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Psychometric evaluations of the simplified Chinese version of the Functional Assessment of Cancer Therapy-Epidermal Growth Factor Receptor Inhibitors 18 (FACT-EGFRI-18-sC) for measuring dermatologic toxicities in metastatic colorectal cancer patients treated with EGFRIs

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Abstract

Background Dermatologic toxicities are common among metastatic colorectal cancer (mCRC) patients receiving epidermal growth factor receptor inhibitors (EGFRIs), adversely affecting their well-being and quality of life (QoL). Currently, no validated tool exists in China to measure these symptoms. This study validated the Simplified Chinese version of the Functional Assessment of Cancer Therapy–EGFRI 18 (FACT-EGFRI-18-sC) for QoL assessment in mCRC patients.

Methods A cross-sectional study was performed via convenience sampling to recruit mCRC patients from two tertiary hospitals in Shenyang, China. Sample size adequacy was confirmed by post hoc power analysis (G*Power 3.1; >80% power for $r \geq 0.3$, $\alpha = 0.05$). Acceptability was assessed by item-level missing data. Reliability was evaluated by Cronbach's α and a 2-week test–retest intraclass correlation coefficient (ICC). Criterion validity was evaluated against the Simplified Chinese version of the patient-reported version of CTCAE (PRO-CTCAE-sC) through non-parametric analyses. Construct validity was assessed via correlations with the Simplified Chinese Body Image Scale (BIS-sC), Karnofsky Performance Status (KPS), and cetuximab cycles using Spearman tests. Diagnostic accuracy and cutoff value were determined via receiver operating characteristic (ROC) analysis.

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Results The final sample ($n = 184$) provided sufficient statistical power, with post hoc analysis revealing 98% power ($\alpha = 0.05$) to detect correlations exceeding 0.3. The FACT-EGFRI-18-sC showed excellent acceptability (no missing data) and satisfactory reliability (Cronbach's $\alpha = 0.899$, ICC = 0.875). Moderate to strong negative correlations with PRO-CTCAE-sC (r = -0.436 to -0.803, $p < 0.001$) and significant FACT-EGFRI-18-sC score differences by dermatologic toxicity status (Z = -4.823 to -7.457, $p < 0.001$) supported criterion validity. Scores of the FACT-EGFRI-18-sC correlated negatively with BIS-sC (r = -0.565 to -0.619, $p < 0.001$), positively with KPS physical/functional subscales ($r = 0.424/0.541$, $p < 0.001$), but not with the social/emotional subscale ($r = 0.125$, $p > 0.05$), confirming construct validity. ROC analysis yielded an area under the curve (AUC) of 0.844 and identified an optimal cutoff of 60.00.

Conclusions The validated FACT-EGFRI-18-sC is a robust tool for QoL assessment in mCRC patients experiencing EGFRI-related dermatologic toxicities, providing a standardized measure to guide toxicity management.

Keywords Colorectal cancer, Dermatologic toxicities, Quality of life, Psychometric evaluations, Reliability, Validity

Background

Globally, colorectal cancer (CRC) is the third most diagnosed malignancy and the second leading cause of cancer death [1]. In China, CRC ranks second in morbidity and fourth in mortality [1, 2]. CRC is a significant public health issue worldwide, with an increasing incidence due to socioeconomic development, dietary changes, unhealthy behaviors, and sedentary lifestyles [3]. Moreover, there is a concerning rise in early-onset CRC among adults younger than 50 years old at diagnosis [1]. Therefore, to alleviate the growing burden of CRC, healthier lifestyle adoption, preventive screening, and treatment modality enhancement are critically important. Over the past decade, the treatment paradigm for CRC has shifted from traditional models like surgery, radiotherapy, and chemotherapy towards precision oncology methods including targeted therapy, immunotherapy, and nanomedicine [4–6]. Promising results have been demonstrated in clinical trials of CRC treatment based on effective systemic therapy [7, 8].

Currently, epidermal growth factor receptor inhibitors (EGFRIs), such as cetuximab and panitumumab, are well established as effective agents for the treatment of metastatic CRC (mCRC) [4, 7, 9]. Despite the efficacy of EGFRIs, more than 85% of the mCRC patients experience dermatologic toxicities, including acneiform rash, xerosis, paronychia, and pruritus [10]. These dermatologic toxicities not only affect patients' physical health (e.g., pain, insomnia, and infection) but also impose profound psychosocial burdens (e.g., anxiety, social withdrawal, and stigmatization), ultimately compromising treatment adherence and quality of life (QoL) [11–13]. Severe cases may necessitate dose reductions or therapy discontinuation, jeopardizing clinical outcomes and survival benefits [14]. However, the management of dermatologic toxicities remains challenging because of the variability in the symptom burden reported by patients and the assessments made by clinicians [14, 15]. The impact of dermatologic toxicities is often underestimated when relying solely on clinician-reported outcome measures [16–19]. The incorporation of patient-reported outcome (PRO) measurements alongside clinician-reported outcome measures can increase the accuracy of dermatologic toxicities reporting and improve treatment approaches in both research and clinical practice [18, 19]. Close monitoring, early recognition, and early management of dermatologic toxicities can help alleviate symptoms, which in turn may improve mCRC patients' QoL.

According to Shaigany et al. [18], among the clinician-reported outcome measures, the National Cancer Institute-Common Terminology Criteria for Adverse Events (NCI-CTCAE) is the most frequently used measurement in research for reporting dermatologic toxicities. For PRO measures, six dermatology instruments are commonly utilized to assess dermatologic toxicities in cancer patients who receive targeted therapy [16, 18]. Of which, four measurements are generic instruments that are used across various skin diseases and patient groups, including the Dermatology Life Quality Index (DLQI), the Skindex-16, the Skindex-29, and the Deutsches Instrument zur Erfassung der Lebensqualität bei Hauterkrankungen (DIELH-24), none of which were developed for targeted cancer therapies [16, 18]. The other two symptom-specific instruments are the Functional Assessment of Cancer Therapy-Epidermal Growth Factor Receptor Inhibitors-18 (FACT-EGFRI-18) and the Hand-Foot Syndrome 14 (HFS-14), both of which are suitable for targeted cancer therapies [16, 18]. Compared with the HFS-14, the FACT-EGFRI-18 developed by Wagner et al. [19], was specifically designed to comprehensively evaluate the impact of the EGFRI-induced dermatologic side effects on QoL and has demonstrated acceptable reliability and validity among English-speaking and Dutch-speaking cancer patients [19–21]. Therefore, the FACT-EGFRI-18 could be an appropriate instrument for assessing dermatologic toxicities in mCRC patients. Although the simplified Chinese version of the FACT-EGFRI-18 (FACT-EGFRI-18-sC) is accessible through the Functional Assessment of Chronic Illness Therapy (FACIT) organization [22], its psychometric properties

