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Comparison of BMI, triponderal mass index and paediatric body adiposity index for predicting body fat and screening obesity in preschool children

Research Article

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Abbreviations:
BAI, body adiposity index; BAIp, paediatric body adiposity index; BIA, bioelectrical impedance analysis; DEXA, dual-energy X-ray absorptiometry; PBF, percentage of body fat; TMI, triponderal mass index

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Abstract

Several novel anthropometric indices, including paediatric body adiposity index (BAIp) and triponderal mass index (TMI), have emerged as potential tools for estimating body fat in preschool children. However, their comparative validity and accuracy, particularly when compared with established indicators such as BMI, have not been thoroughly investigated. This cross-sectional study enrolled 2869 preschoolers aged 3–6 years in Wuhan, China. The non-parametric Bland–Altman analysis was employed to evaluate the agreement between BMI, BAIp and TMI with percentage of body fat (PBF), determined by bioelectrical impedance analysis (BIA), serving as the reference measure of adiposity. Additionally, receiver operating characteristic curve analysis was conducted to assess the effectiveness of BMI, BAIp and TMI in screening for obesity. BAIp demonstrated the least bias in estimating PBF, showing discrepancies of 3·64 % (95 % CI 3·40 %, 4·12 %) in boys and 3·95 % (95 % CI 3·79 %, 4·23 %) in girls. Conversely, BMI underestimated PBF by 3·89 % (95 % CI 3·70 %, 4·37 %) in boys and 4·81 % (95 % CI 4·59 %, 5·09 %) in girls, while TMI also underestimated PBF by 5·15 % (95 % CI 4·90 %, 5·52 %) in boys and 5·68 % (95 % CI 5·30 %, 5·91 %) in girls. BAIp exhibited the highest AUC values (AUC = 0·867–0·996) in boys, whereas in girls, there was no statistically significant difference between BMI (AUC = 0·936, 95 % CI 0·921, 0·948) and BAIp (AUC = 0·901, 95 % CI 0·883, 0·916) in girls ($P = 0.054$). In summary, when considering the identification of obesity, BAIp shows promise as a screening tool for both boys and girls.

Childhood obesity is a global concern, with approximately 39 million children under five being overweight or obese worldwide in 2020[1]. China has seen a significant rise in preschool obesity, increasing from 3·1 % in 2013 to 10·4 % in 2020[2]. Childhood obesity often persists into adulthood, elevating the risk of chronic illnesses and premature death[3]. Early detection of childhood obesity is vital for preventing future health issues[4], necessitating accurate, user-friendly and cost-effective assessment tools.

For decades, BMI has widely served as a valuable tool for tracking obesity prevalence[5]. It has also linked obesity status with an increased risk for CVD[6], type 2 diabetes[7] and mortality[8]. However, as an indirect measure of body fat mass, BMI's association with body fatness is not entirely accurate[9]. Besides, BMI does not offer insight into body fat distribution, a crucial aspect of health assessment[9]. For example, individuals with the same BMI but higher proportions of visceral adipose tissue and ectopic fat depots face an elevated risk of CVD[10,11]. The triponderal mass index (TMI), recently introduced by Peterson *et al.*, offers a potentially more accurate alternative, calculated as weight (kg)/height (m^3)[12]. It has been suggested that this measurement may be a more effective predictor of percent body fat and metabolic syndrome than BMI[13]. Moreover, TMI is observed to be fairly consistent throughout childhood and adolescence[14]. Therefore, utilising a single cut-off value for TMI can be a practical and convenient approach[12]. However, it has remained unclear whether TMI is superior to BMI in predicting body fat and identifying obesity in preschool children. An alternative measurement, the body adiposity index (BAI), has also been proposed. It is calculated as hip circumference (HC) in centimetres divided by height in metres (HM) to the 1·5th power, minus 18[15] (BAI = HC/(HM)$^{1.5}$ − 18), primarily for adults. Some studies have suggested that BAI outperformed BMI in estimating body fat percentage in young adults[16]. However, inconsistent results have been found in Chinese children and adolescents, with BMI often being considered a better tool for estimating whole-body and central body fat[17]. Building on the concept of BAI, the paediatric body adiposity index (BAIp) has recently been developed specifically as a screening tool for childhood obesity[18,19], calculated as HC divided by height in HM to the 0·8th power, minus 38 (BAIp = HC/(HM)$^{0·8}$ – 38)[20]. However, if BAIp is suitable for the Chinese population remains unexamined. Furthermore, although previous research has shown promise for BAIp in epidemiological research, Filgueiras M *et al.* have raised concerns about its accuracy compared with body fat[21]. Therefore, it remains unclear which index is the optimal one for evaluating body composition, necessitating a comparative analysis of the reliability of each indicator.

