded weights before the baseline visit, we were unable to record actual weight loss but the MUST instructions include the alternative that if recent weight loss cannot be calculated, self-reported weight loss can be used (Internet; available from: www.bapen.org.uk/pdfs/must/must_full.pdf). We had no external validation of this self-recalled weight loss. Indeed in studies of the MUST, if height could not be measured accurately, recalled height or knee height was used to calculate height, and if weight could not be measured accurately, recalled weight was used[14].

Disease severity is difficult to assess in SSc. The best validated method is that of Medsger, *et al*[16,48], but this method provides specific scores for different organ systems, and no overall severity score has been validated. In our study we relied on the physician global assessment of disease severity. We have previously shown that the physician global assessment of disease severity, the mRSS, and the sum of the individual organ system severity scores according to the method of Medsger, *et al* behave similarly[49].

Not all our patients meet the ACR criteria for SSc[27]. We purposely did not limit our analyses to only those who met the criteria because we and others feel that these criteria are probably outdated and lack sensitivity. We have shown that adding factors such as anticentromere antibodies, telangiec-

tasia, and nailfold capillary abnormalities tends to confirm that all our patients do have SSc[50].

We hypothesized that a diminished oral aperture and/or a dry mouth might lead to decreased nutrient intake and thus to malnutrition. Although the bivariate analysis does suggest a role for a diminished oral aperture, the multivariate analysis did not confirm that. We are currently performing a more detailed study of oral health abnormalities in SSc and will attempt to address this issue in more detail.

Importantly, we did not use a specific GI questionnaire as part of our assessment. A new and valuable questionnaire has recently been developed[21], but was not available when we collected our data. Our list of GI symptoms, however, did reflect the consensus of scleroderma experts in that it was compiled from the case report forms used at major North American scleroderma centers. Indirectly, the association between the number of GI complaints and the MUST scores tends to validate our simple GI assessment tool. In addition, in other studies we have demonstrated an association between this simple score and quality of life and this also tends to validate this measure[51]. In the adjusted model the number of GI complaints had just borderline significance as the lower 95% confidence interval was 1.1. This may be an indication that although there appears to be validity to our scale, there certainly could be better GI assessment tools, such as that of Khanna, *et al*[21].

The risk for malnutrition in SSc is relatively high, with over 28% of patients being at medium or high risk. Malnutrition is associated with more GI complaints, with early and more severe disease, and with possible malabsorption. We conclude that patients with SSc should be screened for malnutrition, and possible underlying causes assessed and treated when possible.

APPENDIX

Canadian Scleroderma Research Group Investigators: J. Pope, London, Ontario; J. Markland, Saskatoon, Saskatchewan; D. Robinson, Winnipeg, Manitoba; N. Khalidi, Hamilton, Ontario; N. Jones, Edmonton, Alberta; A. Masetto, Sherbrooke, Quebec; E. Kaminska, Hamilton, Ontario; P. Docherty, Moncton, New Brunswick; J-P. Mathieu, Montreal, Quebec; E. Sutton, Halifax, Nova Scotia; M. Abu-Hakima, Calgary, Alberta; S. LeClercq, Calgary, Alberta; D. Smith, Ottawa, Ontario; S. Ligier, Montreal, Quebec; M. Fritzler, Advanced Diagnostics Laboratory, Calgary, Alberta.