(e.g., acceptability, reliability, and validity) have not yet been validated in mainland Chinese mCRC patients. Preliminary data on the FACT-EGFRI-18-sC internal consistency reliability of the FACT-EGFRI-18-sC among lung cancer patients are available in mainland China but lack comprehensive validation (e.g., acceptability, test-retest reliability, criterion, and construct validity) [23, 24]. The lack of validated measures for mCRC patients limits effective assessment of dermatologic toxicities. Therefore, this study aims to examine the psychometric properties of the FACT-EGFRI-18-sC, confirming its suitability for use among mCRC patients who received EGFRIs treatment in mainland China.

Methods

Participants and procedure

This cross-sectional study was conducted in two tertiary hospitals in Liaoning, Mainland China. Between June 2024 and February 2025, all inpatients who met the eligibility criteria were invited to participate in the study during their scheduled chemotherapy appointments. A total of 184 stage IV CRC inpatients receiving EGFR inhibitors were included in the final sample via convenience sampling. The inclusion criteria were (1) diagnosed with stage Ⅳ CRC, (2) received at least one cycle of EGFRIs treatment (cetuximab), (3) 18 years or older, (4) able to complete questionnaires independently or with the help of a researcher, and (5) willing to participate in the study. The exclusion criteria were (1) dermatologic toxicities caused by radiotherapy, and other medications or treatments (determined by clinicians or researchers based on skin characteristics and the patient's treatment regimen), (2) patients with any other concomitant skin disorders (e.g., eczema, ichthyosis, or neurodermatitis), (3) patients with critical and life–threatening conditions, or (4) patients with serious cognitive impairment or mental disorders (e.g., dementia, schizophrenia, or Parkinson's disease).

All participants were recruited and completed the survey during hospitalization. Two weeks later [25], a convenience sampling method was used to select 50 participants to complete the FACT-EGFRI-18-sC again to assess test–retest reliability. Clinicians or nurses assisted researchers in screening and identifying the eligibility of the participants at the study hospitals. Prior to inviting patients to take part in the study, the researcher provided detailed information to explain the purpose, procedures, and completion requirements of the survey. Patients who agreed to participate were asked to provide written consent. Each participant was asked to complete all questionnaires of the survey anonymously and independently. If participants were unable to fill in these questionnaires by themselves, the researcher helped to conduct the filling process by inquiring about reading each item word-by-word sequentially. After all the questionnaires were completed, each item was reviewed by the researcher to clarify the missing or scribbled answers to ensure the completeness and accuracy of the data. The data were independently double-entered into IBM SPSS (version 25.0) by two researchers to ensure accuracy and correct any potential entry errors. Ethical approval was obtained from the human research ethics committee of the author's institution [no 2024075FS (KT)-027-02].

Sample size calculation

The sample size is calculated based on the formula by Bonett [26], as shown below, where k represents the number of items, $z_{\alpha/2}$ and z_{β} are points on the standard normal distribution exceeded with probability $\alpha/2$ and β, respectively, c is the value of Cronbach's α at the null hypothesis, and $\widetilde{p}_k$ is the expected value of Cronbach's α. The expected value is determined by expert opinion or previous studies, with a Cronbach's α greater than 0.70 indicating acceptable reliability. To ensure an instrument demonstrates excellent internal consistency, it is recommended to test the hypothesis with c set above zero, such as $c = 0.50$ [27].

$$n = \{2k/(k-1)\}\left(z_{\alpha/2} + z_{\beta}\right)^2 / \ln\left(\widetilde{\delta}\right) + 2$$

$$\widetilde{\delta} = (1-c)/(1-\widetilde{p}_k)$$

In our study, the FACT-EGFRI-18-sC comprises 18 items ($k = 18$), with a power (1-β) of 90% ($z_{\beta}=z_{0.1}=1.282$), an alpha level of 0.05 ($z_{\alpha/2}=z_{0.025}=1.96$), and c and $\widetilde{p}_k$ set at 0.50 and 0.70, respectively. The minimum required sample size calculated is 88. Allowing for a potential 20% dropout rate, the final sample size is determined to be at least 106. Our sample size meets this criterion. To confirm the adequacy of our sample size, a post hoc power analysis is performed using G*Power (Version 3.1; Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany) with the following parameters: correlation effect size = 0.3, statistical power = 0.80, and α = 0.05 (2-tailed) [28, 29]. This analysis verified that our final sample (n = 184) provided sufficient statistical power for the study.

For the analysis of test-retest reliability, the required sample size is estimated using Bonett's formula for the intraclass correlation coefficient (ICC) [30]. A two-measurement design ($k = 2$) is adopted, with the expected ICC ($\widetilde{\rho}_1$) set at 0.80, which represents a target in the "good" reliability range. The primary precision target is defined as a 95% confidence interval (CI) total width (ω) no greater than 0.20, with a two-tailed significance level of α = 0.05 ($z_{\alpha/2} = 1.96$). On the basis of these assumptions, the final sample size is determined to be 50, which

meets the COSMIN study design checklist criterion for receiving an "adequate" quality rating for test-retest reliability [31].

$$n = \frac{8z_{\frac{\alpha}{2}}^2 \left\{ \left(1 - \widetilde{\rho}_1\right)^2 \left(1 + (k-1)\,\widetilde{\rho}_1\right)^2 \right\}}{\{k\,(k-1)\,\omega^2\}} + 1$$

Measures

Sociodemographic information

Sociodemographic information included participants' age, gender, marital status, education level, family monthly income, cancer familial history, and cetuximab administration cycles.