Understanding the relationships between adiposity markers and body fat is essential for enhancing the clinical identification of childhood obesity, guiding research efforts to comprehend its association with related diseases and developing precise interventions. Therefore, this investigation aims to verify the validity of BMI, BAIp and TMI in predicting the percentage of body fat (PBF) and screening obesity in a sample of Chinese preschool children, using bioelectrical impedance analysis (BIA) as the reference method.

Methods

Participants

Children aged 3–6 years in Wuhan were enrolled in this study. Wuhan was chosen due to its demographic mix and urban characteristics. The data were obtained from two cross-sectional surveys as part of the Wuhan Healthy Start Project for Preschool Children. To optimise resources and ensure regional diversity, a total of thirty-five kindergartens from Jianghan and Hanyang (two representative districts in Wuhan) were included in this study. The first survey was carried out from 2021 to 2022, utilising a cluster random sampling method to select all children from nine kindergartens in the Jianghan District of Wuhan for investigation. The second survey was conducted in 2023, and thirty kindergartens were randomly selected by cluster sampling from Jianghan and Hanyang districts, with all children in these kindergartens included in the survey (four kindergartens overlapped with the previous survey, but with no duplication of participants). Initially, 3227 children were surveyed. After excluding cases of parental refusal and children's absence due to illness or other factors, a final sample of 2869 children aged 3–6 years was included for analysis (Fig. 1).

In our study, informed consent was obtained from legal guardians of all participating children. We adhered to ethical standards by providing detailed information about the study objectives, procedures, potential risks and benefits to the participants or their guardians. Consent forms were written in clear and understandable language, ensuring that the guardians had adequate time to review the information and ask questions before providing consent.

Anthropometric index

Children's height, weight, waist circumference and HC were collected by uniformly trained researchers with a standard procedure. Kangwa WS-RT-2U physical examination instrument and non-elastic tape measure were employed for measurements. To reduce the measurement error, all indicators were measured twice. If the differences between the two consecutive values exceeded 5 mm for height or 100 g for weight, a third measurement was conducted until the difference fell within these thresholds. The final value used was the average of the two closest measurements. BMI, BAIp and TMI (kg/m^3) were calculated as: BMI(kg/m^2) = Weight (kg)/ [Height (m)]^2; BAIp(0·01 m$^{-0·5}$) = Hip Circumference/(Height)$^{0·8}$ – 38; TMI(kg/m^3) = Weight(kg)/ [Height (m)]^3.

Assessment of percentage of body fat using bioelectrical impedance analysis

Body fat was determined by multifrequency BIA using an InBody 230 analyser (Inbody230 system, InBody Corp), with tetrapolar eight-point tactile electrodes. Measurements were taken at two different frequencies (20 and 100 kHz) on each segment (right arm, left arm, trunk, right leg and left leg), with participants bearing feet and wearing light clothing. The measurement was taken 2 h after a meal, and children were instructed not to exercise excessively before the measurement to minimise the possible influence on the BIA values. During the measurement, children stood on the device for weight measurement, and then their identification number, age, sex and height were entered into the device for PBF calculation. Impedance measurements were obtained with the children standing still while holding hand grips that were slightly abducted. The device then used the manufacturer's algorithm to calculate and output data, including fat mass, fat-free mass and PBF.

Definition of obesity

Currently, there is no widely recognised cut-off value for preschool children's PBF to determine obesity. The study by Williams *et al.*[22] suggests using 25 % and 30 % as cut-off values to define obesity in boys and girls, respectively. However, preschool children experience rapid growth and development, leading to significant fluctuation in their body composition with age. Using the same cut-off value across different age groups may compromise diagnostic accuracy[23]. Therefore, many studies have adopted the 95th percentile of PBF (P_{95}) as the diagnostic criterion for obesity. For example, Mi *et al.* used P_{95} of PBF as the diagnostic standard for obesity based on dual-energy X-ray absorptiometry (DEXA) measurement data[24]. However, this standard cannot be widely applied, including in our study, due to the difficulty in obtaining DEXA data, especially for epidemiology study. Previous studies have shown that BIA and DEXA methods can be used interchangeably at the population level[25]. Therefore, in this study, we established the reference values of PBF based on BIA data from our study population, defining PBF > 95th percentile as obesity.

