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Short communication

Disease-related nutritional risk and mortality in systemic sclerosis☆

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SUMMARY

Background & aims: To evaluate the relationship between mortality and nutritional risk associated with disease activity in Systemic Sclerosis (SSc).
Methods: A single-centre prospective cohort study involving 160 SSc outpatients (median age, 62 years [25th–75th, 54–68]). Nutritional risk was assessed by the Malnutrition Universal Screening Tool (MUST), a screening tool that combines anthropometric parameters of nutritional status (body mass index [BMI] and percentage of unintentional weight loss [WL]) with the presence of an "acute disease" (as defined by a disease activity score ≥3 according to Valentini's criteria).
Results: Prevalence of high nutritional risk (MUST score ≥2) was 24.4% [95%CI, 17.4–31.3]. A low nutritional risk (MUST = 1) was detected in 30% of our study sample. In hazard analysis (median follow-up duration = 46 months [25th–75th percentile, 31–54]), high nutritional risk was significantly associated with mortality (HR = 8.3 [95%CI, 2.1–32.1]). The performance of the model based on nutritional risk including disease activity (Harrell's c = 0.74 [95%CI, 0.59–0.89]) was superior to that based on active disease alone (HR = 6.3 [95%CI, 1.8–21.7]; Harrell's c = 0.68 [95%CI, 0.53–0.84]). Risk scored only by anthropometric parameters (prevalence, 9.4% [95%CI, 4.6–14.2]) was not associated with mortality: HR = 2.8 [95%CI, 0.6–13.2].
Conclusions: In SSc outpatients MUST significantly predicts mortality. The combined assessment of nutritional parameters and disease activity significantly improves the evaluation of mortality risk. Disease-related nutritional risk screening should be systematically included in the clinical workup of every SSc patient.

1. Introduction

Malnutrition is now considered the most frequent comorbidity in many chronic diseases, with relevant consequences on the patient's prognosis.[1] Accordingly, regardless of the healthcare setting, the inclusion of nutritional screening procedures in clinical assessment is becoming mandatory.[2] In this perspective, the use of suitable multidimensional screening tools, such as the Nutritional Risk Screening tool (NRS-2002) or the Malnutrition Universal Screening Tool (MUST), which take into account the effect of the underlying disease, has been associated with improved outcome prediction.[1,2]

Different studies have shown that nutritional derangements are frequent in Systemic Sclerosis (SSc) and evidence of implications for outcome has been also provided.[3–7] On the one hand, disease activity has been associated with malnutrition and outcome.[5,8] On the other, anthropometric indexes of nutritional impairment, such as body mass index (BMI) and unintentional weight loss (WL), appeared not associated with mortality,[5] as BMI in SSc patients seems to be similar to that of the general population.[4,5] The use of multidimensional screening tools in SSc has been considered only by the Canadian Scleroderma Research Group.[4] In their study, Baron et al. used the MUST because it is recommended by the European Society of Clinical Nutrition and Metabolism due to its high degree of reliability (low inter-observer variation) and association with outcome.[2,9] However, the effect of the underlying disease in

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patient's assessment was not taken into account. The scoring of nutritional risk relied only on BMI and WL and prevalence of patients at risk was likely underestimated.[4] With this background, the aim of the present study was to investigate the real prevalence of nutritional risk by MUST in SSc when disease activity is included in the assessment procedure. Moreover, as the validation of a nutritional screening tool depends mainly on the ability to predict nutrition-related complications, the second endpoint was to evaluate the association between MUST and mortality.

2. Methods

2.1. Study design

This was a validation study based on a re-analysis of the data pertaining an ongoing observational study at the Rheumatology Unit of the Fondazione IRCCS Policlinico San Matteo (Pavia, Italy). Further information (methodology adopted and the study design) on the present study are detailed elsewhere.[3] In summary, all consecutive SSc outpatients, as classified by Le Roy[10] attending our Rheumatology Unit from February 2007 to September 2008 were screened for study inclusion. Patients were excluded in case of refusal and/or age <18 years. The study was approved by the local Institutional Ethics Committee and written informed consent to the study was obtained.