Simplified Chinese version of the Functional Assessment of Cancer Therapy-Epidermal Growth Factor Receptor Inhibitors 18 (FACT-EGFRI-18-sC)

The FACT-EGFRI-18-sC is a PRO measurement including 18 items that assesses dermatologic toxicities (e.g. skin, nail, and hair) symptom burden and QoL (physical, social/emotional, and functional status) in cancer patients receiving EGFRIs in the past 7 days [19, 22]. The FACT-EGFRI-18-sC has three subscales, including physical (7 items), social/emotional (6 items), and functional (5 items) well-being [32]. Each item is evaluated using a 5-point Likert scale ranging from 0 (not at all) to 4 (very much); items requiring reverse scoring are scored accordingly [22]. The total score can range from 0 to 72, with a higher score indicating a better QoL. The FACT-EGFRI-18-sC, which was licensed for use in this study, was obtained from the FACIT organization [22]. The FACT-EGFRI-18-sC has been applied in studies involving lung cancer patients, where Cronbach's α coefficient for the total scale ranged from 0.867 to 0.919 [23, 24].

Simplified Chinese version of the patient-reported version of the common terminology criteria for adverse events (PRO-CTCAE-sC)

The patient-reported version of the common terminology criteria for adverse events (PRO-CTCAE) was developed by the National Cancer Institute (NCI) that reflecting 78 symptomatic side effects for cancer treatment [17]. Each symptomatic side effect is evaluated by 1 to 3 attributes (presence/absence, frequency, severity, interference, or amount), collectively forming 124 unique items [33]. Each item is assessed individually, without merging attributes [33]. Responses are provided on a 5-point Likert scale (0 = none, 1 = mild, 2 = moderate, 3 = severe, 4 = very severe), or via an absent/present code (0 = absent, 1 = present) [17, 33]. The PRO-CTCAE has been widely validated in more than 60 languages, such as German, Dutch, Japanese, which could be accessible through from the NCI official website (http://healthcaredelivery.cancer.gov/pro-ctcae) [33]. The PRO-CTCAE-sC has been successfully developed and linguistically validated in Chinese cancer patients, and the results supported content validity and acceptability [34]. Although the NCI-CTCAE was widely used in clinical practice and research to assess treatment toxicities among cancer patients, it does not allow for patient self-reporting of symptomatic adverse effects [18]. In contrast, the PRO-CTCAE-sC offered a standardized platform for cancer patients to self-report treatment-related side effects [17, 34]. Therefore, the PRO-CTCAE-sC was chosen as the instrument for evaluating criterion validity.

Simplified Chinese version of the body image scale (BIS-sC)

The body image scale (BIS) is a 10-item self-report measurement including two subscales (appearance concern and body perception) assessing distress related to a distorted body image and associated with shame in cancer patients [35]. Items are rated on a 4-point Likert-type scale from 0 (not at all) to 3 (very much) and summed to create a total score (ranging from 0 to 30), and a higher score indicates a more severe body image [35]. The BIS has been widely linguistically validated in different kinds of languages and various cancer patients worldwide [36–39]. The simplified Chinese version of the BIS (BIS-sC) has been validated in patients with colorectal cancer, and the Cronbach's α coefficient of the total scale was 0.92 [39]. In this study, the Cronbach's α coefficient of the scale was 0.944. Dermatologic toxicities often affected patients' appearance, leading to negative body image and QoL [12, 13]. In addition, both the FACT-EGFRI-18-sC and BIS-sC have similar measurement concepts [22, 39]. It was hypothesized that their scores would be significantly correlated. Therefore, the BIS-sC was selected as an instrument for evaluating construct validity.

Karnofsky performance status (KPS)

The Karnofsky performance status (KPS) was developed by Karnofsky et al. [40]. This scale consists of 11 items for assessing the functional status of cancer patients. The KPS is an objective assessment that is determined by clinicians according to the status of the patients related to illness, self-care ability, and daily activities [40]. The score of the KPS ranges from 100 (normal function) to 0 (death), and a higher score indicates better patient health [40]. The KPS has been widely applied in diverse kinds of cancer patients and countries including China [41–43]. Since dermatologic toxicities can markedly affect patients' self-care abilities, daily activities, adaptation to illness and treatment, as well as psychological well-being [12], it was hypothesized that the total, physical, and functional subscale scores of the FACT-EGFRI-18-sC would be significantly correlated with the KPS, whereas no correlation would be observed between the social/

emotional subscale score of the FACT-EGFRI-18-sC and the KPS. Thus, the KPS was chosen as an instrument to evaluate construct validity.

Statistical analysis

All statistical analyses were performed in IBM SPSS (version 25.0). Descriptive statistics were used to summarize the demographic information of the samples. Continuous variables were evaluated for normality via the Shapiro–Wilk test. Normally distributed data were presented as the means (SDs), non-normally distributed data as the medians (IQRs), and categorical variables as counts (%).

Acceptability was determined by calculating the percentage of missing data for all FACT-EGFRI-18-sC items, with an overall item response rate above 80% considered acceptable [22, 44]. The FACT-EGFRI-18-sC was not translated from English to Chinese, as it was obtained directly from the FACIT organization, which prohibit modification of any items [22]. Therefore, item completion rates served as an important indicator of the measure's acceptability.

Internal consistency reliability was established by calculating the Cronbach's α coefficient and test-retest reliability was evaluated by the intraclass correlation coefficient (ICC). Cronbach's α greater than 0.70 and an ICC greater than 0.75 indicate acceptable reliability, respectively [45, 46]. Test–retest reliability was established by calculating 2-way random effects of average measure ICCs for absolute agreement between 2 tests [47, 48].

The validity evaluation included criterion validity and construct validity (convergent validity and discriminant validity). The scores of FACT-EGFRI-18-sC, BIS-sC, and KPS were non-normally distributed, and the PRO-CTCAE-sC instrument comprised both binary nominal variables and ordinal polytomous variables. Thus, the criterion validity was assessed between the FACT-EGFRI-18-sC and PRO-CTCAE-sC using non-parametric analyses, including Spearman rank correlation test and Mann-Whitney U test. Convergent and discriminant validity of the FACT-EGFRI-18-sC were assessed via Spearman rank correlation tests with the BIS-sC, KPS, and cetuximab administration cycles. The value of the Spearman's correlation coefficient (r) less than 0.30 was considered weak correlation, 0.30 to 0.70 was considered moderate correlation, and greater than 0.70 was considered strong correlation [49].

The diagnostic accuracy and cutoff point of the FACT-EGFRI-18-sC scale were determined via receiver operating characteristic (ROC) analysis. The area under the curve (AUC) was calculated. A model or test with perfect discriminatory ability would have an AUC of 1.0, whereas a model unable to distinguish between individuals with or without the chosen outcome would have an AUC of 0.50 [50]. The optimal cutoff was selected by balancing sensitivity and specificity and maximizing the Youden index, thereby detecting true toxicity cases while minimizing false positives in clinical practice. Participants were diagnosed with dermatologic toxicities according to the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 [51]. All significance levels were set at $p < 0.05$.

