Zhang *et al.*
European Journal of Medical Research (2025) 30:142
https://doi.org/10.1186/s40001-025-02392-y

European Journal of Medical Research

RESEARCH

Open Access

BIA-derived muscle indicator thresholds for malnutrition risk prediction in children with β-thalassemia: a cross-sectional study

Luyang Zhang[1†], Jiewen Long[1†], Li Wang[2], Lijuan Zhang[1], Yanlan Yang[1*] and Sandip Patil[1*]

Abstract

Background Malnutrition is a significant concern in children with β-thalassemia, impacting their growth and overall health. This study aimed to establish optimal thresholds for predicting malnutrition risk in children with β-thalassemia using muscle mass indicators derived from Bioelectrical Impedance Analysis (BIA).

Methods A cross-sectional study was conducted with 162 pediatric patients diagnosed with β-thalassemia. Nutritional status of them was assessed using the World Health Organization (WHO) Child Growth Standards and references. BIA was performed to obtain fat-free mass (FFM), skeletal muscle mass (SMM), and soft lean mass (SLM). Propensity score matching (PSM) was used to control for age and gender. Receiver Operating Characteristic (ROC) curves were constructed to evaluate the diagnostic performance.

Results SLM-change < 6% demonstrated the highest sensitivity [0.82, 95% confidence interval (CI) 0.72–0.92] and a negative predictive value of 0.83 (95% CI 0.74–0.93), while FFM-change < 4% showed more balanced performance with a sensitivity of 0.58 (95% CI 0.45–0.71) and a specificity of 0.65 (95% CI 0.56–0.74). Percentage change indicators (FFM-change, SLM-change, and SMM-change) exhibited remarkable stability before and after PSM, indicating minimal influence from age and gender.

Conclusions This study established novel, age-adaptive thresholds (SLM-change < 6% and FFM-change < 4%) for predicting malnutrition risk in children with β-thalassemia. The findings suggest that these thresholds could serve as effective references to assess nutritional status across different age groups, providing new perspectives for personalized nutritional management strategies.

Keywords β-Thalassemia, Malnutrition, Bioelectrical impedance analysis, Muscle mass, Pediatric nutrition

Introduction

Malnutrition is a critical challenge in children with β-thalassemia, affecting 33.6–44.3% of children with underweight or low body mass index and 37.7–44.3% with short stature [1, 2]. Due to specific limitations, traditional nutritional assessment methods are unable to precisely identify nuanced shifts in nutritional status or accurately detect changes in specific body tissues, such as fat-free mass (FFM), soft lean mass (SLM), and skeletal muscle mass (SMM) [3]. The altered fluid status commonly observed impacts both standard

†Luyang Zhang and Jiewen Long Both authors contributed equally to the first authorship.

*Correspondence:
Yanlan Yang
yylan1981@163.com
Sandip Patil
sandippatil1309@yahoo.com
[1] Department of Haematology and Oncology, Shenzhen Children'S Hospital, 7019 Yitian Road, Shenzhen, Guangdong, China
[2] Department of Clinical Nutrition, Shenzhen Children'S Hospital, 7019 Yitian Road, Shenzhen 518000, Guangdong, China

© The Author(s) 2025. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc-nd/4.0/.

anthropometric measurements, such as weight, and more detailed assessments of body composition, including fat mass, FFM, and total body water [4]. The nutritional status of affected children is closely correlated with their muscle mass and function [5]. Importantly, research by Ooi et al. indicated that muscle depletion is a crucial component of malnutrition, characterized by decreased SMM and impaired muscle function [6]. Furthermore, reduced muscle mass has been established as a core diagnostic criterion for malnutrition in adults worldwide [7]. Despite extensive research on malnutrition assessment, a significant gap remains in validated muscle mass thresholds for the pediatric population, particularly for children with chronic conditions, such as β-thalassemia. To address these limitations, the Global Leadership Initiative on Malnutrition (GLIM) working group [8] advocates for some quantitative techniques to assess muscle mass. These techniques include X-ray absorptiometry (DXA), computed tomography (CT), and bioelectrical impedance analysis (BIA). However, the routine clinical use of DXA and CT is constrained by their high cost, invasive nature, and radiation exposure [9]. In contrast, BIA serves as a non-invasive, rapid, and convenient method for evaluating body composition [10], demonstrating high accuracy and reliability in assessing the body composition of children [11].

BIA has gained widespread recognition for muscle mass evaluation and is now incorporated into diagnostic criteria by authoritative organizations, such as the European Working Group on Sarcopenia in Older People (EWGSOP2) [12]. Notably, reduced muscle mass is associated with poor prognosis in pediatric populations [13]. While its clinical value in detecting muscle depletion and predicting outcomes is well-established, the GLIM experts emphasize the necessity of establishing cutoff values for each measurement and method. They also stress the importance of adopting rigorously validated, ethnicity- and gender-specific muscle mass threshold criteria to improve the accuracy of malnutrition diagnosis [8]. The establishment of validated threshold values is clinically significant, as muscle mass and strength vary across populations due to ethnic differences. This allows for accurate identification of at-risk individuals and enables appropriate clinical intervention through population-specific criteria [14, 15]. This study aims to establish optimal BIA-derived muscle indicator thresholds for predicting malnutrition in children with β-thalassemia. These thresholds will provide clinicians with a rapid and reliable tool for assessing nutritional risk, facilitating early intervention when needed. Our findings may also provide valuable insights into the broader application of BIA in pediatric nutritional assessment for various chronic conditions.

Subjects and methods

Study population

A total of 162 children with β-thalassemia, admitted for regular blood transfusion therapy, were enrolled from the Department of Hematology and Oncology, Shenzhen Children's Hospital from November 2023 to August 2024. The inclusion criteria were as follows: (1) those with a definite diagnosis of β-thalassemia requiring regular blood transfusion therapy; (2) those aged from 2 to 18 years; (3) those without severe pleural or peritoneal effusion; (4) those who can comply with height, weight, and InBody measurements; and (5) those with available informed consent signed by both the patients and their legal guardians. Exclusion criteria were as follows: (1) those receiving surgical intervention within 24 h prior to assessment and (2) those with cardiac pacemakers. The patient recruitment process is depicted in Fig. 1. This study was approved by the Ethics Committee of Shenzhen Children's Hospital (Approval Number: 2023–13302).

