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Original Paper

The influence of body fat percentage in the anthropometric prediction of cardiac structure size in infants

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Abstract

Predicting normal values of cardiovascular structure size are essential in managing congenital and pediatric heart diseases. Conventionally, normal values of cardiovascular structure size are predicted based on body surface area (BSA), which is calculated from the infant's weight and height. However, the predicted normal values may be more accurate if the actual body composition measurement is considered because there are large individual differences in lean body mass (LBM) and fat mass (FM). The objective of this study was to evaluate the efficacy of measuring body fat percentage using the PEA POD Infant Body Composition System, a novel pediatric body composition measurement tool, in assessing cardiovascular structures focused on the diameters of the aortic valve (AVD) and mitral valve (MVD) and the left ventricular mass (LVM) in infants. We evaluated the associations between diameters of the AVD and MVD, LVM, and percent body fat (%BF) using the PEA POD system at term-equivalent age (37-42 weeks). AVD and MVD were not significantly different between groups with high or low %BF, whereas the differences between the predicted normal values and AVD and between the predicted normal values and MVD were significantly larger in the high %BF group than those in the low %BF group ($p<0.05$ and $p<0.01$, respectively). The high %BF group had significantly larger LVM/height$^{2.16}$ than the low %BF group ($p<0.05$), whereas no significant difference in LVM/BSA was found between the two groups. Body composition analysis is crucial for evaluating cardiovascular structure in infants because the existing methods for predicting normal values for valve diameter and LVM are significantly influenced by %BF.

Key words: body composition, left ventricular mass, aortic valve, mitral valve, infants

Introduction

Children with congenital heart disease are potentially at high risk of malnutrition because of fluid restriction associated with congestive heart failure, prolonged mechanical ventilation, and perioperative intensive care[1-3]. Malnutrition during the newborn period leads to excessive fat accumulation, subsequent metabolic syndromes, and even impaired neurodevelopment[4]. Theoretically, history of sarcopenia during infancy may also cause subsequent excessive fat accumulation during the catch-up growth period. To achieve individually-tailored management of congenital and pediatric heart diseases, the prediction of the normal values of cardiovascular structure size is essential. Conventionally, the normal values of cardiovascular structure size are predicted based on body surface area (BSA), which is calculated from an individual's weight and height[5, 6]. However, such predicted values may be inaccurate in patients complicated with impaired nutritional status because individual body composition may differ depending on the intensity of administered therapies. The overestimation or underestimation of the predicted normal values of cardiovascular structure size influences the decision of treatment strategy and even the determination of the optimal timing of cardiac surgery

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considering the patient's somatic growth. Therefore, the predicted normal value may be ideal if actual body composition measurements are considered, as there are large individual differences in lean body mass (LBM) and fat exist among individuals. The PEA POD Infant Body Composition System (Cosmed Inc., Concord, MA, USA) is a novel pediatric body composition measurement tool that uses the air displacement method, and is applicable for infants weighing from 1 to 8 kg. The accuracy of the PEA POD system is as high as reference techniques, such as dual-energy X-ray absorptiometry (DEXA) and bioelectrical impedance analysis, deuterium oxide dilution, and magnetic resonance imaging. Compared with the aforementioned reference techniques, the PEA POD system is simple to operate, takes approximately 7 min for measurement at bedside, and can be repeated because it does not expose the subject to radiation and does not require sedation. Therefore, the PEA POD system was recently considered the gold standard for noninvasive evaluation of body composition[7, 8]. However, there is a paucity of data on the application of the PEA POD system for assessing cardiovascular structures. Establishing an ideal individually tailored management strategy for congenital and pediatric heart diseases using the PEA POD system (i.e., developing a new regression equation for pediatric cardiovascular structures based on individual body composition) is important for proper patient management. Thus, this study was conducted to evaluate the efficacy of percent body fat (%BF) measured using the PEA POD Infant Body Composition System for assessing cardiovascular structures focused on the diameters of the aortic valve (AVD) and mitral valve (MVD), and the left ventricular mass (LVM) in infants.