Results

Demographic characteristics

A total of 200 mCRC patients participated in this study, with 184 (92.0%) valid questionnaires received. The other 16 (8.0%) invalid questionnaires were excluded due to more than 50% of items being unanswered, which was attributed to reasons such as physical discomfort, unwillingness to continue, or having other matters to attend to. Post hoc power analysis confirmed that the final sample ($n = 184$) achieved 98% power to detect the hypothesized correlation effect size > 0.3 (α = 0.05, 2-tailed), exceeding the conventional 80% threshold.

The average age of the participants was 61.01 years (SD = 7.34), with a range of 46 to 75 years; 108 participants (58.7%) were elderly individuals aged 60 years or older. Among the participants, 118 (64.1%) were males and 160 (87.0%) were married. The majority of the participants reported compulsory education (67.4%), an average monthly income of 1,000–2,999 RMB (35.9%), and without familial history of cancer (80.4%). The median cetuximab administration cycle of the participates was 4 (IQR = 6), with a range of 1 to 17 cycles, and 52.7% received less than 5 cycles (Table 1).

Acceptability

No missing values were observed for the FACT-EGFRI-18-sC, with a missing data rate of 0.0% (0 out of 184), which demonstrated excellent acceptability.

Reliability

The overall Cronbach's α coefficient of the FACT-EGFRI-18-sC was 0.899, and that of the three subscales ranged from 0.815 to 0.872, which indicated satisfactory internal consistency. Test-retest reliability over 2 weeks, evaluated in 50 participants, was acceptable for the FACT-EGFRI-18-sC (ICC = 0.790–0.875), indicating robust reliability (Table 2).

Criterion validity

Moderate to strong negative correlations were found between the total and subscale scores of the FACT-EGFRI-18-sC and the PRO-CTCAE-sC item scores for skin dryness, acne, hair loss, itching, and hand–foot syndrome (r = -0.436 to -0.803, $p < 0.001$), supporting the criterion validity. In particular, the total and physical

Table 1 Demographic characteristics of the participants ($n = 184$)

Variables	Number (*n*)	Percentage (%)
Age (years)		
< 60	76	41.3
≥ 60	108	58.7
Gender		
Male	118	64.1
Female	66	35.9
Marital status		
Married	160	87.0
Single/divorced/widowed	24	13.0
Education level		
Compulsory education	124	67.4
Upper secondary education	20	10.9
Tertiary education	40	21.7
Income (average/month, RMB)		
< 1000	42	22.8
1000–2999	66	35.9
3000–4999	53	28.8
≥ 5000	23	12.5
Cancer familial history		
Yes	36	19.6
No	148	80.4
Cetuximab administration cycles		
< 5	97	52.7
5–9	58	31.5
≥ 10	29	15.8

Table 2 Internal consistency and test-retest reliability of the FACT-EGFRI-18-sC

FACT-EGFRI-18-sC	Number of items	Cronbach's α ($n = 184$)	Test-retest ($n = 50$)	
			ICC	95% CI
Total	18	0.899	0.875	(0.819, 0.920)
Physical	7	0.872	0.832	(0.755, 0.893)
Social/emotional	6	0.815	0.790	(0.693, 0.867)
Functional	5	0.826	0.809	(0.719, 0.879)

ICC: Intraclass correlation coefficient; CI: confidence interval

subscale scores of the FACT-EGFRI-18-sC demonstrated strong inverse correlations with skin dryness, acne, itching, and hand-foot syndrome, with correlation coefficients ranging from – 0.701 to -0.803. In addition, the social/emotional subscale score of the FACT-EGFRI-18-sC exhibited a strong inverse correlation coefficient of -0.733 with hair loss. However, the total, physical, and functional subscale scores were moderately negatively correlated with hair loss (ranging from – 0.466 to -0.684). As well as the social/emotional and functional subscale scores of the FACT-EGFRI-18-sC displayed moderate negative correlations with skin dryness, acne, itching, and hand–foot syndrome (ranging from – 0.436 to -0.650, $p < 0.001$) (Table 3). These results demonstrate that more severe dermatologic toxicities are associated with lower QoL in mCRC patients receiving EGFRIs.

The Mann–Whitney U test results further substantiated the criterion validity of the FACT-EGFRI-18-sC. Significant differences in total and each subscale of the FACT-EGFRI-18-sC score distributions were observed between participants with and without dermatologic toxicities (Z = -4.823 to -7.457, $p < 0.001$), such as rash, hives, nail ridging/discoloration, and sensitivity to sunlight (Table 3). The FACT-EGFRI-18-sC effectively distinguishes QoL impacts between mCRC patients with and without dermatologic toxicities, confirming its clinical usefulness. These results collectively underscore the strong criterion validity of the FACT-EGFRI-18-sC in detecting and quantifying dermatological toxicities.

Construct validity

Moderate negative correlations were detected between the FACT-EGFRI-18-sC total score and the BIS-sC score, including its subdimensions (appearance concern and body perception) (r = -0.565 to -0.619, $p < 0.001$). Similarly, the physical and functional subscales of the FACT-EGFRI-18-sC showed moderate negative correlations with the BIS-sC and its subdimensions (r = -0.361 to -0.428, $p < 0.001$). However, the social/emotional subscale exhibited strong negative correlations with the BIS-sC total score (r = -0.710, $p < 0.001$) and moderate negative correlations with its subdimension scores (r = -0.627 to -0.676, $p < 0.001$). These findings collectively demonstrate that poorer body image, heightened appearance concerns, and negative body perception are significantly associated with reduced QoL across the physical, functional, and social/emotional domains in mCRC patients receiving EGFRIs therapy. In addition, significantly moderate correlations were observed for the total, the physical subscale, and functional subscale scores of the FACT-EGFRI-18-sC with the KPS ($r = 0.424$ to 0.541, $p < 0.001$). In contrast, no correlation was noted for the social/emotional subscale score of the FACT-EGFRI-18-sC with the KPS ($r = 0.125$, $p > 0.05$). These findings suggest that mCRC patients with better performance status tend to report higher overall, physical, and functional QoL, whereas emotional/social well-being appears to be independent of functional performance status in this population. Moderate inverse correlations were shown between the total and subscale scores of the FACT-EGFRI-18-sC with the number of cetuximab treatment cycles (r = -0.317 to -0.581, $p < 0.001$), suggesting that longer EGFRIs treatment duration was associated with poorer QoL. These findings support the convergent and discriminant validity of the FACT-EGFRI-18-sC (Table 4).