Study design and data collection

This study adopts a cross-sectional design to evaluate the efficacy of BIA-derived muscle indicators in predicting malnutrition risk and while controlling for potential confounding variables. Within 24 h after admission, relevant data were collected from children. Baseline demographic information, including age, gender, and disease-related data, was extracted from medical records. Height and weight were measured on-site, and BMI was subsequently calculated. Nutritional status was assessed using the Screening Tool for the Assessment of Malnutrition in Paediatric (STAMP) [16], selected for its validated use in pediatric populations and high reliability (sensitivity 70%, specificity 91%). STAMP evaluates three domains: clinical nutritional implications, current nutritional intake, and differences in weight/height centile chart. Each domain is scored from 0 to 3, yielding a total score range of 0–9 points. Concurrently, body composition was analyzed using BIA to obtain specific values of FFM, SMM, SLM [9, 17, 18]. For each of these indicators, we calculated their respective '-change' indicators (FFM-change, SMM-change, and SLM-change). These indicators represent the percentage change relative to the lower limit of the InBody S10 standard range. The percentage change is calculated as follows: (actual measured value–lower limit of standard range)/lower limit of standard range * 100%. Continuous variables (FFM, SLM, SMM, FFM-change, SLM-change, and SMM-change) were utilized to predict the binary outcome (presence or absence of malnutrition

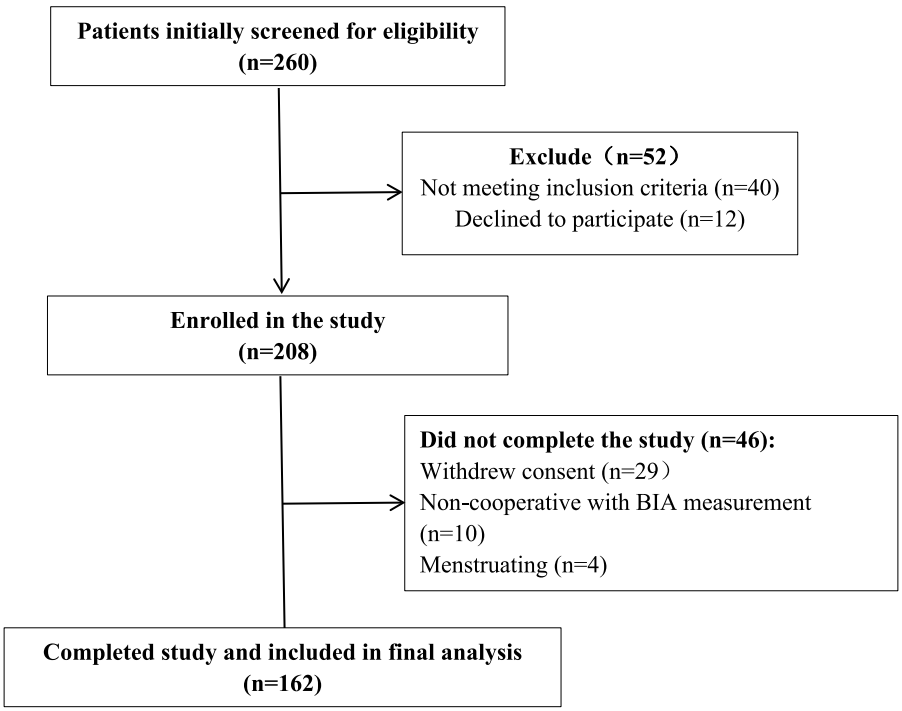

Fig. 1 Patient recruitment process

risk). Given the age-dependent increase in muscle mass among children, this study aimed to identify age-independent indicators. This was achieved through comparisons between normal/overweight and wasting/stunting groups in both unmatched and age–gender matched cohorts. Indicators that remained stable across these analyses were considered reliable predictors of malnutrition risk across pediatric age groups.

Bioelectrical impedance analysis

BIA was performed using the InBody S10 Body Composition Analyzer (InBody Co., Ltd., Seoul, Korea) with multi-frequency bioelectrical impedance technology at six different frequencies (1, 5, 50, 250 and 500 kHz as well as 1 MHz). After the BIA measurement, the reference ranges for FFM, SMM, and SLM were obtained directly from the built-in database of the InBody S10 system. However, these reference ranges were not specifically designed for children with β-thalassemia. The InBody BIA device underwent daily automatic calibration before the first measurement and also received regular maintenance by certified technicians. Measurements were conducted in the morning before transfusion, and the protocol is specified as follows. First, children were instructed fast for 4 h, void their bladders, and remain in the supine position for 15 min prior to assessment. During the measurement, they stayed supine with upper limbs slightly abducted and lower limbs modestly separated, ensuring no contact among extremities and torso while maintaining muscular relaxation. Contact electrodes were sanitized with alcohol wipes before being fixed to the thumbs and middle finger electrodes bilaterally. In and Out electrodes were then secured to the ankles of both lower extremities. In this manner, the FFM, SMM, and SLM of the children were assessed.

Variables for diagnostic performance analysis

To assess the diagnostic performance of BIA measurements, we analyzed several key variables. The predictor variables included BIA-derived muscle indicators: FFM, SLM, and SMM, along with their respective percentage changes relative to the lower limit of standard range (FFM-change, SLM-change, and SMM-change). These percentage changes were calculated using the formula described earlier.

The Z-scores provided by the WHO growth standards (2006) [19] and growth references (2007) [20] were applied to the pediatric cohort. These assessment metrics represent the WHO-recommended standard system for analyzing anthropometric data in children, enabling age- and gender-standardized measurements and direct comparison with international reference populations. The criteria were stratified by age. For children under 5 years, weight-for-height Z-scores (WHZ) were used. For children aged 5 years and older, BMI Z-scores (BMI-Z) were applied. The children were classified based on

the following conditions: wasting (WHZ or BMI-Z < −2 standard deviations (SD)), overweight or obesity (WHZ or BMI-Z > 2 SD), or stunting (height-for-age Z-score (HAZ) < −2 SD) [21, 22].

Statistical analysis

This cross-sectional study used sample size estimation based on the anticipated prevalence of the primary outcome variables and the desired precision. The sample size was calculated using the 'precise' package in R software (version 4.2.2). It was assumed that the prevalence of malnutrition among children with β-thalassemia is 30% [1] and the width of the 95% confidence interval (CI) is approximately 15% (i.e., ± 7.5%). The calculations indicated that at least 155 children were required to achieve the desired precision, and the target sample size was set at 173 based on a potential attrition rate of 10%.

The data were statistically analyzed using R software (version 4.2.2). Categorical variables were described by frequencies or percentages and compared using the chi-square test. The Shapiro–Wilk test was employed to assess normality of continuous variables. Normally distributed data were expressed as mean ± SD, while non-normally distributed data were presented as median (interquartile range, IQR). Between-group comparisons were conducted using Student's t test or the Mann–Whitney U test, as appropriate. Spearman's correlation analysis was performed to examine relationships among variables. Propensity score matching (PSM) was performed using the MatchIt package, with a 1:1 ratio and a calliper of 0.2 [23], to match the wasting/stunting and normal/overweight groups. Receiver Operating Characteristic (ROC) curves were constructed before and after matching, and the area under the curve (AUC) was calculated. The optimal cutoff values were determined using Youden Index. In addition, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were computed. No imputation methods were applied for missing data. Statistical significance was set at a two-sided $\alpha = 0.05$.