Materials and methods

Infants with normal cardiac structures, born from July 2019 to July 2020, were included in this study. Patient features, including gestational age, birth weight, standard deviation (SD) score of birth weight, and medications were obtained from each patient's medical records. AVD and MVD and LVM were measured using transthoracic echocardiography. %BF was measured using the PEA POD Infant Body Composition System. These data were obtained at term-equivalent age, that is, between 37 and 42 weeks. AVD and MVD and LVM and infant's height were measured within a week from the date of body composition measurement. The exclusion criteria were as follows: 1) patients with unstable condition requiring close monitoring of vital signs; 2) those with serious underlying diseases, such as lethal chromosomal abnormalities; 3) those with bronchopulmonary dysplasia and significant congenital heart disease; 4) those requiring oxygen supplementation, mechanical ventilation, or continuous inotrope infusion at term-equivalent age; and 5) those with any other factors resulting in ineligibility.

The correlations between gestational age and either the SD score of birth weight or %BF were evaluated. The following parameters were compared between two groups of subjects, namely, the high and low %BF groups: 1) AVD and MVD; 2) the difference between the normative AVD and MVD predicted by the existing nomogram based on BSA and those predicted using raw data on AVD and MVD; and 3) LVM and two forms of indexed LVM (i.e., LVM/BSA and LVM/height$^{2.16}$), based on a previously reported nomogram for calculating indexed LVM in infants[9, 10]. The high and low %BF groups were divided at the median %BF.

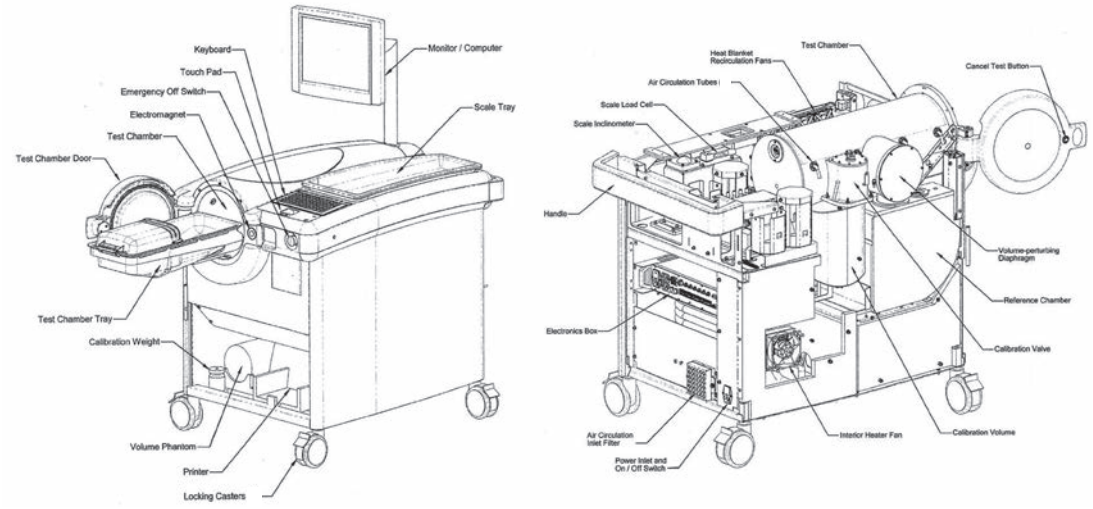
Echocardiography was performed using a Philips CX50 portable ultrasound system (Bothell, WA, USA), and an 8-MHz sector-type probe was used in all subjects. AVD, MVD, and LVM were measured using transthoracic echocardiography according to the recommended quantification methods during the performance of pediatric echocardiography[11]. All evaluations were performed by a single examiner. Each sample was measured by a single pediatric cardiologist. M-mode traces were obtained using the parasternal long- or short-axis view. AVD and MVD were measured from the parasternal long-axis and four-chamber views, respectively. LVM was calculated using the Devereux equation as follows: LVM=0.8 {1.04 [(left ventricular (LV) cavity dimension+posterior wall thickness+interventricular septal thickness)^3−(LV cavity dimension)^3]} + 0.6. LV cavity dimension, posterior wall thickness, and interventricular septal thickness were measured from the M-mode trace at the level just below the mitral annulus using the leading edge-to-leading edge technique. Measurements were averaged over three consecutive cardiac cycles. AVD and MVD were measured using the inner edge-to-inner edge technique. AVD was obtained in a parasternal long-axis view at systole, whereas MVD was measured in an apical four-chamber view at diastole. Both were measured at the moments of maximum diameter. Images determined as inappropriate for accurate measurement were excluded. To examine

the variability of echocardiographic measurements, interobserver and intraobserver coefficients for all subjects were calculated. To assess interobserver variability, images were measured by two independent raters who were blinded to the patients' profiles. To assess intraobserver variability, the same observer who was blinded to the initial measurements repeated the measurements for all subjects on two different occasions.