Statistical analysis

MedCalc version 20.027 and R 4.1.5 were used for statistical analysis, with a P-value < 0·05 considered statistically significant. Kolmogorov–Smirnov tests were applied to check for the assumption of normal distribution (P < 0·05). Continuous variables are presented as median (P_{25}, P_{75}), and group comparisons were conducted with non-parametric test. Generalised additive model (GAMLSS) was used to establish percentile reference curves of PBF in children. GAMLSS is an extension of the Lambda-Mu-Sigma (LMS) method, which uses four distribution parameters: median, CV, skewness and kurtosis. The P_5, P_{10}, P_{25}, P_{50}, P_{75}, P_{80}, P_{85} and P_{95} of sex- and age-specific PBF were estimated, and the percentile curves were drawn. Gamlss

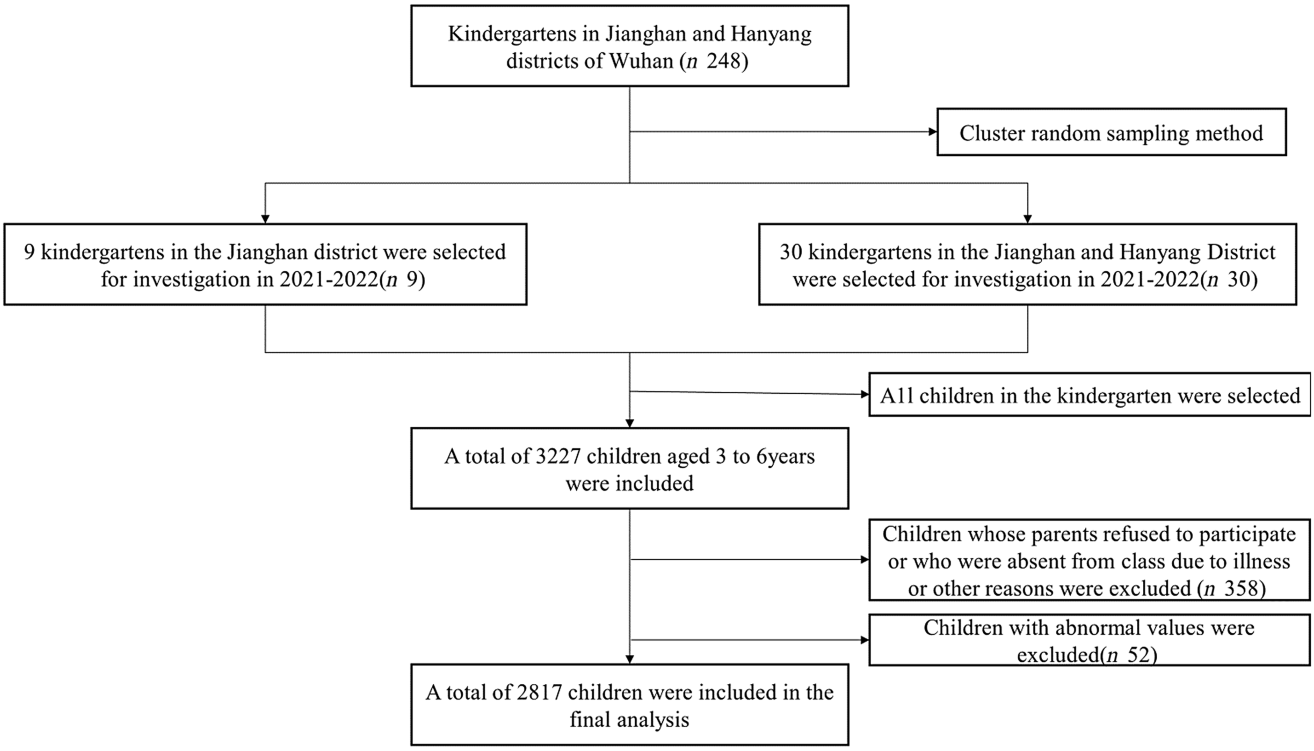

Fig. 1. Flow chart showing inclusion and exclusion of children from Wuhan Healthy Start Project.

package in R 4.1.2 was used for analysis. The non-parametric Bland–Altman plots were used to assess the agreement between BMI, BAIp and TMI with standard body fat measure. The studentised bootstrap method was utilised to establish the limits of agreement, defined as the 2·5th and 97·5th percentiles of differences. The receiver operating characteristic curve was used to evaluate the performance of BMI, BAIp and TMI in correctly classifying children as obesity. The P95 of PBF was established as the standard reference value of obesity, and MedCalc 20.027 software was used to draw and analyse the receiver operating characteristic curve and calculate the AUC.

To ensure data accuracy, the dataset was refined by applying specific exclusion criteria. Entries with a variance of more than 25 units between each index (BMI, BAIp and TMI) and PBF were deemed unsuitable and subsequently removed.