Results

Patient characteristics

A total of 162 children were enrolled, including 93 boys (57.4%) and 69 girls (42.6%), with a mean age of 8.93 ± 3.61. In the unmatched cohort [normal/overweight: $n = 105/2$ (64.8%/1.2%); wasting/stunting: 55 (34%)], children in the wasting group were significantly older than those in the normal nutrition group (11.29 ± 3.29 years vs 7.71 ± 3.13 years, $p < 0.001$). Based on the PSM results, 43 children were included in each group (10.4 ± 3.05 years vs 10.16 ± 2.88 years, $p = 0.706$), achieving good balance in baseline age and gender, as detailed in Table 1. Nutritional risk assessment using the STAMP revealed that all children were at moderate (n = 136, 84%) or high (n = 26, 16%) risk of malnutrition.

Correlation analysis

Spearsan's correlation analysis was conducted to examine the relationships of muscle mass indicators (FFM, SLM, and SMM) and their changes (FFM-change, SLM-change, SMM-change) to WHZ/BMI-Z and HAZ. Notably, changes in muscle mass indicators showed positive correlations with WHZ/BMI-Z ($P < 0.001$). A positive trend was also observed between changes in muscle mass and HAZ. The detailed correlation plots are presented in Figs. 2, 3.

Diagnostic performance of nutritional status assessment indicators

Among the evaluated indicators, SLM-change < 6 exhibited the best performance, demonstrating the highest sensitivity of 0.82 (95% CI 0.72–0.92) and the highest NPV of 0.83 (95% CI 0.74–0.93), but a relatively low specificity of 0.47 (95% CI 0.37–0.56). FFM-change < 4 showed a more balanced performance, with sensitivity of 0.58 (95% CI 0.45–0.71) and specificity of 0.65 (95% CI 0.56–0.74). SLM < 18 had the lowest specificity of 0.38 (95% CI 0.29–0.48), while FFM < 17 showed the least favourable overall performance with sensitivity of merely 0.22 (95% CI 0.11–0.33. Notably, SLM-change < 6 and FFM-change < 4 presented relatively high PPVs of 0.44 and 0.46, respectively. The comprehensive performance metrics for each nutritional status assessment indicator at their optimal cutoff values are provided in Table 2. The confusion matrix for diagnostic performance is presented in Additional files 1–6.

Comparison of AUC values (before and after matching) and indicator stability analysis

Comparative analysis of AUC values before and after matching revealed substantial stability in the percentage change relative to the lower limit of the standard range (e.g., FFM-change, SLM-change, and SMM-change). Specifically, the AUC for FFM-change exhibited only a slight shift from 0.62 (95% CI 0.53–0.72) before matching to 0.61 (95% CI 0.49–0.73) after matching. Similarly, SLM-change demonstrated a minimal change from 0.68 (95% CI 0.59–0.77) to 0.65 (95% CI 0.54–0.77) before and after matching. In contrast, the measured values (e.g., FFM, SLM, and SMM) generally displayed more pronounced fluctuations in AUC values after matching, as illustrated in Fig. 4.

Table 1 Demographic and clinical characteristics of children with β-thalassemia in the matched and unmatched groups

	Matched (PSM)				Unmatched (before PSM)			
	Normal/ overweight ($n=43$)	Wasting/stunting ($n=43$)	*P*	Missing (%)	Normal/ overweight ($n=107$)	Wasting/stunting ($n=55$)	*P*	Missing (%)
Age [year, median (IQR)]	10.30 [7.85, 11.55]	10.80 [7.75, 12.75]	0.675	0	7.00 [5.20, 9.90]	11.10 [8.30, 13.90]	< 0.001	0
Gender (%)				0				0
F	15 (34.9)	16 (37.2)	1		49 (45.8)	20 (36.4)	0.326	
M	28 (65.1)	27 (62.8)			58 (54.2)	35 (63.6)		
Height [cm, median (IQR)]	129.00 [118.50, 138.00]	128.50 [115.75, 133.50]	0.422	0	117.00 [106.00, 129.00]	130.00 [118.50, 140.55]	< 0.001	0
Weight [kg, median (IQR)]	26.00 [20.05, 33.45]	23.00 [18.60, 28.50]	0.054	0	20.00 [17.45, 25.70]	24.60 [19.75, 31.00]	0.002	0
BMI [kg/m^2, median (IQR)]	15.26 [14.64, 16.84]	14.47 [13.80, 15.84]	0.004	0	15.14 [14.43, 15.98]	14.72 [13.94, 16.22]	0.231	0
STAMP [pts, median (IQR)]	3.00 [3.00, 3.00]	3.00 [3.00, 5.00]	< 0.001	0	3.00 [3.00, 3.00]	3.00 [3.00, 5.00]	< 0.001	0
PA [°, median (IQR)]	4.70 [4.30, 4.90]	4.50 [4.00, 4.80]	0.039		4.50 [4.10, 4.90]	4.40 [4.00, 4.80]	0.621	
FFM [kg, median (IQR)]	21.10 [18.30, 25.25]	19.50 [16.40, 22.00]	0.051	0	17.20 [14.25, 21.35]	20.60 [17.00, 24.30]	0.001	0
SLM [kg, median (IQR)]	19.80 [16.45, 23.55]	18.20 [14.80, 22.20]	0.107	0	16.20 [13.45, 19.80]	19.00 [15.50, 22.95]	0.003	0
SMM [kg, median (IQR)]	10.50 [8.70, 12.85]	9.50 [7.60, 10.75]	0.041	0	8.10 [6.35, 10.55]	9.90 [7.95, 11.95]	0.001	0
FFM_change [%, median (IQR)]	5.02 [1.04, 9.90]	3.12 [− 7.16, 7.01]	0.07	0	6.01 [1.50, 10.56]	3.28 [− 4.87, 7.01]	0.009	0
SLM_change [%, median (IQR)]	3.83 [0.21, 7.23]	1.08 [− 8.51, 4.61]	0.014	0	4.88 [0.48, 9.66]	1.23 [− 6.54, 4.83]	< 0.001	0
SMM_change [%, median (IQR)]	3.12 [− 2.18, 7.07]	− 0.92 [− 11.91, 3.31]	0.031	0	1.77 [− 3.09, 6.37]	0.00 [− 10.04, 4.17]	0.057	0

P values < 0.001 indicated strong statistical significance. Normal: height-for-age, weight-for-height or BMI Z-scores ≥ −2SD; overweight: weight-for-height or BMI Z-scores > 2 SD; wasting: weight-for-height or BMI Z-scores < −2SD; stunting: height-for-age Z-score < −2SD

PSM propensity score matching, *IQR* interquartile range, *STAMP* screening tool for the assessment of malnutrition in paediatric, *BMI* body mass index, *FFM* fat-free mass, *SLM* soft lean mass, *SMM* skeletal muscle mass; change = (actual measured value−lower limit of standard range)/lower limit of standard range * 100%

Optimal cutoff values for nutritional status assessment indicators

The optimal cutoff values for BIA-derived muscle indicators in predicting malnutrition risk were determined using the Youden index, as shown in Additional files 7–12. The optimal cutoff values for predicting malnutrition risk in children with β-thalassemia were determined as follows: FFM_change < 4%, SLM_change < 6%, and SMM_change < 3%, as depicted in Fig. 5.