Body composition was measured using air displacement plethysmography (ADP) with the PEA POD Infant Body Composition System (Fig. 1). The determination of body composition by the PEA POD system is based on modeling the body into two compartments, the fat mass (FM) and the lean body mass (LBM) compartments. The LBM compartment consists of protein, water, minerals, and glycogen. FM and LBM are calculated from body weight and the FM and LBM, and body densities. The FM density is a constant equal to 0.9007 g/ml, and the LBM densities used are age- and sex-specific values based on the results obtained from multicompartment studies. Body density is calculated from the body mass measured using an electronic scale and body volume measured using ADP, which utilizes the relationships between pressure and volume and the gas laws of Boyle and Poisson. The PEA POD system has two chambers, the test and reference chambers, which are equal in volume and have the same design and materials. These chambers are separated by a volume-perturbing diaphragm. The pressure changes resulting from the volume perturbations are measured and used to compute test chamber volumes. The subject volume is determined by subtracting the test chamber volumes measured both empty and with the subject inside[12]. Each measurement using the PEA POD system was performed according to the following protocol: First, the automatic volume calibration began by closing the test chamber door. During the 2-min volume calibration, subject information was entered, including gender, length, and age, and body mass was measured on the PEA POD scale. After volume calibration was finished, the door of the test chamber was opened. After placing the subject in the test chamber, the volume measurement began by closing the test chamber door again. At the end of volume measurement, the test chamber door was opened and the subject was removed from the test chamber. The average of the two measurements was used. When there was a large deviation between the two measurements, a third measurement was performed, and the average of two similar values was used.

The predicted normal values of AVD and MVD were calculated as $16.79 \times BSA^{0.5337}$ and $26.25 \times BSA^{0.4658}$, respectively[5]. The following differences were calculated as follows: (predicted normal values based on BSA-measured values of AVD) was defined as "difference (normal-AVD)" and (predicted normal values based on BSA-measured values of MVD) was defined as "difference (normal-MVD)". We did not consider comparisons between sexes because previous studies have reported no significant sex differences in the cardiovascular structures of infants[13, 14].

This study was approved by the Ethics Committee



COSMED E & OE. PEA POD® Infant Body Composition Operator's Manual. P/N 210-4004 Rev. 2015;11-12

Fig. 1. The PEA POD Infant Body Composition System[12]

Measurement items

• Body fat percentage • Lean body mass percentage • Fat mass • Lean body mass • Body mass • Body volume • Body density • Fat mass density • Fat free mass density • Body surface area

of Showa University (approval number: 2863). Statistical analyses were performed using JMP Pro (version 15.0.0; SAS Institute Inc.). The Wilcoxon rank sum test was used for continuous variables, and Fisher's exact test was used for categorical variables for comparing the two groups. *P*-values of less than 0.05 were used to denote statistical significance. Interobserver and intraobserver reliability were determined using intraclass correlation coefficients (ICCs).

Results

Patient features are shown in Table 1. A total of 67 infants were evaluated. The median gestational age and birth weight were 35.3 weeks (range, 24.9–40.6 weeks) and 2,007 g (range, 533–3,567 g), respectively. The median SD score of birth weight was −0.4 g (range, −3.4–2.0 g). The median age, body weight, and %BF at evaluation were 85 days (range, 7–198 days), 2,644 g (range, 1,979–3,832 g), and 15.3% (range, 7.5%–24.9%), respectively. The number of patients born preterm, degree of prematurity, and birth weight were smaller in the low %BF group. Although steroids were used in one patient, the patient was included because only a single small dose was administered (Table 1).

