Clinical characteristics and risk model of lower gastrointestinal involvement in systemic sclerosis

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Abstract

Objective

Systemic sclerosis (SSc) is a systemic autoimmune disease that could involve multiple organs. Lower gastrointestinal involvement (LGIT) in systemic sclerosis (SSc-LGIT) is a serious manifestation and has a poor prognosis. This study aims to explore the related risk factors of SSc-LGIT that require hospitalisation and build a clinical risk model.

Methods

SSc patients with LGIT admitted to Peking Union Medical College Hospital (PUMCH) were enrolled between December 2003 and December 2023. The controls were selected in SSc patients without LGIT in the same period after matching age and gender at a ratio of 1:3. Clinical data of both groups was collected to build the SSc-LGIT clinical prediction model by machine learning using R software.

Results

A total of 42 SSc patients with LGIT and 126 matched SSc patients without LGIT were enrolled. Compared to the control group, SSc-LGIT patients had lower level of body mass index (BMI), haemoglobin (HB), albumin (ALB). Cardiomyopathy and puffy finger were more common, but arthritis/arthralgia was less. Higher hs-CRP and a higher rate of anti-Ro-52 antibody positivity were found in these patients. A multivariate analysis revealed BMI, cardiomyopathy, HB, ALB, hs-CRP as independent related factors for SSc-LGIT, and a clinical risk model containing these five items was built.

Conclusion

A clinical risk model of SSc-LGIT was established and it has demonstrated capability in predicting the risk of severe lower gastrointestinal involvement in systemic sclerosis.

Key words

systemic sclerosis, lower gastrointestinal involvement, clinical risk model

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Introduction

Systemic sclerosis (SSc) is a systemic autoimmune disease, and many organs could be involved, especially the lung and gastrointestinal (GI) tract (1). Gastrointestinal involvement continues to pose a significant challenge for physicians, as it is frequently present in the majority of patients, often from the early stage of the disease (2). A cohort study in China indicated that 84.6% of patients with SSc had GI manifestations (3). However, early diagnosis of intestinal involvement remains difficult, and the prognosis is poor due to a lack of effective treatments. Almost all parts of the lower GI tract can be involved in SSc (4, 5), including the small intestine, colon, and anorectum, leading to a range of symptoms such as abdominal bloating, small intestinal bacterial overgrowth (SIBO), intestinal pseudo-obstruction (IPO), nutritional malabsorption, faecal incontinence (4). These symptoms could cause great distress to patients, resulting in social isolation and anxiety (6), while the high risk of malnutrition caused by intestinal involvement is closely linked to a poor prognosis (7). The prevalence of SIBO in patients with SSc varies widely in different studies, ranges from 11%-60% (4, 6, 8). Longer disease duration, a significant reduction in weight within 6 months, and a high score in UCLA SCTC GIT (University of California Los Angeles Scleroderma Clinical Trial Consortium Gastrointestinal Tract Instrument 2.0) evaluation had been proposed as the risk factors of SIBO in SSc (9, 10). Although the occurrence of IPO in SSc patients is rarer than SIBO, it could lead to poorer outcomes such as severe malnutrition, parenteral nutrition or even mortality (11, 12). A retrospective analysis showed that older age, male, dcSSc, myopathy, and opioid use were predictive factors for IPO (13). The effectiveness of immunotherapy for IPO remains uncertain. Furthermore, colon and anorectum involvements can manifest as dysmotility and faecal incontinence (4, 14).

Additionally, there also is an unmet need for objective evaluation methods and treatments for lower GI involvement in the clinical field (6). Consequently, the early diagnosis and timely, effective treatment of lower GI involvement in SSc pose considerable challenges for both clinicians and patients.

This study aims to identify related factors of severe lower GI involvement in SSc patients requiring hospitalisation, develop a clinical risk model for lower GI involvement in SSc patients, and assist clinicians in identifying high-risk patients.

Materials and methods

The study was approved by the local ethics committee (ethics number: I-23PJ1024) and was concluded in accordance with the 1964 Declaration of Helsinki.