Clinical assessment was performed by the same rheumatologists (V.C. and S.B.) and included the following issues:

- Demography (sex and age).
- Medical history: age of disease's onset (date of the first non-Raynaud's symptom), presence of Raynaud's phenomenon, disease duration, comorbidities, previous and current therapy.
- Limited/diffuse disease subset on the basis of the extent of skin involvement (by Le Roy's criteria[10]).
- Modified Rodnan Skin Score (mRSS): 17 body areas were examined through clinical palpation and scored on a 4-point ordinal scale by the examiner, according to skin thickness (scale range 0–51, from no skin thickening to severe involvement in all body areas).[11]
- Visceral involvement (according to the EULAR Scleroderma Trials and Research group Database [EUSTAR] recommen dations).[8,12]
- Biochemistry: 8–12-h fasting venous blood samples were drawn on the same day and assessed for full auto-antibodies profile (anti-centromere, anti-topo-I or other) and erythrocyte sedimentation rate.
- Anthropometry: body mass index (BMI; calculated as weight [kg]/height $[m]^2$), and history of 6-month previous unintentional weight loss (WL).
- Dietary intake: quantitative assessment of macronutrients intakes was performed through the completion of a 3-day food diary including 2 non consecutive working days and a weekend day of the week preceding the clinical examination.

2.2. Disease activity[8]

It is based on different aspects of disease including some that vary over time. This index appears simple and easy to use as it evaluates both clinical items and some basic laboratory investigations, parameters which are currently evaluated in each centre. It consists of 10 variables with weights ranging from 0.5 to 2.0 and resulting in a total score ranging from 0 to 10 (lowest and highest activity, respectively). The selection of this set of criteria was carried out by the jackknife approach after analyzing the clinical charts of 290 patients with SSc from 19 European medical centres and identifying those items that were most significantly correlated (multiple regression) with a gold standard score of disease activity (subjectively defined by three members of the protocol management team). In scoring the patient, the following items are considered (Table 1): an elevated mRSS (>20); the presence of scleredema, digital necrosis and arthritis; an elevated erythrocyte sedimentation rate (>30 mm/1st hour); the presence of hypocomplementaemia (C3 and/or C4); a deterioration, as evaluated by the patient, of skin, vascular and cardiopulmonary manifestations in the month preceding the assessment; a reduced carbon monoxide transfer factor (<80% of the predicted value).

2.3. Malnutrition universal screening tool (MUST)

The MUST is based on three clinical parameter that have been associated with poor outcome: BMI, unintentional WL in the previous 3–6 months and acute disease or absent nutritional intake for more than 5 days. Each parameter is rated as follows: BMI>20 kg/m^2 = 0; 18.5–20.0 kg/m^2 = 1; <18.5 kg/m^2 = 2; WL<5% = 0; WL 5–10% = 1; WL>10% = 2; acute disease or absent nutritional intake for more than 5 days: absent = 0; present = 2. Therefore, the total score (sum of the sub-scores from the three parameters) enables the evaluation of the overall risk of malnutrition as follows: 0 = low; 1 = medium; 2 = high.[9]

Similarly to the study by Baron et al., as all the participants were outpatients, their nutritional intake was ongoing and they were scored as zero for the last issue of the tool. However, given the significant association between disease activity score ≥3 and mortality,[8] 2 points were assigned to this clinical feature when rating the parameter "acute disease".

2.4. Predictive validity of MUST

The validity of MUST categorisation was tested in the prediction of mortality. Patient survival was defined as the time between the date of enrollment and the date of death from any cause or the date of last contact or last known to be alive.

2.5. Statistics

The prevalence of malnutrition was computed together with its exact 95% binomial confidence interval (95%CI). Data were described as mean and standard deviation (SD) or median and 25th–75th percentiles if continuous and as counts and percent if categorical.

Kaplan Meier cumulative survival was computed. Cox proportional hazard model (including time-dependent) was used to

Table 1
Criteria included in the disease activity scoring system.[8]

Criteria	Score
mRSS >20	1.0
Scleredema	0.5
Δ Skin[a]	2.0
Digital necrosis	0.5
Δ Vascular[a]	0.5
Arthritis	0.5
↓ TLCO (<80% of predicted value)	0.5
Δ Cardiopulmonary[a]	2.0
ESR>30 mm/1st hour	1.5
Hypocomplementaemia (C3 and/or C4)	1.0
Total maximum disease activity score	10.0

Abbreviations: mRSS, modified Rodnan skin score; TLCO, carbon monoxide transfer factor; ESR, erythrocyte sedimentation rate.

[a] Deterioration, as evaluated by the patient, of the condition in the month preceding the assessment.