A significant negative correlation was found between %BF and gestational age, but no significant correlation was observed between %BF and SD score of birth weight (Fig. 2). The median %BF was 15.3%. In total, 33 and 34 patients were classified into the low %BF group (<15.3%) and high %BF group (≥15.3%), respectively. Regarding echocardiographic measurements, eight M-mode images for LVM, one B-mode image for the aortic valve, and four B-mode images for the mitral valve were excluded because of inadequate quality for accurate measurements. Interobserver and intraobserver reliability were acceptable (ICCs were 0.86 and 0.99, respectively).

The mean ± SD values of AVD, MVD, and LVM in the two groups were 6.7 ± 0.6cm, 10.2 ± 0.9cm, and 5.1 ± 1.4g, respectively. No significant differences in AVD and MVD were observed between the high and low %BF groups (Fig. 3a and 3b), whereas differences (normal–AVD) and (normal–MVD) were significantly larger in the high %BF group than in the low %BF group ($p<0.05$ and $p<0.01$, respectively) (Fig. 3c and 3d). LVM and LVM/height$^{2.16}$ were significantly higher in the high %BF group than those in the low %BF group ($p<0.05$ and $p<0.05$, respectively) (Fig. 4a and 4b), whereas LVM/BSA was similar in both groups (Fig. 4c).

Table 1. Patient features

	Total (n=67)	Low %BF group (n=33)	High %BF group (n=34)	*P*-value
Male/female (N)	35/32	19/14	16/18	NS
Term/preterm birth (N)	20/47	18/15	2/32	< 0.01
Gestational age (weeks)	35.3 (24.9–40.6)	37.0 (32.6–40.6)	32.7 (24.9–39.0)	< 0.01
Birth weight (g)	2,007 (533–3,567)	2,243 (1,467–3,567)	1,570 (533–3,345)	< 0.01
SD score of birth weight	−0.4 (−3.4–2.0)	−0.6 (−3.4–1.5)	−0.4 (−2.7–2.0)	NS
Age at body composition measurement (days)	85 (7–198)	144 (7–197)	81 (15–198)	NS
Corrected age at body composition measurement (weeks)	39.3 (37.0–41.6)	39.3 (37.7–41.3)	39.6 (37.0–41.6)	NS
Anthropometry at mesurement				
Height (cm)	47.2 (42.0–53.0)	47.0 (42.0–53.0)	48.0 (42.8–53.0)	< 0.01
Weight (g)	2,644 (1,979–3,832)	2,442 (1,979–3,531)	2,802 (2,161–3,832)	< 0.01
Body surface area (cm^2)	1,954 (1,655–2,438)	1,864 (1,655–2,389)	2,015 (1,746–2,438)	< 0.01
PEA POD data at term equivalent age				
Lean body mass (g)	2,230 (1,805–3,053)	2,109 (1,805–3,053)	2,284 (1,826–2,966)	NS
Fat mass (g)	383 (163–867)	278 (163–477)	553 (334–867)	< 0.01
%BF	15.3 (7.5–24.9)	11.4 (7.5–15.1)	19.5 (15.3–24.9)	< 0.01

%BF, body fat percentage; SD, standard deviation; NS, not significant. The values are expressed as median (range).

Discussion

Several studies have reported the influence of body composition on cardiovascular system in adults and old children, but not in infants at term equivalent age[15, 16]. In adults, it has been reported that indexation for LBM measured by bioelectrical impedance analysis removed gender differences for LVM and reduced the influence of adiposity compared with existing LVMI[15]. In children aged 7 to 13 years of age, it was also reported that higher levels of body fat measured using DEXA were associated with unfavorable levels of LV geometry and function[16]. To our knowledge, this report is the first study that has evaluated the association between body composition and the cardiovascular system in infants, using the PEA POD system. Regarding the association between %BF and prematurity, a strong negative correlation was found between %BF and gestational age. This observation was similar to the findings of a meta-analysis[17], where body composition was measured using the PEA POD system, dual-