REFERENCES

1. Cossio M, Menon Y, Wilson W, deBoisblanc BP. Life-threatening complications of systemic sclerosis. Crit Care Clin 2002;18:819-39.
2. Parodi A, Sessarego M, Greco A, et al. Small intestinal bacterial overgrowth in patients suffering from scleroderma: clinical effectiveness of its eradication. Am J Gastroenterol 2008;103:1257-62.
3. Ebert EC. Gastric and enteric involvement in progressive systemic sclerosis. J Clin Gastroenterol 2008;42:5-12.
4. Nishimagi E, Tochimoto A, Kawaguchi Y, et al. Characteristics of patients with early systemic sclerosis and severe gastrointestinal tract involvement. J Rheumatol 2007;34:2050-5.
5. Kaye SA, Lim SG, Taylor M, Patel S, Gillespie S, Black CM. Small bowel bacterial overgrowth in systemic sclerosis: detection using direct and indirect methods and treatment outcome. Br J Rheumatol 1995;34:265-9.
6. Jaovisidha K, Csuka ME, Almagro UA, Soergel KH. Severe gastrointestinal involvement in systemic sclerosis: report of five cases and review of the literature. Semin Arthritis Rheum 2005;34:689-702.
7. Ng SC, Clements PJ, Berquist WE, Furst DE, Paulus HE. Home central venous hyperalimentation in fifteen patients with severe scleroderma bowel disease. Arthritis Rheum 1989;32:212-6.
8. Levien DH, Fiallos F, Barone R, Taffet S. The use of cyclic home hyperalimentation for malabsorption in patients with scleroderma involving the small intestines. JPEN J Parenter Enteral Nutr 1985;9:623-5.
9. Grabowski G, Grant JP. Nutritional support in patients with systemic scleroderma. JPEN J Parenter Enteral Nutr 1989;13:147-51.
10. Brown M, Teubner A, Shaffer J, Herrick AL. Home parenteral nutrition — an effective and safe long-term therapy for systemic sclerosis-related intestinal failure. Rheumatology 2008;47:176-9.
11. Cohen S. The gastrointestinal manifestations of scleroderma: pathogenesis and management. Gastroenterology 1980;79:155-66.
12. Lundberg AC, Akesson A, Akesson B. Dietary intake and nutritional status in patients with systemic sclerosis. Ann Rheum Dis 1992;51:1143-8.
13. Herrick AL, Worthington H, Rieley F, et al. Dietary intake of micronutrient antioxidants in relation to blood levels in patients with systemic sclerosis. J Rheumatol 1996;23:650-3.
14. Stratton RJ, Hackston A, Longmore D, et al. Malnutrition in hospital outpatients and inpatients: prevalence, concurrent validity and ease of use of the 'malnutrition universal screening tool' ('MUST') for adults. Br J Nutr 2004;92:799-808.
15. Elia M. Screening for malnutrition: A multidisciplinary responsibility. Development and use of the 'malnutrition universal screening tool' ('MUST') for adults. Malnutrition Advisory Group (MAG), a Standing Committee of British Association for Parenteral and Enteral Nutrition. Redditch: BAPEN; 2003.
16. Medsger TA Jr, Bombardieri S, Czirjak L, Scorza R, Della Rossa A, Bencivelli W. Assessment of disease severity and prognosis. Clin Exp Rheumatol 2003;21:S42-6.
17. LeRoy EC, Black C, Fleischmajer R, et al. Scleroderma (systemic sclerosis): classification, subsets and pathogenesis. J Rheumatol 1988;15:202-5.
18. Khanna D, Furst DE, Clements PJ, et al. Responsiveness of the SF-36 and the Health Assessment Questionnaire Disability Index in a systemic sclerosis clinical trial. J Rheumatol 2005;32:832-40.
19. Khanna D, Clements PJ, Furst DE, Chon Y, Elashoff R, Roth MD, et al. Correlation of the degree of dyspnea with health-related quality of life, functional abilities, and diffusing capacity for carbon monoxide in patients with systemic sclerosis and active alveolitis: results from the Scleroderma Lung Study. Arthritis Rheum 2005;52:592-600.
20. Khanna D, Yan X, Tashkin DP, Furst DE, Elashoff R, Roth MD, et al. Impact of oral cyclophosphamide on health-related quality of life in patients with active scleroderma lung disease: results from the scleroderma lung study. Arthritis Rheum 2007;56:1676-84.
21. Khanna D, Hays RD, Park GS, Braun-Moscovici Y, Mayes MD, McNearney TA, et al. Development of a preliminary scleroderma gastrointestinal tract 1.0 quality of life instrument. Arthritis Rheum 2007;57:1280-6.
22. Tashkin DP, Elashoff R, Clements PJ, Roth MD, Furst DE, Silver RM, et al. Effects of 1-year treatment with cyclophosphamide on outcomes at 2 years in scleroderma lung disease. Am J Respir Crit Care Med 2007;176:1026-34.
23. Avouac J, Sordet C, Depinay C, Ardizonne M, Vacher-Lavenu MC, Sibilia J, et al. Systemic sclerosis-associated Sjogren's syndrome