Table 3 Criterion validity between the FACT-EGFRI-18-sC and the PRO-CTCAE-sC ($n = 184$)

Item of the PRO-CTCAE-sC (attribute)	FACT-EGFRI-18-sC			
	Total	Physical	Social/Emotional	Functional
1. Rash (presence/absence)	-7.187 [a]*	-6.739 [a]*	-6.154 [a]*	-4.867 [a]*
2. Skin dryness (severity)	-0.790 [b]*	-0.724 [b]*	-0.635 [b]*	-0.650 [b]*
3. Acne (severity)	-0.735 [b]*	-0.745 [b]*	-0.450 [b]*	-0.551 [b]*
4. Hair loss (amount)	-0.684 [b]*	-0.567 [b]*	-0.733 [b]*	-0.466 [b]*
5. Itching (severity)	-0.781 [b]*	-0.803 [b]*	-0.460 [b]*	-0.602 [b]*
6. Hives (presence/absence)	-7.457 [a]*	-6.659 [a]*	-6.473 [a]*	-5.837 [a]*
7. Hand-foot syndrome (severity)	-0.715 [b]*	-0.701 [b]*	-0.436 [b]*	-0.634 [b]*
8. Nail ridging (presence/absence)	-6.668 [a]*	-6.427 [a]*	-5.789 [a]*	-4.823 [a]*
9. Nail discoloration (presence/absence)	-7.064 [a]*	-6.951 [a]*	-5.223 [a]*	-5.439 [a]*
10. Sensitivity to sunlight (presence/absence)	-7.090 [a]*	-6.633 [a]*	-4.974 [a]*	-5.653 [a]*

[a] Mann–Whitney U, *Z*

[b] Spearman rank correlation analysis, *r*

*$P < 0.001$ (2-tailed)

Table 4 Correlation coefficients between FACT-EGFRI-18-sC, BIS-sC, KPS, and cetuximab administration cycles ($n = 184$)

Measurement	FACT-EGFRI-18-sC			
	Total	Physical	Social/Emotional	Functional
BIS-sC -Total	-0.619*	-0.409*	-0.710*	-0.378*
BIS-sC -appearance concern	-0.591*	-0.366*	-0.676*	-0.388*
BIS-sC -body perception	-0.565*	-0.361*	-0.627*	-0.428*
KPS	0.446*	0.541*	0.125 (0.090) **	0.424*
Cetuximab administration cycles	-0.558*	-0.581*	-0.317*	-0.452*

*$P<0.001$ (2–tailed), **$P>0.05$ (2–tailed)

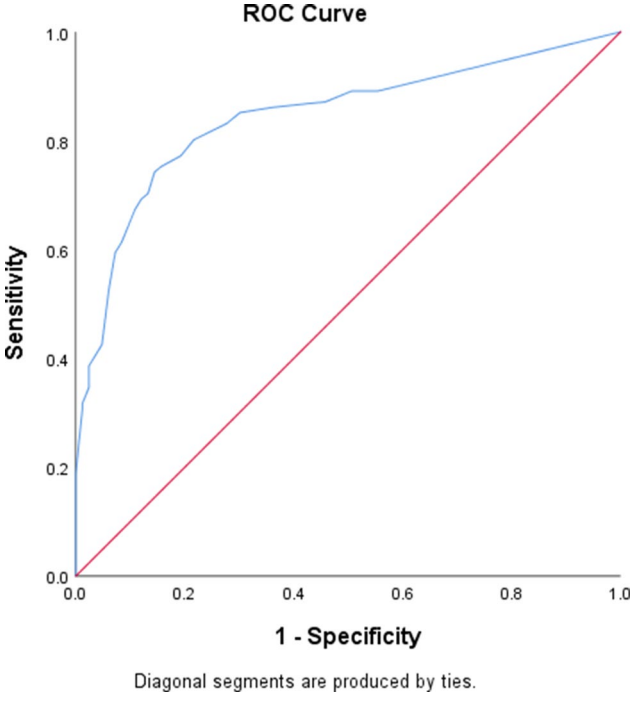

Fig. 1 AUC of the FACT-EGFRI-18-sC

Receiver operating characteristic analysis

The result demonstrated robust diagnostic performance of the FACT-EGFRI-18-sC, with an AUC of 0.844 (Fig. 1), indicating a strong ability to discriminate between mCRC patients experiencing greater versus lesser impacts of dermatologic toxicities on QoL. The maximum Youden index was 0.598, which identified a threshold of 60.00 as the optimal cutoff (Table 5).

This means that patients scoring below 60 are likely to experience a greater impact of dermatologic toxicities on their QoL, while those scoring above 60 generally report better QoL with less interference from dermatologic issues. At the threshold of 60.00, the sensitivity was 0.743, meaning that approximately 74% of mCRC patients whose QoL was significantly affected by dermatologic toxicities were correctly identified (Table 5). The specificity was 0.855, indicating that approximately 86% of mCRC patients with minimal impact were accurately excluded (Table 5).

Discussion

Dermatologic toxicities are common adverse events in mCRC patients undergoing treatment with EGFRIs and often lead to significant physiological and psychosocial challenges, such as pain, insomnia, infection, and depression [10–13]. These issues can negatively impact patients' overall health and QoL. Therefore, understanding dermatologic toxicities caused by EGFRIs from patients' perspectives is crucial, as these adverse effects are best described by the patients themselves and can significantly influence adherence to long-term therapy. In China, research on patient-reported symptoms and concerns regarding EGFRI-induced dermatologic toxicities among mCRC patients remains in its early stage, with a notable lack of validated instruments. The FACT-EGFRI-18-sC is currently the only available assessment tool in mainland China but has not been evaluated for its psychometric

Table 5 Various cutoff scores for the FACT-EGFRI-18-sC ($n = 184$)