Results

Characteristics of subjects

The 2869 participants consist of 1471 (51·27 %) boys and 1398 (48·73 %) girls, with means ages of 4·33 and 4·32 years, respectively. Boys generally exhibit greater height, weight, WC, HC, BMI and TMI than girls. Conversely, girls typically present a higher PBF ($P < 0·05$). There is no sex difference in age and BAIp. Demographic information is presented in Table 1.

Percentile reference value of percentage of body fat in children of different ages and sexes

The reference values of percentile PBF (P_5, P_{10}, P_{25}, P_{50}, P_{75}, P_{85}, P_{90}, P_{95}) of children of different ages and sexes are shown in Table 2. The PBF percentile curves for boys and girls are shown in Fig. 2. The PBF of boys and girls showed a steady decline with the increase of age. However, a significant decline in PBF was evident among boys aged 3–6 years, compared with girls.

Non-parametric Bland–Altman analysis of the differences between BMI, paediatric body adiposity index and triponderal mass index with PBF

The non-parametric Bland–Altman plot in Fig. 3 depicts the concordance and median of the differences of BMI, BAIp and TMI with PBF. Among the three measures, BAIp demonstrated the least mean bias in both boys 3·64 % (95 % CI 3·40 %, 4·12 %) and girls 3·95 % (95 % CI 3·79 %, 4·23 %) regarding PBF. This indicates that BAIp underestimated PBF by 3·64 % in boys and 3·95 % in girls. In contrast, BMI and TMI showed more significant bias. BMI underestimated PBF by 3·89 % (95 % CI 3·70 %, 4·37 %) in boys and 4·81 % (95 % CI 4·59 %, 5·09 %) in girls. Similarly, TMI underestimated PBF by 5·15 % (95 % CI 4·90 %, 5·52 %) and 5·68 % (95 % CI 5·30 %, 5·91 %) for boys and girls, respectively. The median of differences for BMI, BAIp and TMI is displayed in Table 3.

Receiver operating characteristic curves for obesity screening using BMI, paediatric body adiposity index and triponderal mass index

We evaluated the effectiveness of BMI, BAIp and TMI in identifying obesity by plotting receiver operating characteristic curves for the three indexes (Fig. 4) and calculating corresponding AUC values, optimal cut-off values, specificity and sensitivity (Table 4). Pairwise comparisons of the AUC for these indexes were performed to identify the optimal indices for obesity screening. The AUC of the indexes were all greater than 0·8, indicating acceptable accuracy and predictive ability for obesity screening. In boys, BAIp demonstrated the highest AUC value (AUC = 0·950,

Table 1. Selected characteristics of the study population

	Total (*n* 2817)		Boys (*n* 1444)		Girls (*n* 1373)		
Variables	Median	P_{25}, P_{75}	Median	P_{25}, P_{75}	Median	P_{25}, P_{75}	*P*
Age (years) (P_{25}, P_{75})	4·31	3·90, 5·04	4·31	3·90, 5·10	4·31	3·89, 5·00	0·373
Age (years), *n* (%)	*n*	%	*n*	%	*n*	%	0·697
3	873	31·97	442	30·57	431	31·39	
4	1208	42·89	612	42·39	596	43·41	
5	572	20·29	306	21·16	266	19·37	
6	165	5·85	85	5·88	80	5·83	
	Median	P_{25}, P_{75}	Median	P_{25}, P_{75}	Median	P_{25}, P_{75}	
Height (cm) (P_{25}, P_{75})	106·55	102·30, 111·70	107·25	103·00, 112·50	105·65	101·40, 111·20	< 0·001
Weight (kg) (P_{25}, P_{75})	17·55	15·80, 20·02	17·98	16·18, 20·74	17·10	15·51, 19·24	< 0·001
WC (cm) (P_{25}, P_{75})	50·70	48·65, 53·25	51·33	49·25, 53·85	50·05	48·10, 52·60	< 0·001
HC (cm) (P_{25}, P_{75})	57·00	54·10, 60·30	57·25	54·40, 60·50	56·75	53·90, 60·05	0·007
BMI (kg/m^2) (P_{25}, P_{75})	15·50	14·66, 16·40	15·69	14·86, 16·60	15·30	14·48, 16·20	< 0·001
BAIp, 0·01 $m^{-0.5}$ (P_{25}, P_{75})	16·11	14·13, 18·21	15·96	14·10, 18·18	16·23	14·14, 18·26	0·397
TMI (kg/m^3) (P_{25}, P_{75})	14·55	13·66, 15·43	14·57	13·79, 15·40	14·50	13·53, 15·47	0·016
PBF (%) (P_{25}, P_{75})	19·80	16·40, 23·70	19·60	16·30, 23·50	20·00	16·60, 23·90	0·041

WC, waist circumference; HC, hip circumference; BAIp, paediatric body adiposity index; TMI triponderal mass index; PBF percentage body fat.