Discussion

Patients with transfusion-dependent β-thalassemia (TDT) require lifelong blood transfusions and iron chelation therapy. These treatments, along with the disease itself, can lead to multiple complications that increase the risk of malnutrition [24, 25]. Previous research has demonstrated that children with TDT tend to experience worsening stunting, wasting, and muscle loss as they age [26]. This progressive deterioration in nutritional status underscores the critical need for early and accurate identification of malnutrition risk. To the best of our knowledge, this study is the first to systematically investigate the optimal thresholds for BIA-derived muscle indicators to predict malnutrition risk in children with β-thalassemia, using wasting or stunting as indicators. Our findings revealed that SLM-change < 6% exhibits the highest sensitivity (0.82, 95% CI 0.72–0.92) and robust NPV (0.83, 95% CI 0.74–0.93), suggesting its potential as an effective initial screening tool. However, it is noteworthy that SLM-change < 6% exhibits a relatively low specificity (0.47, 95% CI 0.37–0.56), which may result in some false-positive results. Therefore, a thorough nutritional assessment is crucial to confirm the diagnosis in clinical practice based on these findings. In contrast, FFM-change < 4% shows a balanced performance, with sensitivity of 0.58 (95% CI 0.45–0.71) and specificity of 0.65 (95% CI 0.56–0.74), suggesting it may be a more suitable tool for predicting malnutrition risk.

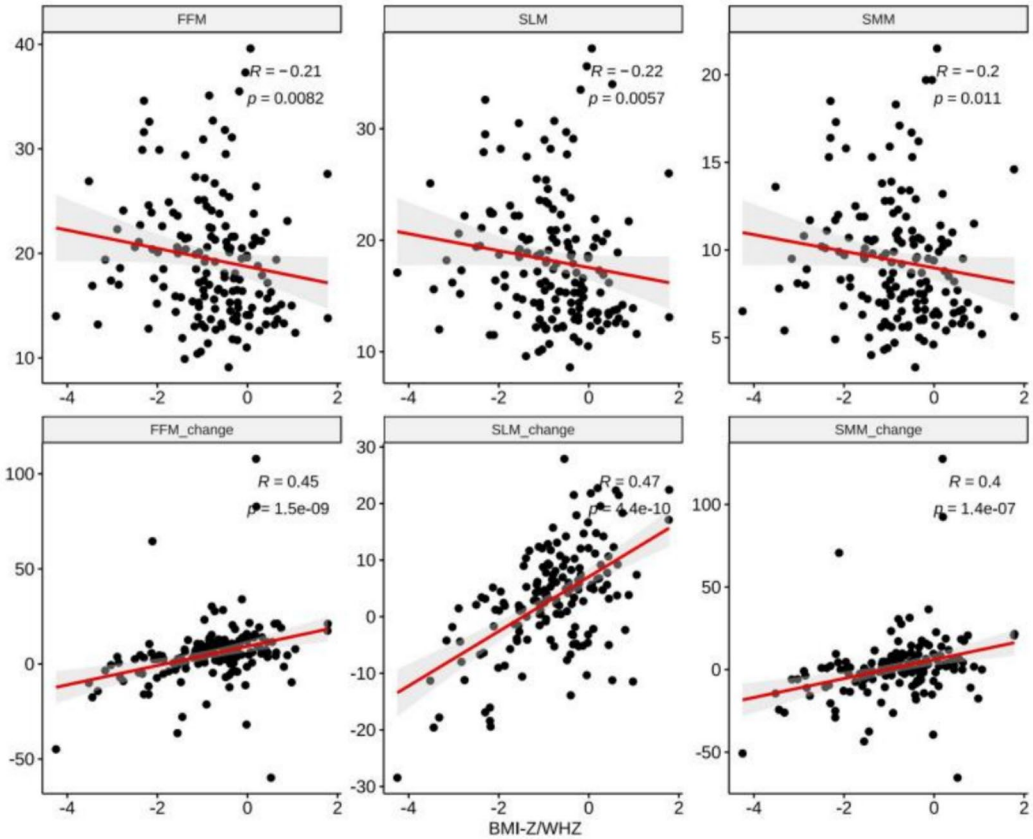

Fig. 2 Correlation analysis between muscle mass indicators and their changes to WHZ/BMI-Z

Our innovative methodological approach tackles the challenge of continuous muscle mass growth during childhood. Since muscle mass in children is predominantly influenced by age rather than gender [27], our proposed cutoff values are expressed as percentages of the lower limits of normal ranges for BIA-derived muscle indicators. This approach accounts for expected muscle mass variations across different ages, eliminating the necessity for multiple age-specific thresholds and enabling clinicians to identify children at potential risk of malnutrition when their indicators fall below these percentage thresholds, thereby prompting further evaluation.

To validate the stability of our percentage-based indicators across different age groups, PSM was employed to controlled potential confounding factors, such as age and gender. The results demonstrated remarkable stability in our indicators (e.g., FFM-change, SLM-change, and SMM-change) before and after matching. Notably, the AUC values for FFM-change and SLM-change showed minimal variation, changing from 0.62 (95% CI 0.53–0.72) and 0.68 (95% CI 0.59–0.77) before matching to 0.61 (95% CI 0.49–0.73) and 0.65 (95% CI 0.54–0.77) after matching, confirming their independence from demographic characteristics. This consistent performance validates the reliability of these indicators as robust candidates for predicting malnutrition risk across various age ranges in children with β-thalassemia.