Study populations and design

All SSc patients admitted to Peking Union Medical College Hospital (PUMCH) due to lower GI involvements between December 2003 and December 2023 were enrolled in the study. All patients fulfilled the 1980 American College of Rheumatology (ACR) or 2013 ACR/European League Against Rheumatism (EULAR) classification criteria for SSc (1). Patients were excluded if:

1. lower GI involvements caused by other reasons, such as drugs and tumours; 2. overlapping other connective tissue diseases, such as systemic lupus erythematosus, and rheumatoid arthritis (Fig. 1).

SSc patients without lower GI involvement were selected as controls using the propensity score method (PSM) based on sex and age at a ratio of 1:3 during the same time.

Lower GI involvement included IPO, SIBO, intestinal malabsorption, GI dysmotility, faecal incontinence, and unclassified involvement. IPO was defined as a clinical and/or radiological appearance of intestinal obstruction without a clearly defined ischaemic, mechanical, or postsurgical cause in patient with SSc (15). SIBO was confirmed by glucose H_2/CH_4 breath test (10) and the gastroenterology consultation, Intestinal malabsorption was confirmed by D-Xylose absorption test abnormal (16) and GI dysmotility was confirmed by GI transit test abnormality (4). Unclassified involvement was

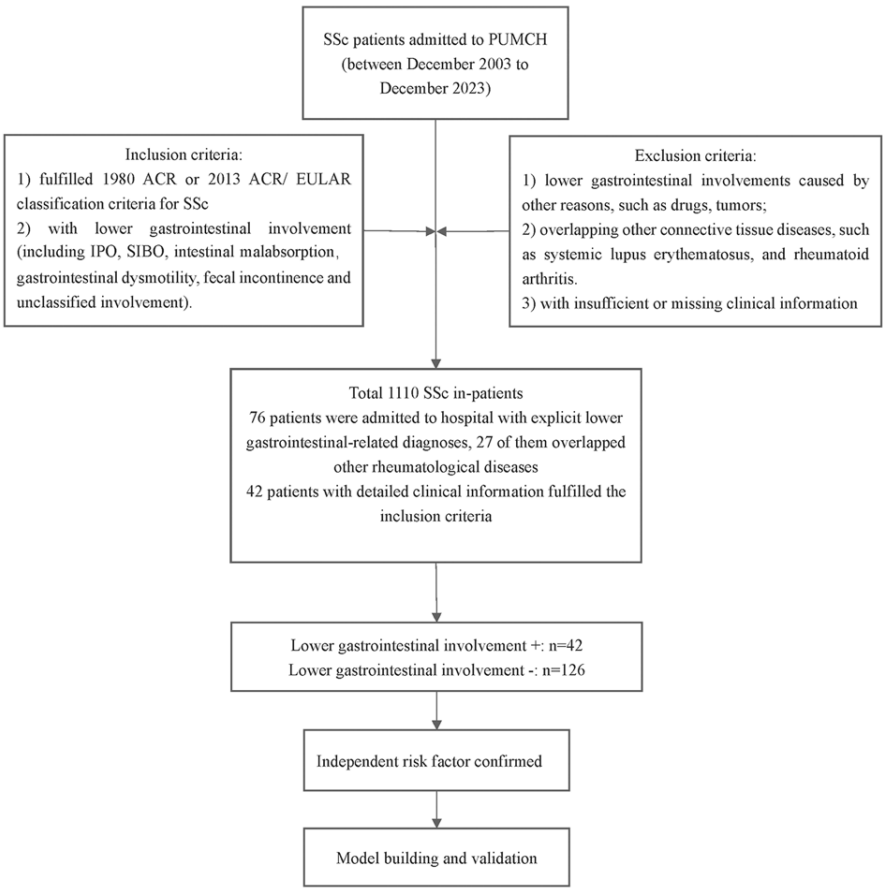

Fig. 1. Enrolment flowchart of participants used for model development and validation.

defined as abdominal bloating or diarrhoea with confirmed imaging abnormality, but unfulfilling the above diagnosis. Imaging tests included intestinal CT, ultrasound (US), and lower gastrointestinal contrast (GC).