Table 2. Percentiles for PBF by age in boys and girls aged 3–6 years

		PBF (%)							
Sex	Year	5th	10th	25th	50th	75th	85th	90th	95th
Boys	3·0	13·28	14·84	17·65	21·18	25·38	28·05	30·08	33·50
	4·0	12·26	13·70	16·30	19·56	23·44	25·90	27·77	30·93
	5·0	11·19	12·51	14·88	17·85	21·40	23·65	25·36	28·23
	6·0	10·00	11·18	13·30	15·96	19·12	21·13	22·66	25·24
Girls	3·0	12·78	14·45	17·36	20·88	24·93	27·44	29·32	32·47
	4·0	12·27	13·88	16·67	20·05	23·94	26·35	28·15	31·17
	5·0	11·68	13·21	15·87	19·09	22·78	25·08	26·80	29·67
	6·0	10·93	12·36	14·84	17·85	21·31	23·46	25·07	27·75

PBF, percentage of body fat.

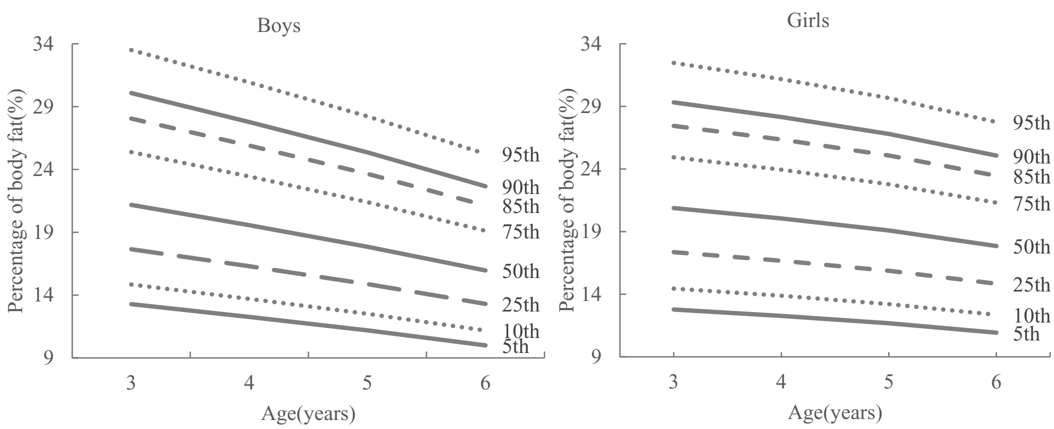

Fig. 2. Percentile curves of percentage of body fat (%) for boys and girls aged 3–5 years.

Table 3. Agreement and proportional bias assessment between BMI, BAIp and TMI for PBF

Indexes	Median of the differences	95 % CI	Lower LoA	95 % CI	Upper LoA	95 % CI	*P*
Boys							
BMI	3·89	3·70, 4·37	−3·99	−4·32, −3·19	14·80	13·48, 15·40	< 0·001
BAIp	3·64	3·40, 4·12	−6·20	−6·87, −5·42	15·38	13·76, 16·11	< 0·001
TMI	5·15	4·90, 5·52	−3·49	−3·99, −2·98	17·28	15·62, 18·32	< 0·001
Girls							
BMI	4·81	4·59, 5·09	−3·35	−4·00, −2·92	15·27	14·57, 16·90	< 0·001
BAIp	3·95	3·79, 4·23	−2·85	−3·38, −2·59	12·99	12·32, 14·63	< 0·001
TMI	5·68	5·30, 5·91	−2·34	−3·18, −1·88	16·84	16·02, 18·87	< 0·001

BAIp, paediatric body adiposity index; TMI, triponderal mass index; PBF, percentage of body fat; LoA, limits of agreement.

