Original Article

Normative Data for Quantitative Calcaneal Ultrasound in Asian Children

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Abstract

Introduction: Dual energy X-ray absorptiometry (DEXA) is currently the gold standard for the assessment of bone mineral density. Quantitative ultrasound (QUS), on the other hand, is a radiation-free alternative for the assessment of bone strength in the paediatric population. Establishing normative data for bone strength specific to the population would allow identification of children at risk of osteoporosis as a consequence of disease and its treatment. This cross-sectional study aims to establish the normal reference range for calcaneal broadband ultrasound attenuation (BUA) measurements in normal Singaporean children aged 6 to 12 years. **Materials and Methods**: Healthy Singaporean children were randomly selected from 11 primary schools for the assessment of calcaneal BUA, using the paediatric Contact Ultrasonic Bone Analyzer (CUBA, McCue Plc, Compton, Winchester, England). The height, weight, body mass index and BUA measurements for each age group and gender were expressed as the mean ± SD. One-way ANOVA was used to compare the mean calcaneal BUA by age and gender of Singaporean children with that of children from the United Kingdom, Turkey and Taiwan. **Results**: A total of 750 healthy Singaporean children (417 males and 333 females) aged 6 to 12 years from 11 primary schools were enrolled. The calcaneal BUA values of Turkish and white British children were not statistically different from this Singaporean cohort. However, the Singaporean calcaneal BUA measurements were significantly higher compared to the Taiwanese children. **Conclusion**: This study provides the first normal reference data to evaluate bone strength in Singaporean children using the paediatric Contact Ultrasonic Bone Analyzer.

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Introduction

Dual energy X-ray absorptiometry (DEXA) is currently the gold standard for the assessment of bone mineral density (BMD). It is the commonest tool used to predict fracture risk in patients at risk of osteoporosis. The limitation of DEXA is that it only measures bone density in two dimensions, and does not provide information on bone architecture and bone remodelling, both of which also contribute to overall bone strength and fracture risk.

Quantitative ultrasound (QUS) is an alternative to DEXA and is used for the assessment of skeletal strength in children and adults.[1-5] It measures the broadband ultrasound attenuation (BUA) and the velocity of sound in bone. The more complex the bone structure, the more sound waves will be absorbed. Hence, normal bone will have a higher attenuation than osteoporotic bone.[2] Since QUS can provide information on bone microarchitecture, it is complementary to BMD in the assessment of overall bone strength and fracture risk.[1] Studies have demonstrated both the effectiveness and validity of BUA as an independent predictor of fracture risk in adults.[6,7] Mughal et al[8] has also demonstrated that calcaneal BUA correlates significantly with total body bone mineral density (r = 0.74, P <0.001) for healthy children and adolescents. Hence QUS can be an alternative to the DEXA in the assessment of bone strength in children under the right clinical setting.

The calcaneum is the preferred site for measuring BUA as it is more easily accessible and consists predominantly of trabecular bone (>90%), similar to the spine. Trabecular bone is metabolically more active than cortical bone, and is more vulnerable to age, disease and therapy-induced bone alterations than cortical bone.[6,9] Hence, calcaneal ultrasound may allow early detection of reduced bone strength, and the identification of children who are at risk

of developing osteoporotic fractures. Moreover, calcaneal QUS is radiation-free, portable and technically easy-to-use in the paediatric outpatient setting. To date, there is no known normative data for BUA for Singaporean children using the CUBA machine.

The aim of this study is to establish a normal reference range of calcaneal BUA in Singaporean children aged 6 to 12 years. We also aim to compare our QUS measurements with the BUA normative data from Taiwanese and non-Asian populations.

Materials and Methods

Fifteen schools were selected by random sampling from all the primary schools in Singapore, and 11 schools consented to participate in this cross-sectional study. Depending on the class size, 3 or 4 students were randomly selected from every class at each level using systematic random sampling. A questionnaire was given to the parents requesting for information on their child's medical history. Subjects were excluded if there was a history of chronic disease which could affect calcium and Vitamin D metabolism, metabolic bone disease, a history of long-term medications such as corticosteroids, anticonvulsants and immunosuppressants which can affect bone metabolism, and anomalies of growth and puberty. Written informed consents were obtained from the parents or guardians of the children. Verbal assents were also obtained from the children at the time of study. This study was approved by the National Healthcare Group Domain Specific Review Boards.

The study was conducted in each school by 2 trained nurses. Height was measured using a wall-mounted measuring tape. Standing weight was measured using the Tanita weighing scale. For both measurements, the children were in their school attire without socks and shoes. The paediatric Contact Ultrasonic Bone Analyzer (CUBA, McCue Plc, Compton, Winchester, England) was used to measure broadband ultrasound attenuation (BUA) over the left heel. The child was seated with the left foot placed in the footwell secured using 2 straps. Ultrasonic coupling jelly was then applied to the sides of the left heel, and transducers were placed on either side of the heel. Inaudible sound waves were transmitted through the calcaneum, and the BUA (in decibels per megahertz) was then measured (Fig. 1). The in-vitro precision for BUA was 0.44% and the in-vivo precision was 1.3%. To maintain quality control, a heel phantom was scanned before each use. Each BUA value recorded was a mean of 2 consecutive measurements.