Data collected included general conditions (age, gender, body mass index (BMI) and subtypes (dsSSc or lcSSc), clinical characteristics (disease duration, Raynaud's phenomenon (RP), puffy finger, digital ulcer, finger gangrene, telangiectasis, arthritis/ arthralgia, myositis, interstitial lung disease (ILD), pulmonary arterial hypertension (PAH), cardiomyopathy, scleroderma renal crisis (SRC), GI symptoms) and laboratory finding were collected and analysis. ILD was defined as the presence of ground-glass opacification or fibrosis on high-resolution CT (HRCT) imaging. PAH was defined as a mean pulmonary arterial pressure >25 mm Hg at rest, together with pulmonary capillary wedge pressure <15 mm Hg determined via right heart catheterisation or pulmonary artery systolic pressure >40 mm Hg at rest based on an echocardiogram. Cardiomyopathy was defined as the left ventricular ejection fraction (LVEF) <50% confirmed by echocardiography or myocardial impairment confirmed by myocardial magnetic resonance imaging, excluding other non-SSc causes, such as coronary heart disease. Disease duration was defined as the time between the first non-Raynaud phenomenon and baseline (hospital admission) (10).

Statistical analyses

Statistical analyses were performed using SPSS 27.0 (SPSS Inc. Chicago, IL, USA) and R v. 4.3.1. Continuous variables which were normally distributed were compared using Student's t-test, and were presented as mean ± standard deviation. Non-normally distributed continuous variables were compared using the Mann-Whitney test, and were presented as median (interquartile range). Categorical variables were compared using the chi-square or Fisher's exact test and presented as count (proportion). Blood biochemistry test data with less than 10% of true counts are filled in using mean interpolation, and data with more than 10% of missing counts are discarded from the whole set.

For the risk prediction model building, we included clinical factors that showed statistically significances ($p<0.05$) in T tests, Wilcoxon Mann Whitney tests and chi-square tests as factors in backward stepwise logistic regression analysis by R (package 'caret'). These factors were selected by the backward stepwise selection, with Akaike's information criterion (AIC) as the stopping rule. The AIC value for the multifactor analysis form was minimised with the fewest number of variables. A nomogram risk prediction model was developed (package 'rms'). The receiver operating characteristic curve (ROC) and Hosmer-Lemeshow test were utilised to check the efficiency and reliability of the model (packages 'pROC', 'calibrate', 'MASS', and 'rms').

Internal validation of the model was carried out using the Bootstrap procedure (package 'risk Regression', and a clinical decision curve analysis (DCA) was conducted to assess the model's clinical utility (package 'rmda').

Results

Clinical characteristics

A total of 42 SSc patients with lower GI involvement were enrolled, with a mean age of 54.36±12.01 years old, 33 of these patients were females (78.57%). The control group comprised 126 patients, with an average age of 53.16±9.831 years old and 101 were females (80.16%).

As shown in Table I, the most common manifestation in lower GI involvement was intestinal pseudo-obstruction (IPO, 24 patients, 57.1%), with 6 of these patients had recurrent attacks (14.29%). Other common manifestations included SIBO, (10, 23.81%), intestinal malabsorption (4, 9.52%), GI dysmotility (4, 9.52%) and faecal incontinence (3, 7.14%). Additionally, 5 patients (11.9%) were classified as unclassified involvements, including 3 patients with abdominal bloating and 2 with diarrhoea.

Table I. The manifestations of lower GI involvement in systemic sclerosis.