Cutoff score	Sensitivity	Specificity	Youden Index
17.0000	0.000	1.000	0.000
19.0000	0.030	1.000	0.030
24.5000	0.040	1.000	0.040
30.0000	0.069	1.000	0.069
33.0000	0.079	1.000	0.079
36.5000	0.119	1.000	0.119
39.0000	0.129	1.000	0.129
41.0000	0.149	1.000	0.149
43.0000	0.188	1.000	0.188
45.0000	0.307	0.988	0.295
46.5000	0.317	0.988	0.305
47.5000	0.347	0.976	0.322
48.5000	0.386	0.976	0.362
50.0000	0.426	0.952	0.378
51.5000	0.525	0.940	0.465
52.5000	0.594	0.928	0.522
53.5000	0.614	0.916	0.530
54.5000	0.644	0.904	0.547
55.5000	0.673	0.892	0.565
57.0000	0.693	0.880	0.573
58.5000	0.703	0.867	0.570
60.0000*	0.743	0.855	0.598
61.5000	0.752	0.843	0.596
62.5000	0.772	0.807	0.580
63.5000	0.802	0.783	0.585
65.0000	0.832	0.723	0.555
66.5000	0.851	0.699	0.550
68.0000	0.861	0.639	0.500
69.5000	0.871	0.542	0.413
70.5000	0.891	0.494	0.385
71.5000	0.891	0.446	0.337
73.0000	1.000	0.000	0.000

* Best cutoff score

properties [19, 20]. This study examined the psychometric properties of the FACT-EGFRI-18-sC among mCRC patients, which demonstrated satisfactory acceptability, reliability, and validity within this specific clinical context. A full validation of the FACT-EGFRI-18-sC using a sample of Chinese mCRC patients will create a culturally appropriate tool for systematically screening and assessing dermatologic toxicities caused by EGFR inhibitors in clinical practice.

In this study, the FACT-EGFRI-18-sC demonstrated excellent acceptability among Chinese mCRC patients, as evidenced by the absence of missing values (0.0%). The internal consistency reliability of the FACT-EGFRI-18-sC total score was acceptable (0.899), aligning with findings from previous research (0.72–0.94) [12, 20, 23, 24]. Furthermore, the Cronbach's α coefficients for the three subscales of the FACT-EGFRI-18-sC ranged from 0.815 to 0.872, consistent with the results reported by Du et al. [23], who primarily assessed reliability in lung cancer patients (0.704–0.949). These results support the satisfactory reliability of the FACT-EGFRI-18 across studies and cancer types (e.g., lung and colorectal cancer) in different cultural contexts. However, a slight difference was noted in comparison with Liu et al.'s study [24], where the Cronbach's α coefficient for the physical domain was reported as 0.673. This difference could be attributed to the participant composition in Liu et al.'s study [24], where the majority were lung cancer patients (97.6%) treated with the TKIs rather than mCRC patients receiving cetuximab. TKIs are small-molecule compounds that are administered orally, whereas cetuximab is a monoclonal antibody that is delivered intravenously, resulting in distinct pharmacologic properties and patterns of skin exposure [4, 10, 23]. Additionally, lung cancer and colorectal cancer are biologically different diseases, with varying EGFR expression levels and mutation profiles, which could further influence the type and severity of drug-induced dermatologic toxicity [12, 23]. Moreover, Liu et al.'s study [24] included a small sample size of only 44 patients, while our study involved a significantly larger sample size of 184 participants. The adequacy of our study sample size (n = 184) was thoroughly validated through both a priori calculation and post hoc power analysis [26, 28, 29]. Particularly, post hoc analysis revealed an excellent statistical power of 98% to detect clinically meaningful correlations (r >0.3) at a significance level of α = 0.05, substantially exceeding conventional thresholds of 80% power [28, 29]. The robust sample size enhances both the reliability of the psychometric findings and the representativeness of mCRC patients with EGFRIs-related dermatologic toxicities, confirming the clinical utility of the FACT-EGFRI-18-sC for routine toxicity assessment in targeted therapy settings. Careful sample size determination is essential when designing a reliability study. If the sample size was inadequate, the study would lack statistical power and produce excessively wide confidence intervals, ultimately compromising the credibility of the results [26]. Unfortunately, the English and Dutch versions of the FACT-EGFRI-18 did not examine its subscales, limiting the possibility of comparisons from a global perspective [19–21, 32]. Moreover, although Chiang et al. [12] used the FACT-EGFRI-18 to identify factors influencing dermatologic toxicities related to the EGFRIs-associated QoL among mCRC patients in Taiwan, China, only the overall Cronbach's α coefficient of the tool was reported. Despite variations in cancer type, sample size, EGFR inhibitor type, and study design [12, 19–21, 23, 24, 32], the FACT-EGFRI-18 consistently demonstrates stable and reproducible measurements of the impact of dermatologic toxicities on QoL, supporting its application in both research and clinical settings.

The test–retest reliability analysis of the FACT-EGFRI-18-sC in our study yielded ICC values between 0.790 and

0.875, confirming its robust reliability. Notably, no studies worldwide have reported ICCs of this tool, making cross-cultural or linguistic comparisons unfeasible. A subsample of 50 participants was selected for test-retest reliability of the FACT-EGFRI-18-sC in our study, which met the minimum (n = 50) recommended for ICC stability [30, 31]. Although an expected ICC of 0.80 was used for sample size estimation, one observed value was 0.790, with all others ≥ 0.80. The small deviation (0.01) is well within the 95% CI of the expected ICC and represents typical sampling variability [30]. Moreover, it still meets the acceptable reliability threshold (ICC ≥ 0.75) [31, 45, 46]. Overall, the FACT-EGFRI-18-sC showed robust reliability, indicating it effectively measured the impact of dermatologic toxicities on mCRC patients' QoL.

In terms of assessing criterion validity for the FACT-EGFRI-18-sC, no universally accepted gold standard exists. While the NCI-CTCAE remains the standard for clinician-reported symptomatic adverse events [18], evidences suggest that direct patient reports offer greater accuracy and consistency [52–55]. To capture dermatologic toxicities more effectively, the NCI developed the PRO-CTCAE [17], which was related to the European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire (QLQ-C30) domains [52]. Given that, the PRO-CTCAE was chosen as the gold standard instrument in this study.