A standardized BIA measurement protocol was implemented in this study. DXA is recognized as the reference method for body composition assessment, but its routine use in pediatric populations is limited due to concerns about radiation exposure and practical constraints, such as cost and accessibility. BIA offers a more practical alternative, particularly for pediatric populations requiring frequent follow-up. The built-in prediction equations of InBody S10, though subject to certain limitations, demonstrate stability in relative change values, making them suitable for monitoring dynamic nutritional status. Our approach aligns with the recommendations of the GLIM working group, emphasizing the use of rigorously validated, race- and sex-specific muscle mass thresholds [8]. By focusing specifically on Asian children, this study effectively controls for racial factors, enhancing the applicability of our findings to this demographic. We

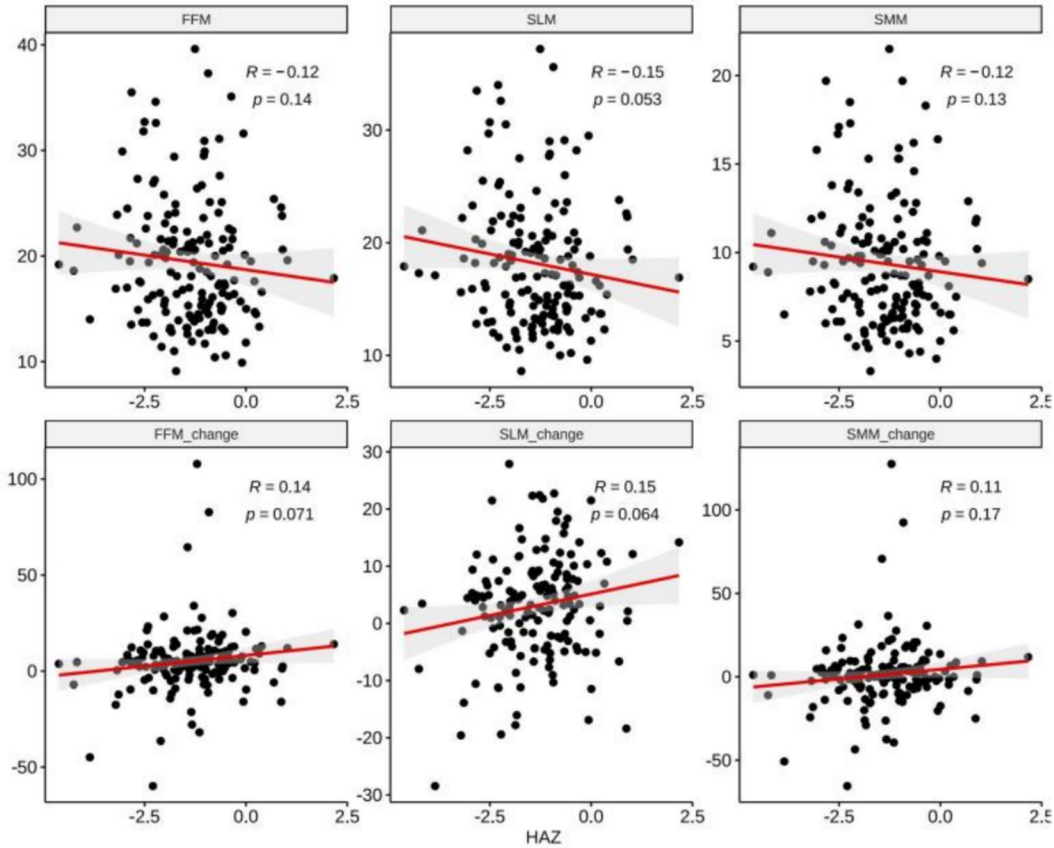

Fig. 3 Correlation analysis between muscle mass indicators and their changes to HAZ

Table 2 Evaluation of diagnostic performance at the optimal cutoff value

Marker (%)	PPV (95% CI)	NPV (95% CI)	SEN (95% CI)	SPE (95% CI)
FFM < 17	0.19 (0.09–0.28)	0.56 (0.46–0.66)	0.22 (0.11–0.33)	0.51 (0.42–0.61)
SLM < 18	0.23 (0.14–0.32)	0.54 (0.43–0.65)	0.36 (0.24–0.49)	0.38 (0.29–0.48)
SMM < 9	0.22 (0.13–0.31)	0.54 (0.43–0.65)	0.33 (0.2–0.45)	0.4 (0.31–0.5)
FFM-change < 4	0.46 (0.35–0.58)	0.75 (0.66–0.84)	0.58 (0.45–0.71)	0.65 (0.56–0.74)
SLM-change < 6	0.44 (0.34–0.54)	0.83 (0.74–0.93)	0.82 (0.72–0.92)	0.47 (0.37–0.56)
SMM-change < 3	0.4 (0.3–0.49)	0.75 (0.65–0.86)	0.73 (0.61–0.84)	0.43 (0.34–0.52)

FFM fat-free mass, *SLM* soft lean mass, *SMM* skeletal muscle mass, *PPV* positive predictive value, *NPV* negative predictive value, *SEN* sensitivity, *SPE* specificity; change = (actual measured value–lower limit of standard range)/lower limit of standard range * 100%

acknowledge that these may vary across different ethnic groups due to genetic and environmental factors [28].

This study exhibits both similarities and significant differences compared to previous literature on muscle mass assessment in children and adolescents. Webber and Barr developed age- and sex-specific reference curves for SMM in healthy children, providing a valuable tool for evaluating muscle development across various age groups [29]. In contrast, this study aimed to establish cutoff values for predicting malnutrition in children with β-thalassemia using BIA-derived muscle indicators. Nonetheless, both studies highlight the importance of considering age and gender for muscle mass assessment.

While studies on using BIA-derived muscle indicators for predicting malnutrition risk in children with β-thalassemia are limited, this study demonstrates significant consistency with several previous studies that focused on establishing optimal diagnostic cutoff points for specific populations. For instance, one study employed CT stratification analysis to ascertain