Lower gastrointestinal involvements	Number	Rate
Intestinal pseudo-obstruction (recurrent track)	24 (6)	57.1 (14.29)
Small intestinal bacterial overgrowth	10	23.81
Intestinal malabsorption	4	9.52
Gastrointestinal dysmotility	4	9.52
Faecal incontinence	3	7.14
Unclassified involvement	5	11.90
Combined diagnosis	number	rate
Intestinal malabsorption + SIBO	3	7.14
Intestinal malabsorption + IPO	1	2.38
Dysmotility + SIBO	1	2.38
Dysmotility + IPO	2	4.76
Faecal incontinence + IPO	1	2.38

IPO: defined as a clinical and/or radiological appearance of intestinal obstruction without a clearly defined ischaemic, mechanical, or postsurgical cause in a patient with SSc; SIBO: confirmed by glucose H2/CH4 breath test and the gastroenterology consultation; intestinal malabsorption: confirmed by D-Xylose absorption test abnormal; gastrointestinal dysmotility: confirmed by gastrointestinal transit test abnormality; unclassified involvement: abdominal bloating or diarrhoea with confirmed imaging abnormality (included intestinal CT, ultrasound (US), and lower gastrointestinal contrast (GC)), but unfulfilling the above diagnosis criteria.
GI: gastrointestinal; SIBO: small intestinal bacterial overgrowth; IPO: intestinal pseudo-obstruction.

Table II. Imaging findings in SSc patients with lower GI involvement.

	CT		Bowel ultrasound (BUS)		Gastrointestinal contrast (GC)	
	+	-	+	-	+	-
IPO	23	0	6	2	0	0
SIBO	4	6	1	0	1	3
Intestinal malabsorption	2	2	1	0	0	0
Dysmotility	3	1	0	1	1	1
Faecal incontinence	0	2	0	0	0	0
Unclassified involvement	2	3	2	0	1	0

GI: gastrointestinal; SSc: systemic sclerosis; BUS: bowel ultrasound; GC: gastrointestinal contrast; IPO: intestinal pseudo-obstruction; SIBO: small intestinal bacterial overgrowth.

Among the patients with lower GI, nearly all patients (n=41) accepted CT scanning, while 11 received bowel ultrasound (BUS) (9 appeared abnormalities) and 7 received gastrointestinal contrast (GC, 4 appeared abnormalities). Among the 24 patients with IPO, 23 underwent CT scan and all of them revealed abnormalities such as bowel dilatation or thickening of the intestinal wall or both. Eight patients with IPO had BUS performed, and 6 of them showed abnormal results. These 6 patients also had abnormal CT, while 2 patients with negative BUS test had bowel dilatation in their CT scanning. All patients with SIBO underwent CT scanning, with 40% exhibiting abnormalities (mostly reported as bowel dilatation), and 1 had abnormal BUS. Four patients with SIBO made GC test and 25% (n=1) appeared abnormal. In patients with intestinal malabsorption, half of the patients (2 in 4) had abnormal CT findings and 1 of them also had abnormal BUS. For patients with faecal incontinence, 2 underwent CT scanning, both of them returned negative results. All intestinal CT scans in IPO patients demonstrated bowel dilatation, with 8 reported the thickening of the intestinal wall. Six abnormal bowel ultrasounds in IPO patients indicated bowel dilatation, and two of them also showed thickening of the intestinal wall.
The frequency of abnormal CT findings in patients with unclassified involvement was 40% (2/5), 2 had abnormal BUS and 1 patient showed abnormal GC (Table II).

Risk factor model building

Data on clinical characteristics and laboratory examinations are summarised in Table III. Patients with lower GI involvement exhibited significantly lower BMI, haemoglobin (HB), albumin (ALB) levels compared to the control group ($p<0.001$). Additionally, cardiomyopathy ($p<0.001$) and puffy finger ($p=0.01$) were more common in patients with lower GI involvement, while arthritis/arthralgia was less common ($p=0.04$). The observation group also displayed higher high-sensitivity C-reactive protein (hs-CRP) ($p=0.04$) and a higher rate of anti-Ro-52 antibody positivity ($p=0.001$). No significant differences were observed in other antibodies (anti Sm, anti RNP, anti SSA, anti SSB, anti scl-70, ACA, ANA) or laboratory findings (lactate dehydrogenase (LDH), uric acid (UA), immunoglobulin G (IgG), immunoglobulin A (IgA), immunoglobulin M (IgM), erythrocyte sedimentation rate (ESR)) ($p>0.05$).
For the risk model analysis, 8 factors (BMI, Puffy finger, cardiomyopathy, arthritis/arthralgia, anti-Ro52 antibody, ALB, hs-CRP, Hb) were included in the backward stepwise logistic regression analysis. Ultimately, five predictors (BMI, cardiomyopathy, ALB, hs-CRP, Hb) were selected in the clinical prediction model processed by using R programme (Table IV).