Moderate to strong negative correlations exist between the FACT-EGFRI-18-sC scores and the ordinal variable item scores of the PRO-CTCAE-sC (r ranging from -0.436 to -0.803) in this study, indicating good criterion validity of the FACT-EGFRI-18-sC. However, comparing the findings on the criterion validity of the FACT-EGFRI-18-sC with those of other studies is challenging. Previous published studies have assessed the criterion validity of the FACT-EGFRI-18 using the NCI-CTCAE, a clinician-reported outcome measure, due to the absence of a gold standard [20, 24]. In Wong et al.'s study [20], agreements between the NCI-CTCAE items most commonly associated with EGFRIs-induced dermatologic toxicities and the FACT-EGFRI-18 items were measured by using the unweighted Kappa statistic to assess the criterion validity. The Kappa coefficients ranged from – 0.02 to 0.53, varying by assessment time and skin symptoms [20]. According to Choen [56], if the Kappa coefficient is equal to or greater than 0.41, moderate or better agreement will be defined. Thus, the criterion validity between the FACT-EGFRI-18 and the NCI-CTCAE is generally fair [20], which might reflect the limitations of the NCI-CTCAE measure itself. In another study conducted by Liu et al. [24], a Spearman correlation test was used to assess the criterion validity between the FACT-EGFRI-18-sC and NCI-CTCAE among 43 lung cancer patients and one CRC patient, revealing moderate correlations between the two measures. However, this study only considered skin dryness, itching, and a nail-related item from the NCI-CTCAE to record dermatologic toxicities, whereas acneiform rash was identified by the Multinational Association of Supportive Care in Cancer (MASCC) [24]. Among dermatologic toxicities, acneiform rash was the most common dermatologic adverse event in cancer patients treated with EGFRIs, which was overlooked in the validity assessment [10, 24]. Furthermore, the study did not specify the particular items of the NCI-CTCAE that were correlated with the FACT-EGFRI-18-sC [24].

In addition to the ordinal variable item scores of the PRO-CTCAE-sC, dichotomous variables related to dermatologic toxicities were also selected to evaluate the criterion validity of the FACT-EGFRI-18-sC via the Mann−Whitney U test. Significant differences in the total and subscale score distributions of the FACT-EGFRI-18-sC were identified between participants with and without dermatologic toxicities (Z = -4.823 to -7.457), including rash, hives, nail ridging/discoloration, and sensitivity to sunlight. These findings collectively highlight the robust criterion validity of the FACT-EGFRI-18-sC in identifying and quantifying dermatologic toxicities. To date, our study is the first to comprehensively evaluate and report criterion validity in this context, effectively bridging this research gap.

Convergent and discriminant validity were assessed by correlating the FACT-EGFRI-18-sC with the BIS-sC, KPS, and cetuximab administration cycles using the Spearman rank correlation test. For convergent validity, moderate to strong negative correlations were detected between the FACT-EGFRI-18-sC and the BIS-sC, including their total scores and subdimensions (r ranging from – 0.361 to -0.710). According to the PRO theory, PRO measures should reflect the aspects of QoL that patients themselves experience [57–59]. In this context, the observed correlations indicate that the FACT-EGFRI-18-sC effectively captures the psychosocial impact of dermatologic toxicities on body image, indicating that it aligns with the theoretical expectations of PRO. These correlations are anticipated, as the EGFRIs-associated health-related QoL is closely linked with body image [12, 13]. According to Chiang et al. [12], patients who experienced more negative body image were more likely to have a poorer EGFRIs-associated health-related QoL. Dermatologic toxicities, such as rash, skin dryness, and hives, can alter a patient's appearance, which may lead to mild to moderate body image distress [12]. Additionally, patients often struggle to adapt to their illness and treatment, while physical symptoms contribute to psychological distress, such as stigma or perceived devaluation [60, 61]. Moreover, Luca et al. [13] noted that 52% of CRC patients reported avoiding social interaction and

experiencing concern, frustration, or depression due to their dermatological toxicities.

In addition, moderate correlations were identified between the total, physical, and functional subscale scores of the FACT-EGFRI-18-sC and the KPS (r ranging from 0.424 to 0.541). These findings aligned with previous research indicating that increased dermatologic toxicities could significantly impact activities of daily living [12]. However, for discriminant validity, no correlation was found between the social/emotional subscale scores of the FACT-EGFRI-18-sC and the KPS (r = 0.125). The potential reason might be that the KPS is an objective measure reflecting patients' illness, self-care ability, and daily activities, without accounting for social/emotional factors [40]. These findings are consistent with PRO theory [57–59], which indicates that the FACT-EGFRI-18-sC appropriately distinguishes between domains that are theoretically related and unrelated to functional status.

Apart from that, the number of cetuximab administration cycles was negatively associated with the FACT-RGFRI-18-sC score, with r ranging from − 0.317 to -0.581, which suggested a lower QoL with the longer treatment durations. These results were similar to those of earlier studies conducted by Wong et al. [20] and Ringash et al. [62]. Wong et al. [20] reported that both the total and subscale scores of the FACT-EGFRI-18 decreased significantly over time, indicating a decline in QoL. Furthermore, the results from Ringash et al.'s [62] international, multicenter, randomized controlled, phase III study demonstrated that with prolonged treatment duration, mCRC patients receiving cetuximab exhibited progressive deterioration in global QoL. Taken together, these results support both convergent and discriminant validity of the FACT-EGFRI-18-sC, which indicate that the FACT-EGFRI-18-sC accurately reflects patients' subjective experiences of dermatologic toxicities, including impacts on body image, functional status, and treatment-related symptom burden.

ROC analysis is an effective method for evaluating diagnostic and predictive accuracy in disease management, offering clear discrimination between individuals with and without the outcome [50]. In this study, we assessed the diagnostic performance of the FACT-EGFRI-18-sC by calculating the AUC, which was found to be 0.844. This score indicates a strong discriminative ability and confirms the effectiveness of the FACT-EGFRI-18-sC as a PRO measure for capturing the impact of dermatologic toxicities on mCRC patients' QoL. Clinically, the cutoff score of 60.00 distinguishes mCRC patients with greater QoL impairment from those relatively unaffected by dermatologic toxicities, with scores ≤ 60 indicating notable impact and scores >60 suggesting minimal interference [19]. Additionally, the balanced sensitivity (74.3%) and specificity (85.5%) of the cutoff indicate that the FACT-EGFRI-18-sC can reliably identify mCRC patients whose QoL is meaningfully affected by dermatologic toxicities, while minimizing misclassification of those with minimal impact, supporting its practical use in clinical monitoring and decision-making. These findings highlight that the FACT-EGFRI-18-sC is not only statistically robust but also clinically interpretable, offering a valuable tool for monitoring mCRC patients, identifying those at greater risk of QoL deterioration due to dermatologic toxicities, and guiding timely supportive care interventions. To our knowledge, this study provides the first ROC-based cutoff value for FACT-EGFRI-18-sC, offering a potential reference for dermatologic toxicities management. Further validation in diverse clinical settings is warranted.