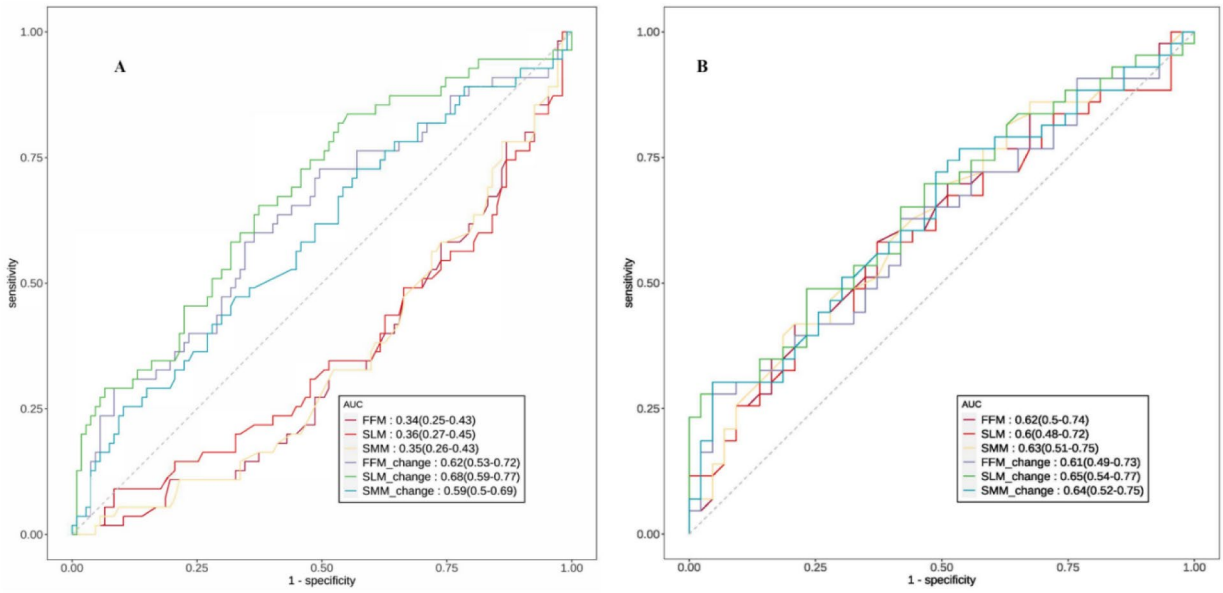

Fig. 4 Comparison of AUC values for muscle mass indicators before and after matching

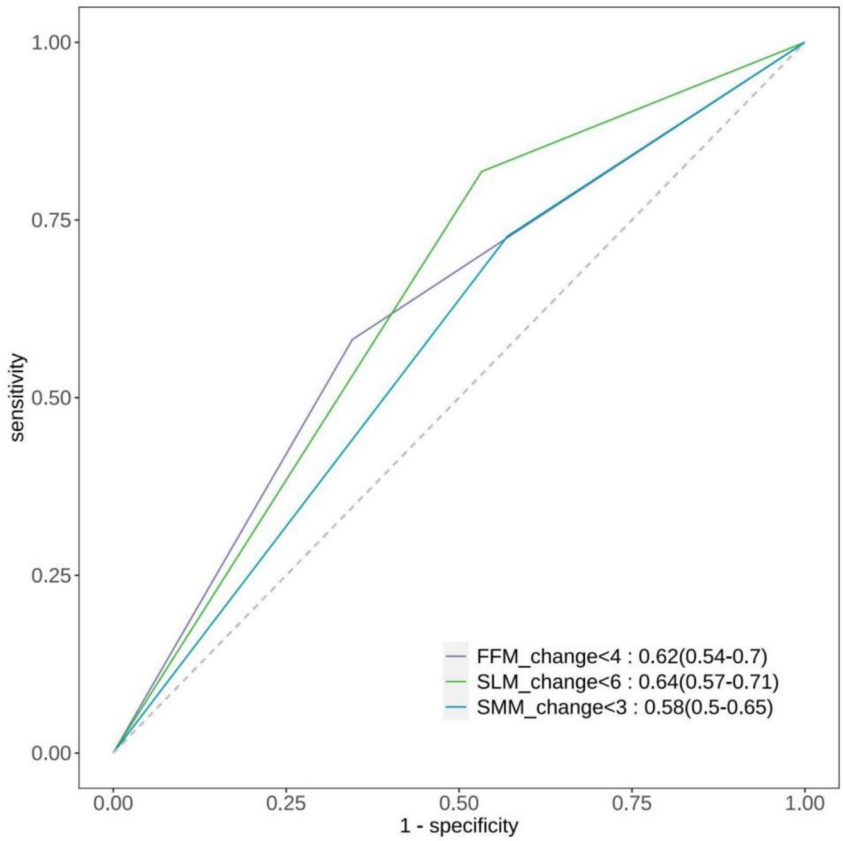

Fig. 5 Optimal cutoff values for nutritional status indicators in children with β-thalassemia

gender-specific cutoffs for low muscle mass, which was associated with mortality in patients with solid tumours [30]. Another study defined gender- and age-specific handgrip strength cutoff values for undernutrition screening in hospitalized patients [31]. Notably, as early as 1981, Frisancho published new norms for upper limb fat and muscle area [32]. These norms refined the use of arm circumference and other anthropometric measurements to calculate muscle indicators to assess nutrition status. Recent studies (e.g., those investigating critical calf circumference values in the elderly [33] and Tran et al.'s research [34] on optimal mid-upper arm circumference (MUAC) cutoffs for screening severe acute malnutrition in Vietnamese children) aimed to determine specific thresholds for assessing nutritional status or muscle condition in specific populations. In a similar vein to our approach of establishing specific thresholds for children with β-thalassemia, Morelli et al. (2023) [35] demonstrated that tailored cutoff values, particularly those that are gender-specific, provide better prognostic value compared to untailored thresholds in patients with head and neck squamous cell carcinoma. This further emphasizes the importance of establishing population-specific thresholds for different clinical conditions.

The BIA employed in this study, particularly the FFM-change and SLM-change indicators, demonstrates unique advantages in predicting malnutrition risk in children with β-thalassemia. Compared to widely used anthropometric methods in previous studies (e.g., MUAC and triceps skinfold thickness) [33, 34], BIA-derived indicators can more precisely quantify the changes in muscle. Traditional arm circumference measurements, while simple to perform, struggle to differentiate between changes in muscle and those in fat tissue. In contrast, the FFM-change and SLM-change indicators adopted in this study directly reflect the alterations in muscle mass. This is particularly crucial for detecting sarcopenic obesity, a condition characterized by normal or high-fat mass but low skeletal muscle mass [36] which may go undetected when relying solely on body weight, arm circumference, or BMI. By utilizing BIA, our method addresses this limitation, providing a more sensitive method to identifying decreased muscle mass, even when traditional anthropometric measurements exhibit normal values.

An 8.2 year-old patient with specific normal SLM range of 18.7–22.9 kg was considered to illustrate the clinical application of our threshold. A potential malnutrition risk will be considered if SLM measurement of this patient shows 17.5 kg, which is more than 6% below the normal range lower limit of 18.7 kg ((17.5–18.7)/18.7 × 100% = −6.4%). This would prompt clinicians to further assess the nutritional status. This approach aligns with the trends in personalized medicine and may offer valuable insights for nutritional assessment in other chronic diseases. The unified threshold we proposed could significantly streamline nutritional assessment processes in clinical settings.