Validation of the model

A nomogram risk prediction model was developed based on the outcomes (Fig. 2a), with each variable being assigned a score. The higher the score, the greater the risk of lower GI involvement in SSc patients. A correction curve was developed to evaluate the model's degree of rectification (Fig. 2b). The Hosmer-Lemeshow test indicated good calibration ($\chi^2=9.54$, $p=0.39$). Internal validation using the Bootstrap 1,000 times self-sampling method yielded a Brier value of 9.1 (95%CI:6.2–12.1) (Fig. 2c). The ROC curve of this model is shown in Figure 2d, with a calculated AUC value of 0.93 (95%CI:0.89–0.97). The clinical decision curve is presented in Figure 2e, indicating that the threshold of 0.01-0.86 has the largest clinical net income.

Discussion

In this study, we developed a clinical risk model of SSc with severe lower GI

Table III. Comparison of characteristics between SSc patients with and without lower GI involvement.

Clinical information	Patients with lower GI involvement (%)	Patients without lower GI involvement (%)	χ^2/Z/t	*p*-value
Age (± SD)	54.3 (12.01)	53.16 (9.83)	0.65	0.20
Sex (F)	33 (78.57)	101 (80.16)	0.22	0.83
BMI (IQR)	17.5 (5.37)/41	22.4 (4.77)/125	5.34	<0.001
Subtypes (dcSSc)	23 (54.76)	59 (46.83)	0.79	0.37
Disease duration (IQR)	56 (114)	65.5 (101)	0.12	0.93
RP	34 (80.95)	114 (90.48)	2.72	0.10
Digital ulcers	11 (26.19)	29 (23.02)	0.18	0.68
Finger gangrene	3 (7.14)	2 (1.59)	1.72	0.19
Telangiectasis	17 (40.48)	38 (30.16)	1.52	0.22
Puffy finger	17 (40.48)	26 (20.63)	6.512	0.01
Myositis	4 (9.53)	14 (11.1)	0.00	1.00
Arthritis/arthralgia	8 (19.05)	46 (36.51)	4.40	0.04
Scleroderma renal crisis	8 (19.0476)	11 (8.73)	2.39	0.12
ILD	30 (71.43)	82 (65.08)	0.57	0.45
PAH	5 (11.9)	22 (17.46)	0.72	0.40
Cardiomyopathy	11 (26.19)	3 (2.38)	20.36	<0.001
Gastroesophageal reflux	24 (57.14)	65 (51.59)	0.39	0.53
Dysphagia	7 (16.67)	31 (24.60)	1.13	0.29
ANA	40 (95.24)	122 (96.83)	0.23	0.63
ACA	11 (26.1905)	21 (16.67)	2.33	0.127
Anti Sm	8 1(0.79)	0.00 1.00		
Anit RNP	7 (16.67)	13 (10.32)	0.68	0.41
Anti SSA	8 (19.05)	22 (17.46)	0.05	0.82
Anti SSB	0	3 (2.38)	0.11	0.31
Anti scl-70	10 (23.81)	36 (28.57)	0.51	0.75
Anti-Ro-52	21 (50)	29 (23.2)/125	10.76	0.001
HB (± SD)	110.81 (21.34)	131.87 (16.4)	6.76	<0.001
ALB (± SD)	34.95 (5.29)	41.3 (4.60)	7.45	<0.001
hs-CRP (IQR)	8.45 (11.53)	4.01 (6.62)	2.03	0.043
WBC (± SD)	3.73 (9.25)	1.67 (3.77	0.705	0.48
PLT (± SD)	221.71 (102.38)	192.95 (65.40)	1.709	0.09
ALT (IQR)	18.50 (14.25)	20.00 (15.25)	0.324	0.75
GGT (IQR)	21.50 (37.00)	21.00 (22.75)	0.497	0.41
ALP (IQR)	79.00 (53.25)	68.00 (29.25)	1.373	0.17
AST (IQR)	21.00 (11.25)	24.00 (9.00)	0.809	0.42
LDH (IQR)	225.00 (135.25)	213.50 (90.50)	0.004	1.00
Cr (IQR)	61.50 (30.25)	61.00 (21.00)	0.302	0.76
UA (IQR)	265.00 (141.50)	286.50 (101.50)	1.525	0.13
IgG (IQR)	11.70 (3.96)	12.52 (5.08)	1.132	0.26
IgA (IQR)	2.37 (1.62)	2.27 (1.32)	0.473	0.64
IgM (IQR)	0.88 (0.70)	0.89 (0.73)	0.725	0.47
ESR (IQR)	14.00 (15.50)	11.00 (19.00	1.169	0.24