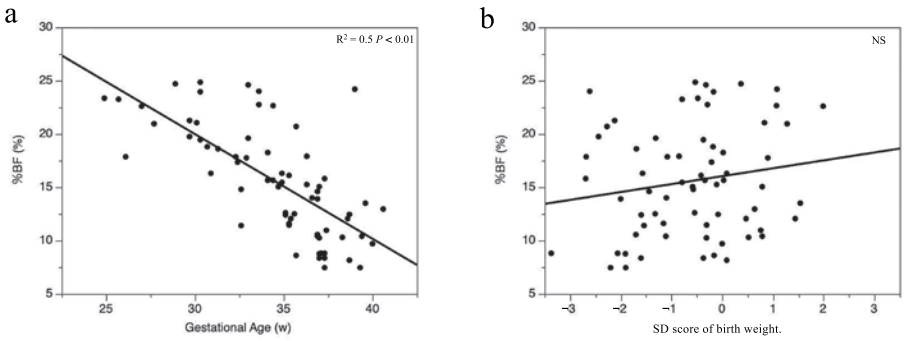


Fig. 2. Association between body fat percentage (%BF) and gestational age (a) and standard deviation (SD) score of birth weight (b)
%BF was significantly negatively correlated with gestational age, but not with the SD score of birth weight.

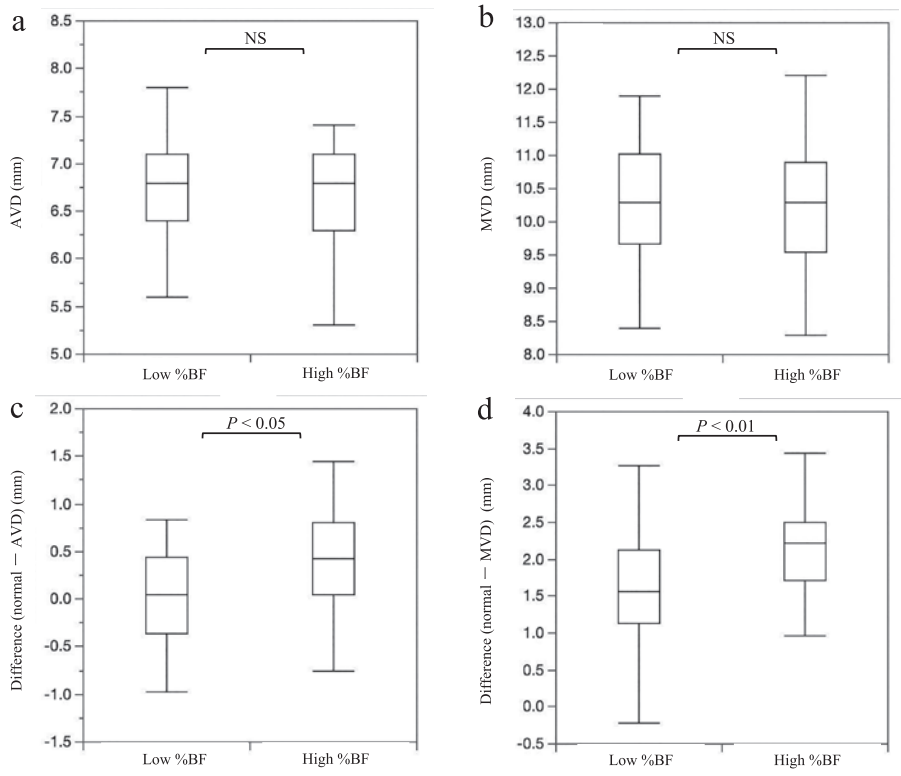


Fig. 3. Comparison of AVD (a), MVD (b), difference (normal-AVD) (c), and difference (normal-MVD) (d) in the high and low %BF groups
There were no significant differences in AVD or MVD. In the high %BF group, differences (normal-AVD) and (normal-MVD) were significantly higher than in the low %BF group.