and relationship to the limited cutaneous subtype: results of a prospective study of sicca syndrome in 133 consecutive patients. Arthritis Rheum 2006;54:2243-9.
24. Van Tubergen A, Debats I, Ryser L, Londono J, Burgos-Vargas R, Cardiel MH, et al. Use of a numerical rating scale as an answer modality in ankylosing spondylitis-specific questionnaires. Arthritis Rheum 2002;47:242-8.
25. Ferraz MB, Quaresma MR, Aquino LR, Atra E, Tugwell P, Goldsmith CH. Reliability of pain scales in the assessment of literate and illiterate patients with rheumatoid arthritis. J Rheumatol 1990;17:1022-4.
26. Furst DE, Clements PJ, Steen VD, Medsger TA Jr, Masi AT, D'Angelo WA, et al. The modified Rodnan skin score is an accurate reflection of skin biopsy thickness in systemic sclerosis. J Rheumatol 1998;25:84-8.
27. Subcommittee for Scleroderma Criteria of the American Rheumatism Association Diagnostic and Therapeutic Criteria Committee. Preliminary criteria for the classification of systemic sclerosis (scleroderma). Subcommittee for scleroderma criteria of the American Rheumatism Association Diagnostic and Therapeutic Criteria Committee. Arthritis Rheum 1980;23:581-90.
28. Health Canada. Canadian guidelines for body weight classification in adults. Ottawa: Health Canada; 2003.
29. Russell C, Elia M. Nutrition screening survey in the UK in 2007: A report by BAPEN, British Association for Parenteral and Enteral Nutrition. [Internet. Accessed Sept 1, 2009.] Availabile from: http://www.bapen.org.uk/res_pub.html.
30. Stafford-Brady FJ, Kahn HJ, Ross TM, Russell ML. Advanced scleroderma bowel: complications and management. J Rheumatol 1988;15:869-74.
31. Elia M, Zellipour L, Stratton RJ. To screen or not to screen for adult malnutrition? Clin Nutr 2005;24:867-84.
32. Jones JM. Validity of nutritional screening and assessment tools. Nutrition 2004;20:312-7.
33. Jones JM. The methodology of nutritional screening and assessment tools. J Hum Nutr Diet 2002;15:59-71; quiz 3-5.
34. Kondrup J, Allison SP, Elia M, Vellas B, Plauth M. ESPEN guidelines for nutrition screening 2002. Clin Nutr 2003;22:415-21.
35. Baker JP, Detsky AS, Wesson DE, Wolman SL, Stewart S, Whitewell J, et al. Nutritional assessment: a comparison of clinical judgement and objective measurements. N Engl J Med 1982;306:969-72.
36. Detsky AS, Smalley PS, Chang J. The rational clinical examination. Is this patient malnourished? JAMA 1994;271:54-8.
37. Elkan AC, Engvall IL, Tengstrand B, Cederholm T, Hafstrom I. Malnutrition in women with rheumatoid arthritis is not revealed by clinical anthropometrical measurements or nutritional evaluation tools. Eur J Clin Nutr 2008;62:1239-47.
38. Gerasimidis K, Drongitis P, Murray L, Young D, McKee RF. A local nutritional screening tool compared to malnutrition universal screening tool. Eur J Clin Nutr 2007;61:916-21.
39. Sieber CC. Nutritional screening tools — How does the MNA compare? Proceedings of the session held in Chicago May 2-3, 2006 (15 Years of Mini Nutritional Assessment). J Nutr Health Aging 2006;10:488-92; discussion 92-4.
40. Kyle UG, Kossovsky MP, Karsegard VL, Pichard C. Comparison of tools for nutritional assessment and screening at hospital admission: a population study. Clin Nutr 2006;25:409-17.
41. Godfrey K. Implementation of the Malnutrition Universal Screening Tool. Nurs Times 2004;100:61.
42. Malnutrition Advisory Group. A consistent and reliable tool for malnutrition screening. Nurs Times 2003;99:26-7.
43. Stratton RJ, King CL, Stroud MA, Jackson AA, Elia M. 'Malnutrition Universal Screening Tool' predicts mortality and length of hospital stay in acutely ill elderly. Br J Nutr 2006;95:325-30.
44. Elia M, Ward LC. New techniques in nutritional assessment: body composition methods. Proc Nutr Soc 1999;58:33-8.
45. King C, Elia M, Stroud M, Stratton R. The predictive validity of the malnutrition universal screening tool ('MUST') with regard to mortality and length of stay in elderly inpatients. Clin Nutr 2003;22:S4.
46. Wood C, Stubbs S, Warwick H, Dunnachie A, Elia M, Stratton R. Malnutrition risk and health care utilisation in orthopaedic patients. Proc Nutr Soc 2004;63:20A.
47. Stratton R, Thompson R, Margetts B, Stroud M, Jackson A, Elia M. Health care utilisation according to malnutrition risk in the elderly: an analysis of data from the National Diet and Nutrition Survey. Proc Nutr Soc 2002;61:20A.
48. Medsger TA Jr. Assessment of damage and activity in systemic sclerosis. Curr Opin Rheumatol 2000;12:545-8.
49. Baron M, Sutton E, Hudson M, Thombs B, Markland J, Pope J, et al. The relationship of dyspnoea to function and quality of life in systemic sclerosis. Ann Rheum Dis 2008;67:644-50.
50. Hudson M, Taillefer S, Steele R, et al. Improving the sensitivity of the American College of Rheumatology classification criteria for systemic sclerosis. Clin Exp Rheumatol 2007;25:754-7.
51. Hudson M, Thombs BD, Steele R, Watterson R, Taillefer S, Baron M. Clinical correlates of quality of life in systemic sclerosis measured with the World Health Organization Disability Assessment Schedule II. Arthritis Rheum 2008;59:279-84.