Table IV. Result of predictive factors selected by R in SSc patients with lower GI involvement.

Factors	β	SE	*p*-value	OR	95%LCI	95%UCI
hs-CRP	0.07	0.03	0.01	1.07	1.02	1.13
Cardiomyopathy	3.25	0.87	<0.001	25.70	4.71	140.30
Arthritis/arthralgia	-1.24	0.69	0.07	0.29	0.08	1.12
ALB	-0.22	0.06	<0.001	0.80	0.71	0.91
Hb	-0.03	0.01	0.07	0.97	0.94	0.99
BMI	-0.23	0.08	0.02	0.80	0.69	0.93

involvement requiring hospitalisation including five items. Five key variables were BMI, Cardiomyopathy, ALB, hs-CRP, and Hb.

The lower GI involvement in SSc is common and can lead to severe, even fatal outcomes. However, timely diagnosis and effective management are still unmet. Until now several studies have investigated factors related to SIBO and IPO in SSc patients (9, 10, 13), while no risk factor model about lower GI involvement in SSc has been put forward yet. We included six categories of SSc lower GI involvements in this study and proposed a clinical prediction model that covered most sites and types of lower GI involvement in SSc inpatients.

Our findings revealed that patients with different disease subtypes might have discrepancies in specific involvements, like ulcers (17). Although the correlation between disease subtypes and lower GI involvement is not fully elucidated, prior research has indicated a higher incidence of IPO in patients with dcSSc (13), while the prevalence of SIBO appears consistent across subtypes (8). Our study unified lower GI involvement as a whole and found no significant differences between SSc subtypes.

Notably, previous research had highlighted that SSc patients were more prone to small bowel dilation compared to patients with IPO arising from other conditions (18), which suggested that small bowel dilation might be a specific characteristic of SSc lower GI involvement that can be observed via imaging. Intestinal imaging techniques such as CT, ultrasound, and radiography play crucial roles in identifying intestinal functional or structural abnormalities in SSc patients. CT is considered as the most commonly used test to evaluate the GI tract in clinical practice. In our cohort, nearly all patients underwent CT scans (41 out of 42), and all IPO patients had abnormal results. CT scans had the highest positivity rate (100%) among IPO patients, but only 40% of patients had abnormal manifestations in SIBO, which may be due to less obvious structural intestinal lesions associated with SIBO. Ultrasound is a safe, non-invasive examination without radiation exposure, but experience and excellent technique were required for the operator. Our study shows that bowel ultrasound is positive in 75% of the patients with IPO, indicating that although ultrasound is not as sensitive as CT, but it could be used as a non-invasive practical tool during follow-up.