Strengths and limitations

One major strength of this study lies in the originality of its research question, as it addresses a significant gap by comprehensively examining the psychometric properties of the FACT-EGFRI-18-sC among mCRC patients receiving EGFIs in mainland China. Another key strength was the assessment of the test-retest reliability of the FACT-EGFRI-18-sC, which demonstrated robust reliability. Additionally, our study was the first to evaluate the criterion validity of the FACT-EGFRI-18-sC using the PRO-CTCAE as the gold standard, a validated patient-reported measure widely adopted in international oncology trials. This approach provides a more accurate, patient-centered assessment of dermatologic toxicities, thereby enhancing both the scientific rigor and clinical relevance of our findings. Moreover, the diagnostic accuracy and optimal cutoff point of the FACT-EGFRI-18-sC were evaluated via ROC analysis, adding to the study's strengths of the study.

However, several limitations must be acknowledged. This study design imposed certain constraints, as it was cross-sectional, conducted at a single site, and based on convenience sampling. These factors may restrict the representativeness of the sample and limit the generalizability of the findings. A cross-sectional study design could not allow for the assessment of the sensitivity of the FACT-EGFRI-18-sC to changes over time. Future studies should adopt a prospective longitudinal design with assessments at baseline and multiple follow-ups to evaluate how the FACT-EGFRI-18-sC evolves. While convenience sampling at a single site ensures feasibility, future studies should employ random sampling and involve multiple centers to enhance generalizability and reduce the introduction of selection bias.

Furthermore, measurement-related limitations should also be noted. Content validity was not formally assessed by cognitive interviews or expert review, which might limit confidence that the items of the FACT-EGFRI-sC

fully capture patients' symptom experiences. Nevertheless, most participants reported understanding the items and provided accurate responses during the survey, suggesting that the findings remain reasonably generalizable to this population. Future studies should incorporate qualitative methods to explore how patients interpret FACT-EGFRI-18-sC items and support culturally sensitive adaptations. Additionally, this study did not account for potential confounding factors, such as comorbidities, concurrent treatments, or other patient-related factors. These factors may affect symptom burden and QoL reporting, psychometric results, and cutoff determination. Future studies should adjust for key confounders to ensure the reliability, validity, and thresholds of the FACT-EGFRI-18-sC across patient subgroups. Above all, these limitations suggest that the psychometric properties and identified FACT-EGFRI-18-sC cutoffs should be applied with caution in other clinical settings.

Conclusions

The FACT-EGFRI-18-sC demonstrated satisfactory psychometric properties and can be applied in Chinese mCRC patients to capture patient-reported dermatologic symptoms and QoL outcomes, supporting clinical monitoring, management decisions, and research assessment. Importantly, all the participants understood the items without missing data, highlighting the cultural adaptability and accessibility of the FACT-EGFRI-18-sC. The validated instrument may also enable cross-country outcome comparisons when applied to comparable populations with consistent methods. Healthcare providers should ensure continuous follow-up to monitor dermatologic toxicities and implement appropriate interventions, such as symptom-directed medications, skincare strategies, and patient education, to reduce symptom severity and improve QoL. However, these conclusions should be interpreted in light of study limitations, including the single-center, cross-sectional design, convenience sampling, lack of formal content validity assessment, and the absence of adjustment for potential confounders. Overall, a robust and well-validated tool such as the FACT-EGFRI-18-sC is essential for monitoring and managing dermatologic toxicities and evaluating the effectiveness of interventions.

Abbreviations

FACT-EGFRI-18	Functional Assessment of Cancer Therapy-Epidermal Growth Factor Receptor Inhibitors-18
FACT-EGFRI-18-sC	Simplified Chinese Version of the Functional Assessment of Cancer Therapy-Epidermal Growth Factor Receptor Inhibitors 18
EGFRIs	Epidermal growth factor receptor inhibitors
mCRC	Metastatic colorectal cancer
QoL	Quality of life
ICC	Intraclass correlation coefficient
CTCAE	Common Terminology Criteria for Adverse Events
PRO-CTCAE-sC	Simplified Chinese version of the patient-reported version of the CTCAE
BIS-sC	Simplified Chinese Body Image Scale
KPS	Karnofsky Performance Status
ROC	Receiver operating characteristic
PRO	Patient-reported outcome
NCI-CTCAE	National Cancer Institute-Common Terminology Criteria for Adverse Events
DLQI	Dermatology Life Quality Index
DIELH-24	Deutsches Instrument zur Erfassung der Lebensqualität bei Hauterkrankungen
HFS-14	Hand-Foot Syndrome 14
AUC	Area under the curve

Acknowledgements

We would like to thank all participants who helped us during this project.

Author contributions

LJZ, HX, and LL designed the study; LJZ wrote the manuscript; LJZ, NN, LNW, and LJZ were responsible for the data collection, HX and LL coordinated and supervised data collection; MYW and XJT input data to IBM SPSS; LJZ, SYN, CL, and DS carried out the analysis; HZ, XLS, YXM, and ZXZ contributed to the interpretation of the results; TW, JY(B)T, NJ, HX, and LL critically reviewed and revised the manuscript. All authors have read and approved the final manuscript.

Funding

This study was supported by the Joint Fund Program of the Science and Technology Department of Liaoning Province (Grant No. 2023-MSLH-181); the Basic Scientific Research Project for Universities, Department of Education of Liaoning Province (Grant No. LJ112410162003); the National Natural Science Foundation of China (Grant No.72204266).

Data availability

All data generated or analyzed during this study are not publicly available due to restrictions by the ethics committee. The dataset supporting the conclusions is available upon request to the corresponding author.

Declarations

Ethics approval and consent to participate

This study was conducted in adherence to the local and international ethical principles including those in the Declaration of Helsinki. The study was approved by the Ethics Committee of Affiliated Hospital of Liaoning University of Traditional Chinese Medicine [no 2024075FS (KT)-027-02]. Written informed consent was obtained from a legally authorized representative for anonymized patient information to be published in this article.

Consent for publication

The findings described in this study have not been previously published, and none of the authors is currently submitting them to another publisher for consideration.

Competing interests

The authors declare no competing interests.

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Received: 3 May 2025 / Accepted: 18 September 2025
Published online: 10 October 2025

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