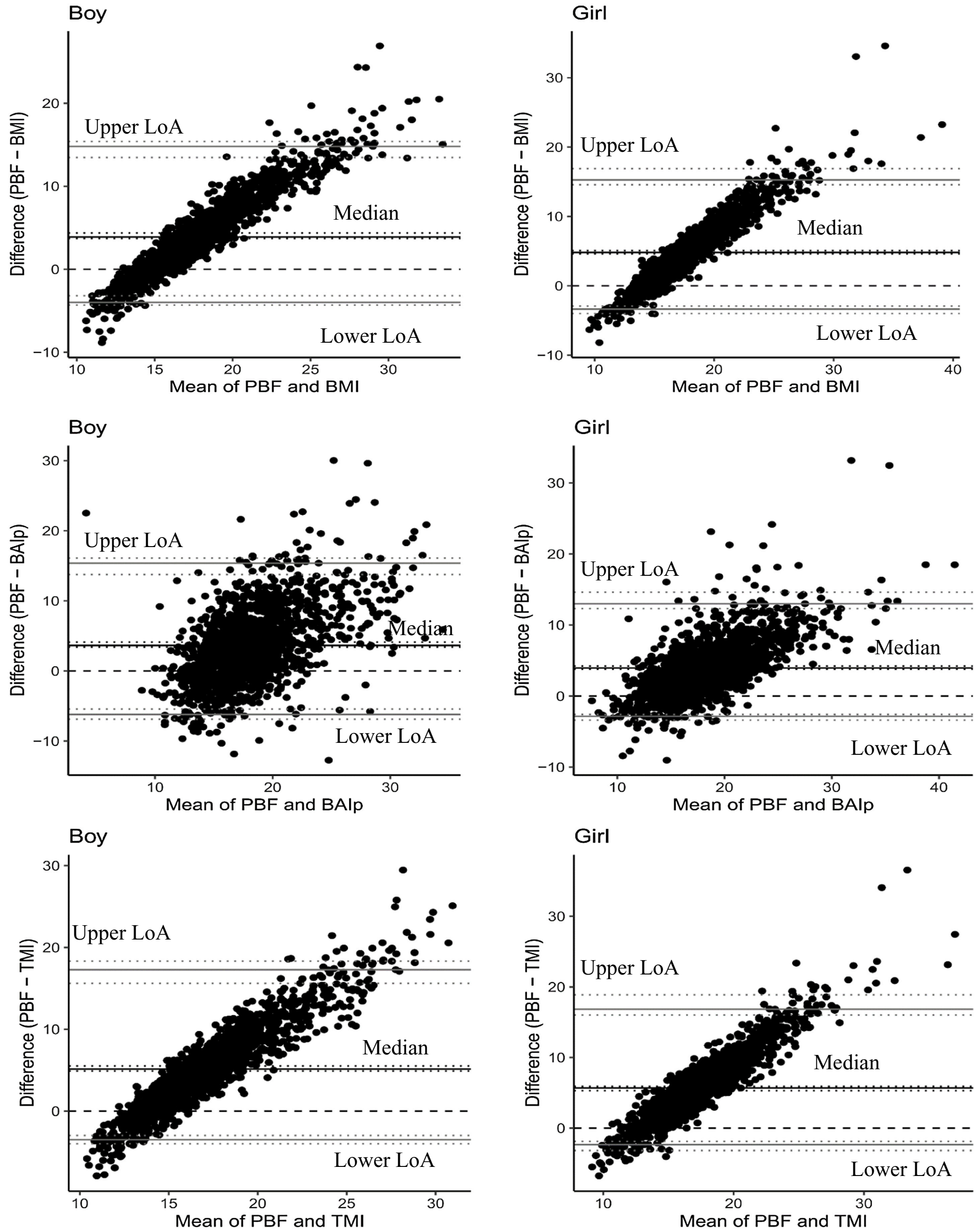

Fig. 3. Non-parametric Bland–Altman plots comparing the agreement between PBF estimated by BMI, BAIp and the TMI with PBF estimated by BIA in boy and girl. LoA, limits of agreement; PBF, percentage of body fat; BAIp, paediatric body adiposity index; TMI, triponderal mass index.