Cardiomyopathy is a significant complication of SSc, presenting risks including sudden cardiac death (19). There was a large burden of subclini-

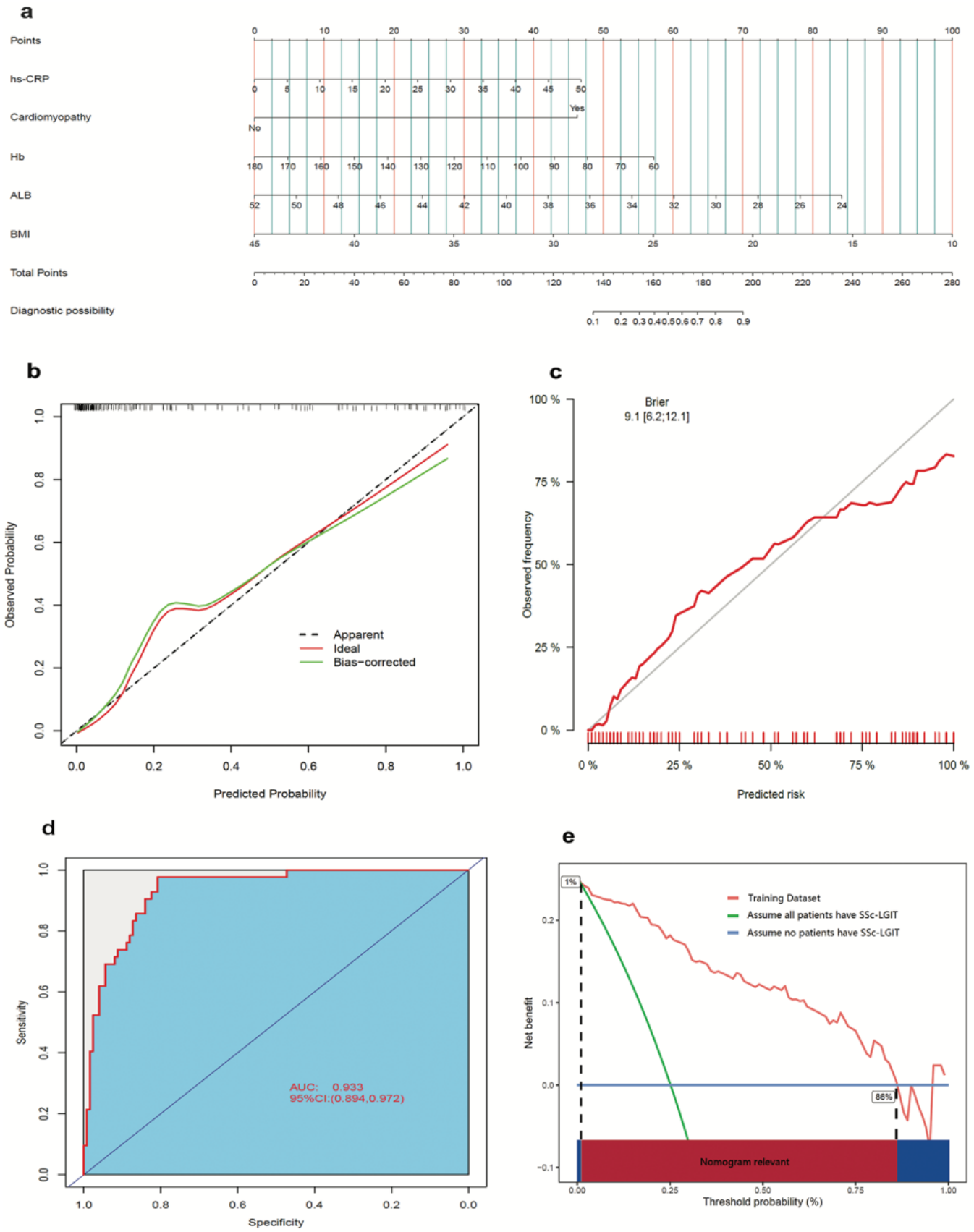

Fig. 2. Validation of the sever SSc-LGIT model.
a) NOMO graph of the clinical risk model of severe SSc-LGIT; **b**) Correction curve of the severe SSc-LGIT clinical risk model; **c**) The ROC curve of the severe SSc-LGIT clinical risk model; **d**) Internal validation result using the Bootstrap 1,000 times self-sampling method yielded; **e**) The clinical decision curve of the severe SSc-LGIT clinical risk model.