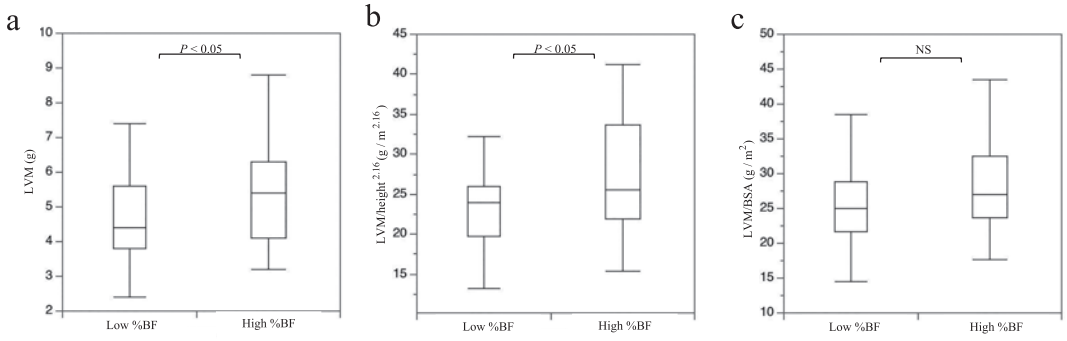


Fig. 4. Comparison of LVM (a), LVM/height$^{2.16}$ (b), and LVM/BSA (c) between the two groups
In the high %BF group, LVM and LVM/height$^{2.16}$ were significantly higher. There was no significant difference in LVM/BSA.

energy X-ray absorptiometry, or magnetic resonance imaging, and suggesting that acquisition of excessive fat mass is a process that occurs during the catch-up growth period under the regulation of several endocrine, nutritional, and environmental factors[18]. This suggests that assessing body composition is necessary, in addition to routine anthropometry, especially in preterm infants at risk of malnutrition.

Regarding AVD and MVD in this study, the normal values predicted by the existing nomogram based on BSA were larger than the actual measured values in the high %BF group. We believe that the calculated BSA was potentially overestimated because LBM in the high %BF group was smaller than that in the low %BF group and was associated with large fat mass. Consequently, existing normal prediction methods for valve diameters may include sources of error associated with individual differences in %BF. Considering the actual body composition measurement may increase prediction accuracy.

To index LVM, we used the two following formulas: LVM/height$^{2.16}$ and LVM/BSA. LVM and LVM/height$^{2.16}$ were significantly larger in the high %BF group, whereas LVM/BSA was not significantly different between the two groups. Historically, the LVM index has been predicted based on BSA. However, LVM indexed by BSA is more likely to be underestimated in young age because of the complex associations between the heart and body growth. Although different LVM indexing methods in children have been proposed, they had similar problems[19-25]. Recently, Chinali *et al.* have reported that LVM/height$^{2.16}$ represents a more reliable approach for subjects aged 0-18 years and in both sexes throughout the entire height ranges[9]. Therefore, in this study, we used both formulas (LVM/height$^{2.16}$ and LVM/BSA). Theoretically, LVM in infancy is determined primarily by the number of cardiac myocytes, which reaches their maximum number during the first year of life[26]. Furthermore, a study has reported that preterm infants have a disproportionate increase in LVM from birth up to 3 months of postnatal age, which represents a physiological compensation for reduced myocardial systolic performance[27]. It was also reported that LVM/BSA increased more extensively during the first month in preterm infants because the immature myocardium in preterm infants exists in a high basal contractile state and has high sensitivity to afterload changes[28-30]. The difference between LVM/height$^{2.16}$ and LVM/BSA was likely a consequence of overestimation by body weight in the high %BF group, which was larger than that in the low %BF group, and was associated with large fat mass with similar LBM. Based on this result, we believe that LVM/height$^{2.16}$ appears more reasonable because it is a metric that is completely independent of weight and fat mass, whereas LVM/BSA can be affected by individual differences in %BF. The high LVM in the high %BF group at term equivalent age suggests that the accelerated increase in LVM may be associated with both postnatal hemodynamic status and nutritional environment. However, because the high %BF group included a high percentage of premature patients, LVM can also be affected by the hemodynamic environment. To determine the exact mechanism of the increased LVM/height$^{2.16}$ in the high %BF group, further investigation of the longitudinal changes in LVM and hemodynamic parameters from birth are necessary.

Limitations

This study has several limitations, including the small number of subjects and lack of an assessment of hemodynamic status, which may affect LVM. We could not evaluate the influence of prematurity itself

on cardiovascular structures.

Conclusions

Body composition analysis, especially on %BF, is essential for evaluating cardiovascular structures in infants. The development of regression equations for cardiovascular structures that consider the body composition is crucial.

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Conflicts of interest/Competing interests

All authors have no conflicts of interest to declare.

Ethics approval

This study was approved by the Ethics Committee of Showa University (approval number: 2863).

Consent to participate

The subjects were enrolled after an informed consent form was explained and signed by their guardians of their own volition.

Consent for publication

All authors consented to the publication of the data.

Availability of data and material

Data are available upon reasonable request.

Code availability

The software package and code are available.

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