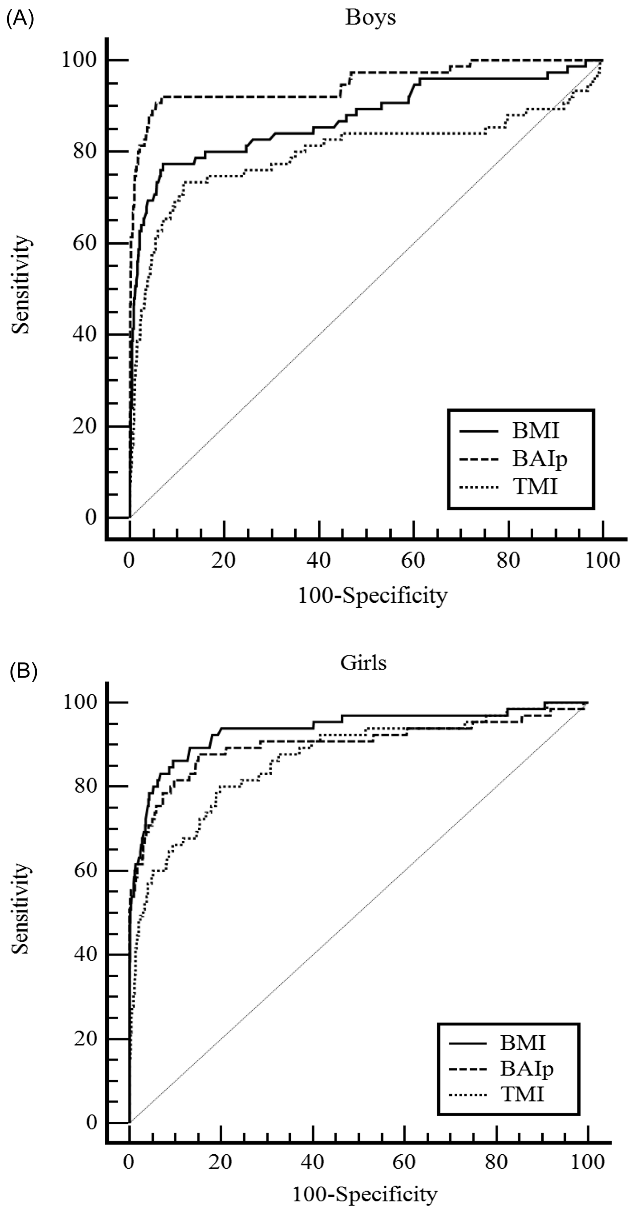

Fig. 4. Receiver operating characteristic curves of BMI, BAIp and TMI for screening obesity by sex. BAIp, paediatric body adiposity index; TMI, triponderal mass index.

95 % CI 0·937, 0·961) among all indexes, followed by BMI (AUC = 0·875, 95 % CI 0·857, 0·892) and TMI (AUC = 0·799, 95 % CI 0·777, 0·819). Both of BMI and TMI has a significantly smaller AUC than BMI ($P < 0·05$). In girls, BMI had the highest ability to recognise obesity (AUC = 0·936, 95 % CI 0·921, 0·948), followed by BAIp (AUC = 0·901, 95 % CI 0·883, 0·916) and TMI (AUC = 0·866, 95 % CI 0·846, 0·883). However, there was no statistically significant difference between BMI and BAIp in girls ($P = 0·054$).

Discussion

The present study evaluated the efficacy of BMI, BAIp and TMI as screening tools for obesity and predicting PBF among preschool children in China. The non-parametric Bland–Altman plots showed that BAIp had better agreement with PBF than BMI and TMI in both boys and girls. In terms of obesity screening, BAIp has demonstrated higher accuracy values and greater effectiveness among boys as compared with BMI and TMI. However, for girls, the AUC value of BMI appeared to be higher than that of BAIp; however, this difference did not reach statistical significance.

This study used the GAMLSS method to fit the percentile reference values of PBF for preschool children aged 3–6 years in Wuhan. From the age of 3–6 years, the PBF showed a downward trend with age in both boys and girls and the decline of PBF is generally more noticeable in boys compared with girls. Previous research observed that children experience a peak in their fat content within the first 9–12 months after birth, owing to their energy requirements for growth. This fat content gradually decreases due to the development of their body structure and metabolism, reaching its minimum between the ages of 3 and 8 years. After this age, fat content starts to increase again, a phenomenon known as adiposity rebound[26]. Our findings indicate that older children have a lower PBF than 3-year-old children, signifying that preschool children are approaching the lowest level of PBF, which occurs before the onset of adiposity rebound. This trend is consistent with the findings of Dong *et al.* who measured the PBF of Chinese children using DEXA[24]. In addition, our study also found sex differences in the PBF across preschool years. Specifically, at the age of 3 years, boys had a higher body fat percentage than girls, while at the age of 4–6 years, girls had a higher body fat percentage than boys. This finding is consistent with the studies conducted by Zhao[27] and Kiumars[28] which also found differences in PBF between boys and girls aged 3–17 years. However, the factors that contribute to the differences in PBF between boys and girls in preschool age have yet to be fully clarified. While it is believed that sex steroids, leptin and insulin-like growth factor I[28] may be involved, further scientific inquiry is necessary to better understand the complex interplay of these factors.