cal cardiac lesions in patients with SSc (20). Dupont. R's research suggested that cardiac involvement in SSc was significantly associated with micronutrient deficiency and malnourished patients had significantly higher summed Medsger disease severity scales (21). Previous studies have suggested 3 stages (neuropathy, myopathy, and finally intestinal fibrosis) in intestinal involvement (22), myopathy is one of the stages. Our study found that cardiomyopathy but not myositis was more common in patients with lower GI lesions, which was consistent with the conclusion from the prospective study that more intestinal and anal GIT profile composed with heart involvement (23). This may suggest that the pathogenesis in intestinal smooth muscle involvement and myocardium involvement may be different from skeletal muscle, the former two more commonly presenting as myopathies but the latter mostly as myositis. This difference was supported by their different treatment responses to glucocorticoid and immunosuppressive therapy, which are effective in myositis but little response in cardiomyopathy or lower GI involvement in our clinical practice.

Existing literatures report that malnutrition adversely impacts the disease prognosis (7, 24, 25), while Baron *et al*. study suggested that body weight loss is the most sensitive indicator of malnutrition (26). The assessment of nutritional condition is required in SSc patients as malnutrition represents a potentially modifiable risk factor with nutritional interventions (27). An observation cohort study showed more than half of SSc patients with intestinal impairment were associated with malnutrition (28), while studies suggested that a single indicator (*e.g*. a single BMI (29) or albumin (30)) is not the ideal marker for assessing malnutrition in SSc patients. Our study demonstrated that SSc patients with lower GI involvement exhibited significantly poorer nutritional status, characterised by lower BMI, HB and ALB compared to the control group, which is in accordance with the previous studies (27, 28). These indicators were included in the SSc-LGIT model and the combination of multiple nutrition-related indicators enhance the effectiveness of the model. Notably, hs-CRP emerged as a relevant inflammatory marker correlating with lower GI involvement in our study, consistent with prior research linking elevated CRP levels to irreversible organ damage in SSc (31).

Antinuclear antibodies (ANA) are considered the strongest independent predictors in SSc with digital microvascular damage (32). They are presented in most of the SSc patients (33). Maclean *et al*. reported that ANA negativity was associated with constipation in the GIT 2.0 (34), and another study showed that SSc patients with negative ANA possibly had more frequent GI involvement (35). However, in our study, patients with lower GI involvement did not show a significantly difference in the rate of ANA positive. This may be due to the small number of patients and the high positive rate of ANA. Moreover, Yen *et al*. reported that anti-Ro52 antibody positivity was associated with GI tract involvement in patients with SSc (36). Our study also found anti Ro52 antibody positivity was more common in SSc patients with lower GI involvement, though no significant difference was found in further analysis (p=0.59).

The nomogram and decision curve in this study show the excellent utility of our model, which relies on routine clinical follow-up data that are easily obtainable, underscoring its applicability in evaluating the risk of developing lower GI complications in SSc patients. Despite the absence of external validation through additional prospective studies, we employed internal validation via Bootstrap procedure to affirm the modelling stability.

There are several limitations in this study. This study was a single-centre retrospective study. Though we used PSM in selecting the control group to reduce the bias, not all patients underwent lower GI-related imaging, thus this might potentially result in selection bias, and underestimate the prevalence of certain manifestations, such as SIBO. According to Christian. von Mühlenbrock *et al*. study, SIBO was evidenced in nearly two-thirds of SSc patients (37). Future multicentre prospective studies are essential to assess the model's reliability comprehensively. Our cohort consisted of patients with diverse lower GI involvement phenotypes, and it was uncertain whether the pathogenesis was the same in these subtypes. Thus, future research focusing on specific GI phenotypes in SSc, such as IPO, will be helpful to unravelling the pathogenesis of specific GI phenotypes.

Conclusion

In summary, our study established a clinical risk model of lower GI involvement in SSc with BMI, Cardiomyopathy, ALB, hs-CRP, Hb. This model demonstrates a reliable capacity to predict the risk of severe lower GI involvement in systemic sclerosis, thereby offering clinicians valuable insights for early diagnosis and intervention. Future research will aim to establish a prospective cohort dedicated to investigating lower GI tract involvement in SSc, facilitating a deeper understanding of the underlying pathogenesis.

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