Limitations

The cross-sectional design of this study is not conductive to assessing the long-term predictive performance of these thresholds. While our focus was on children with β-thalassemia, the disease itself may influence body composition. Specially, the BIA methodology assumes a constant hydration of fat-free mass (73.2%), which may not fully applicable to patients with altered fluid status and muscle mass, potentially affecting the generalizability of our results to other conditions. Furthermore, the findings of this single-center study with a relatively homogeneous patient population may be influenced by disease, geographic and ethnic factors, highlighting the need for population-specific validation studies. While our method provides a unified threshold for predicting malnutrition risk, it does not differentiate between acute and chronic malnutrition. Future research with larger sample sizes, multi-center designs, and detailed subgroup analyses will be crucial in enhancing the clinical utility of these indicators.

Conclusion

This study established optimal thresholds for predicting malnutrition risk in children with β-thalassemia, using wasting or stunting as indicators based on muscle indicators measured by BIA. The thresholds identified are FFM-change < 4% and SLM change < 6%. By developing these single, age-adaptive thresholds, we address a current research gap and provide valuable reference standards for clinical practice. These thresholds facilitate early detection of malnutrition risk, allowing for timely interventions before significant nutritional deterioration occurs. Overall, these findings offer new perspectives and practical tools for assessing the nutritional status of children with β-thalassemia in clinical settings, potentially improving their nutritional outcomes through early preventive measures.

Abbreviations

AUC	Area under the curve
BIA	Bioelectrical impedance analysis
BMI	Body mass index
CI	Confidence interval
CT	Computed tomography
DXA	Dual-energy X-ray absorptiometry
EWGSOP2	European working group on Sarcopenia in older people
FFM	Fat-free mass
GLIM	Global leadership initiative on malnutrition
IQR	Interquartile range
MUAC	Mid-upper arm circumference
NPV	Negative predictive value
PPV	Positive predictive value

PSM	Propensity score matching
ROC	Receiver operating characteristic
SD	Standard deviation
SEN	Sensitivity
SLM	Soft lean mass
SMM	Skeletal muscle mass
SPE	Specificity
STAMP	Screening tool for the assessment of malnutrition in paediatric
WHO	World Health Organization

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s40001-025-02392-y.

Additional file 1

Author contributions

L.Z. and J.L. contributed equally to this work as co-first authors. L.Z. conceptualized and designed the study. J.L. was responsible for data acquisition and analysis. L.W. performed the statistical analysis. Li.Z. contributed to data interpretation. S.P. and Y.Y. supervised the project and were responsible for manuscript review and editing. All authors contributed to manuscript revision, read, and approved the submitted version.

Funding

This work has been supported by the Sanming Project of Medicine in Shenzhen SZSM202211033; Supported by the Shenzhen Fund for Guangdong Provincial High-level Clinical Key Specialties (SZGSP012); Supported by Shenzhen Key Medical Discipline Construction Fund (SZXK034); Supported by Guangdong High-level Hospital Construction Fund; Supported by Shenzhen High-level Hospital Construction Fund.

Availability of data and materials

The datasets generated during and/or analysed during the current study are not publicly available, but are available from the corresponding author on reasonable request Prof Sandip Patil.

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Ethics Committee of Shenzhen Children's Hospital (Approval Number: 2023–13302). Written informed consent was obtained from all participants' legal guardians (parents or authorized caregivers) prior to enrollment. For children aged 8 years and above, written assent was also obtained after age-appropriate explanation of the study procedures. For children under 8 years, verbal assent was obtained through child-friendly explanation of the study. The entire consent process was conducted in accordance with the Declaration of Helsinki.

Consent for publication

Informed consent was obtained from all individual participants included in the study.

Competing interests

The authors declare no competing interests.

Received: 12 November 2024 Accepted: 18 February 2025
Published online: 27 February 2025

References

1. Mirhosseini NZ, Shahar S, Ghayour-Mobarhan M. Factors affecting nutritional status among pediatric patients with transfusion-dependent beta thalassemia. Med J Nutrition Metab. 2013;6(1):45–51.
2. Mirhosseini NZ, Shahar S, Ghayour-Mobarhan M, Banihashem A, Kamaruddin NA, Hatef MR, et al. Bone-related complications of transfusion-dependent beta thalassemia among children and adolescents. J Bone Miner Metab. 2013;31(4):468–76. https://doi.org/10.1007/s00774-013-0433-1.
3. Holmes CJ, Racette SB. The utility of body composition assessment in nutrition and clinical practice: an overview of current methodology. Nutrients. 2021;13(8):2493. https://doi.org/10.3390/nu13082493.
4. Larson-Nath C, Goday P. Malnutrition in children with chronic disease. Nutr Clin Pract. 2019;34(3):349–58. https://doi.org/10.1002/ncp.10274.
5. Tostes NF, Da CASD, Martucci RB. Association between nutritional status and muscle strength in pediatric cancer patients. Clin Nutr ESPEN. 2021;43:436–41. https://doi.org/10.1016/j.clnesp.2021.03.009.
6. Ooi PH, Thompson-Hodgetts S, Pritchard-Wiart L, Gilmour SM, Mager DR. Pediatric sarcopenia: a paradigm in the overall definition of malnutrition in children? JPEN J Parenter Enteral Nutr. 2020;44(3):407–18. https://doi.org/10.1002/jpen.1681.
7. Cederholm T, Jensen GL, Correia M, Gonzalez MC, Fukushima R, Higashiguchi T, et al. Glim criteria for the diagnosis of malnutrition—a consensus report from the global clinical nutrition community. Clin Nutr. 2019;38(1):1–9. https://doi.org/10.1016/j.clnu.2018.08.002.
8. Barazzoni R, Jensen GL, Correia M, Gonzalez MC, Higashiguchi T, Shi HP, et al. Guidance for assessment of the muscle mass phenotypic criterion for the global leadership initiative on malnutrition (glim) diagnosis of malnutrition. Clin Nutr. 2022;41(6):1425–33. https://doi.org/10.1016/j.clnu.2022.02.001.
9. Sergi G, De Rui M, Stubbs B, Veronese N, Manzato E. Measurement of lean body mass using bioelectrical impedance analysis: a consideration of the pros and cons. Aging Clin Exp Res. 2017;29(4):591–7. https://doi.org/10.1007/s40520-016-0622-6.
10. Jackson AA, Johnson M, Durkin K, Wootton S. Body composition assessment in nutrition research: value of bia technology. Eur J Clin Nutr. 2013;67(Suppl 1):S71–8. https://doi.org/10.1038/ejcn.2012.167.
11. Brantlov S, Jodal L, Lange A, Rittig S, Ward LC. Standardisation of bioelectrical impedance analysis for the estimation of body composition in healthy paediatric populations: a systematic review. J Med Eng Technol. 2017;41(6):460–79. https://doi.org/10.1080/03091902.2017.1333165.
12. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyere O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019;48(1):16–31. https://doi.org/10.1093/ageing/afy169.
13. Mager DR, Hager A, Ooi PH, Siminoski K, Gilmour SM, Yap J. Persistence of sarcopenia after pediatric liver transplantation is associated with poorer growth and recurrent hospital admissions. JPEN J Parenter Enteral Nutr. 2019;43(2):271–80. https://doi.org/10.1002/jpen.1414.
14. Peterson MD, Zhang P, Saltarelli WA, Visich PS, Gordon PM. Low muscle strength thresholds for the detection of cardiometabolic risk in adolescents. Am J Prev Med. 2016;50(5):593–9. https://doi.org/10.1016/j.amepre.2015.09.019.
15. Ates BE, Soysal P, Dokuzlar O, Kocyigit SE, Aydin AE, Yavuz I, et al. Validation of population-based cutoffs for low muscle mass and strength in a population of turkish elderly adults. Aging Clin Exp Res. 2020;32(9):1749–55. https://doi.org/10.1007/s40520-019-01448-4.
16. Mccarthy H, Dixon M, Crabtree I, Eaton-Evans MJ, Mcnulty H. The development and evaluation of the screening tool for the assessment of malnutrition in paediatrics (stamp(c)) for use by healthcare staff. J Hum Nutr Diet. 2012;25(4):311–8. https://doi.org/10.1111/j.1365-277X.2012.01234.x.
17. Kyle UG, Bosaeus I, De Lorenzo AD, Deurenberg P, Elia M, Gomez JM, et al. Bioelectrical impedance analysis–part i: review of principles and methods. Clin Nutr. 2004;23(5):1226–43. https://doi.org/10.1016/j.clnu.2004.06.004.
18. Ward LC, Brantlov S. Bioimpedance basics and phase angle fundamentals. Rev Endocr Metab Disord. 2023;24(3):381–91. https://doi.org/10.1007/s11154-022-09780-3.
19. WHO Multicentre Growth Reference Study Group, de Onis M. WHO child growth standards based on length/height, weight and age. Acta Paediatr. 2006;95:76–85.
20. World Health Organization. Growth Reference Data for Children From 5 to 19 Years, 2007. Geneva: WHO (2007) at: https://www.who.int/tools/growth-reference-data-for-5to19-years.