The result of the non-parametric Bland–Altman plot indicated that BAIp had better agreement with PBF than BMI and TMI in both boys and girls. Previous study have indicated that BMI has only a fair correlation with body fat[29], and Vanderwall *et al.* reported that in children under 9 years, BMIz demonstrate a weak to moderate predictive effect for both total fat mass and PBF[30]. Compared with BMI, BAI gives more consideration to the characteristics of body shape and fat distribution, rather than solely focusing on the proportion between weight and height[31]. According to Aarbaoui, the disparity in PBF assessed by BIA compared with the estimation derived from BAIp did not exhibit statistical significance nor practical clinical relevance. Therefore, utilising BAIp could be a simpler and more reliable method for determining PBF in paediatric population[20]. However, inconsistent with studies involving school-age children[32] and adolescents[33], TMI did not demonstrate superior performance in predicting PBF in this research. This might be attributed to the younger age of the participants, as the predictive ability of TMI for PBF may be influenced by children's growth and developmental characteristics[34]. Our results demonstrated that the BAIp proves to be a more reliable indicator of obesity in boys compared with BMI and TMI, whereas BMI has similar screening performances to BAIp in girls. This contrasts with findings from Yu, who conducted a cross-sectional study in the Chinese population aged 6–60 years and found that BMI was more highly correlated with PBF than BAI[17]. Similarly, Ye reported that BAI is not an ideal index for obesity screening and that it is less closely related to PBF than BMI and TMI in Chinese children and adolescents[34]. The different

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Table 4. Comparison of the receiver operator characteristic curves for various anthropometric indices in predicting obesity

				Comparison of AUC						
				BAIp		TMI				
Sex	Variables	AUC	95 % CI	*Z*	*P*	*Z*	*P*	Sensitivity	Specificity	Optimal cut-offs
Boys	BMI	0·875	0·857, 0·892	2·324	0·020	4·180	< 0·001	77·3	93·0	17·776
	BAIp	0·950	0·937, 0·961			4·180	< 0·001	92·0	93·3	20·410
	TMI	0·799	0·777, 0·819					73·3	88·7	16·005
Girls	BMI	0·936	0·921, 0·948	1·924	0·054	3·935	< 0·001	86·2	90·5	16·924
	BAIp	0·901	0·883, 0·916			1·463	0·143	87·7	84·9	19·130
	TMI	0·866	0·846, 0·883					80·0	80·3	15·619

BAIp, paediatric body adiposity index; TMI, triponderal mass index.

conclusions may have arisen due to the utilisation of BAIp rather than BAI as the assessment index for childhood obesity in our study. Aarbaoui indicated that BAI, which was developed using an adult sample, is not valid for children, as it may overestimate the PBF of young people[34]. The observed difference in the effectiveness of BMI, BAIp and TMI for obesity screening in preschool children between sexes could stem from physiological disparities in body fat distribution and composition. In the case of girls, similar to BAIp, BMI also exhibited a favourable effect in obesity screening. This may be attributed to the observed tendency for girls to accumulate fat at a faster rate at this age. Therefore, the favourable performance of BMI in girls could potentially be linked to the higher PBF of girls at this particular age. Freedman indicated that the accuracy of BMI varies according to the degree of body fatness and BMI tends to be a reliable indicator of excess adiposity in relatively fat children[35].

As for the limitations of the study, first, we used the BIA method to measure body fat content rather than more accurate techniques such as DEXA and CT, which might introduce measurement bias. Additionally, the cross-sectional nature of this study could have limited our ability to assess the accuracy of BMI, BAIp and TMI in tracking changes in body fat over time. Furthermore, while our study focused on children aged 3–6 in Wuhan, the results may not be directly extrapolated to the entire population of children in that age group across China. Factors such as regional variations in lifestyle, diet and socio-economic status could influence the generalisability of our findings. Therefore, caution should be exercised when applying our results to the broader population of children aged 3–6 in China.

Conclusion

In conclusion, this study indicated that compared with BMI and TMI, BAIp showed better agreement with PBF. BAIp could potentially serve as a promising alternative screening tool for obesity in both boys and girls. This finding suggests that BAIp could serve as a valuable screening tool for identifying obesity risk with greater accuracy, thereby providing a reliable foundation for early intervention. Consequently, it is recommended that the public health sector consider incorporating BAIp into routine child health surveillance programmes to enhance the precision of screening and the effectiveness of interventions.

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J. D. Z. conceptualised and designed the study, supervised the overall study implementation and reviewed and revised the manuscript. Y. M. W. drafted the initial manuscript, conducted the initial analyses and revised the manuscript. K. X. conceptualised and designed the study and collected data. P. Z. Y. T. and W. L. D. helped in data collection. M. Y. W., M. N. W., Y. F. J., W. Q. X. and J. M. Z. reviewed the manuscript for important intellectual content.

The authors declare that they have no competing interests.

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of Tongji Medical College, Huazhong University of Science and Technology (project identification code: (2020) IEC (A179)).

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

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