21. Becker P, Carney LN, Corkins MR, Monczka J, Smith E, Smith SE, et al. Consensus statement of the academy of nutrition and dietetics/american society for parenteral and enteral nutrition: indicators recommended for the identification and documentation of pediatric malnutrition (undernutrition). Nut Clin Practice Off Publ Am Soc Parenteral and Ente Nutr. 2015;30:147–61. https://doi.org/10.1177/0884533614557642.
22. World Health Organization. The double burden of malnutrition: priority actions on ending childhood obesity. Geneva: World Health Organization; 2020.
23. Austin PC. Optimal caliper widths for propensity-score matching when estimating differences in means and differences in proportions in observational studies. Pharm Stat. 2011;10(2):150–61. https://doi.org/10.1002/pst.433.
24. Soliman AT, De Sanctis V, Elalaily R, Yassin M. Insulin-like growth factor- i and factors affecting it in thalassemia major. Indian J Endocrinol Metab. 2015;19(2):245–51. https://doi.org/10.4103/2230-8210.131750.
25. Schiaffino S, Mammucari C. Regulation of skeletal muscle growth by the igf1-akt/pkb pathway: insights from genetic models. Skelet Muscle. 2011;1(1):4. https://doi.org/10.1186/2044-5040-1-4.
26. Wang L, Zhang L, Yang Y, Luo Y, Wang L, Patil S. Association of age to nutritional status and muscle mass in children with transfusion-dependent beta-thalassemia: a cross-sectional study. Front Nutr. 2024;11:1493502. https://doi.org/10.3389/fnut.2024.1493502.
27. Liu J, Yan Y, Xi B, Huang G, Mi J. Skeletal muscle reference for chinese children and adolescents. J Cachexia Sarcopenia Muscle. 2019;10(1):155–64. https://doi.org/10.1002/jcsm.12361.
28. Heymsfield SB, Peterson CM, Thomas DM, Heo M, Schuna JJ. Why are there race/ethnic differences in adult body mass index-adiposity relationships? A quantit critical review. Obes Rev. 2016;17(3):262–75. https://doi.org/10.1111/obr.12358.
29. Webber CE, Barr RD. Age- and gender-dependent values of skeletal muscle mass in healthy children and adolescents. J Cachexia Sarcopenia Muscle. 2012;3(1):25–9. https://doi.org/10.1007/s13539-011-0042-6.
30. Prado CM, Lieffers JR, Mccargar LJ, Reiman T, Sawyer MB, Martin L, et al. Prevalence and clinical implications of sarcopenic obesity in patients with solid tumours of the respiratory and gastrointestinal tracts: a population-based study. Lancet Oncol. 2008;9(7):629–35. https://doi.org/10.1016/S1470-2045(08)70153-0.
31. Guerra RS, Fonseca I, Pichel F, Restivo MT, Amaral TF. Handgrip strength cutoff values for undernutrition screening at hospital admission. Eur J Clin Nutr. 2014;68(12):1315–21. https://doi.org/10.1038/ejcn.2014.226.
32. Frisancho AR. New norms of upper limb fat and muscle areas for assessment of nutritional status. Am J Clin Nutr. 1981;34(11):2540–5. https://doi.org/10.1093/ajcn/34.11.2540.
33. Kawakami R, Murakami H, Sanada K, Tanaka N, Sawada SS, Tabata I, et al. Calf circumference as a surrogate marker of muscle mass for diagnosing sarcopenia in Japanese men and women. Geriatr Gerontol Int. 2015;15(8):969–76. https://doi.org/10.1111/ggi.12377.
34. Hai TT, Bardosono S, Wiradnyani L, Hop LT, Ngan H, Phuong HN. The optimal mid-upper-arm circumference cutoffs to screen severe acute malnutrition in vietnamese children. AIMS Publ Health. 2020;7(1):188–96. https://doi.org/10.3934/publichealth.2020016.
35. Morelli C, Formica V, Bossi P, Rofei M, Guerriero S, Riondino S, et al. Untailored vs Gender—and body-mass-index-tailored skeletal muscle mass index (smi) to assess sarcopenia in advanced head and neck squamous cell carcinoma. Cancers. 2023;15(19):4716. https://doi.org/10.3390/cancers15194716.
36. Prado CM, Heymsfield SB. Lean tissue imaging: a new era for nutritional assessment and intervention. JPEN J Parenter Enteral Nutr. 2014;38(8):940–53. https://doi.org/10.1177/0148607114550189.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.