Statistical Analysis

Data analysis was performed using SPSS version 16.0 for windows. Data were presented as the mean ± 2SD. One-way ANOVA was utilised to compare BUA values by gender and age. A linear regression model was calculated to examine the relationship between BUA values and age, height, weight and BMI. A P value <0.05 was considered statistically significant.

Results

Demographic Characteristics

A total of 750 healthy Singaporean children (417 males and 333 females) were recruited from 11 primary schools. There were 545 Chinese (72.6%), 128 Malays (17.1%), 66 Indians (8.8%) and 11 children of other races (1.5%). The racial distribution was comparable to the Singapore Census for the similar age groups. These subjects were divided into groups by age and sex (Tables 1A and 1B). We have included the national normative values for weight and height for children of the same age range in these tables. Tables 1A and 1B, and Figure 2 summarise the BUA measurements by age and gender, and demonstrate that the BUA progressively increased with age.
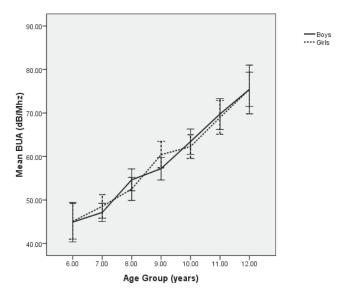

Fig. 1. Measuring BUA over the left heel using the CUBA machine.

Fig. 2. BUA (Mean ± 2 SE) for age for Singaporean boys and girls.

Table 1A. Demographic Features and BUA Values for Singaporean Boys

Age (yrs)		Weight (kg) Study Population	Weight (kg) Singaporean Population	Height (cm) Study Population	Height (cm) Singaporean Population	BMI (kg/m²)	BUA
6 – 6.99	(23)	25.23 ± 6.48	24.12	121.43 ± 6.07	118.62	16.94 ± 3.28	44.94 ± 10.94
7 – 7.99	(70)	23.92 ± 4.77	26.09	123.67 ± 5.14	123.39	15.56 ± 2.42	47.15 ± 8.79
8 – 8.99	(72)	27.97 ± 6.79	29.50	130.72 ± 5.58	128.72	16.24 ± 3.06	54.64 ± 10.57
9 – 9.99	(65)	30.60 ± 7.81	32.68	134.16 ± 6.63	133.97	16.82 ± 3.21	57.23 ± 10.55
10 – 10.99	(77)	35.52 ± 11.04	37.15	138.41 ± 7.19	139.23	18.28 ± 4.23	63.44 ± 12.72
11 – 11.99	(65)	39.09 ± 11.30	41.83	146.08 ± 8.64	146.44	18.12 ± 4.15	69.78 ± 14.41
12 – 12.99	(45)	44.02 ± 10.63	46.79	153.21 ± 8.75	152.65	18.58 ± 3.29	75.46 ± 13.08

Table 1B. Demographic Features and BUA Values for Singaporean Girls

Age (yrs)		Weight (kg) Study Population	Weight (kg) Singaporean Population	Height (cm) Study Population	Height (cm) Singaporean Population	BMI (kg/m²)	BUA
6 – 6.99	(28)	21.85 ± 5.30	23.19	120.11± 5.69	118.27	15.00 ± 2.68	45.11 ± 10.84
7 – 7.99	(58)	24.50 ± 8.08	25.15	123.80 ± 6.74	122.47	15.70 ± 3.33	48.54 ± 10.36
8 – 8.99	(47)	27.32 ± 8.72	28.03	129.74 ± 7.13	127.88	15.99 ± 3.75	52.53 ± 9.02
9 – 9.99	(54)	31.76 ± 8.52	32.13	135.45 ± 6.99	134.19	17.13 ± 3.69	60.43 ± 11.08
10 – 10.99	(49)	33.71 ± 7.48	36.34	138.88 ± 6.55	140.47	17.32 ± 2.70	62.29 ± 9.59
11 – 11.99	(49)	39.41 ± 9.65	41.18	147.43 ± 7.93	147.02	17.94 ± 3.12	68.99 ± 13.69
12 – 12.99	(48)	41.68 ± 10.28	46.23	152.44 ± 7.49	152.68	17.78 ± 3.24	75.41 ± 19.41

The BUA measurements were compared with previously reported studies of other paediatric populations (Table 2). Although the BUA measurements of Singaporean children showed no significant differences between boys and girls, the Singapore BUA measurements were significantly higher than that of Taiwanese children ($P <0.05$).

The influence of age, height, weight and BMI on BUA were examined. For both boys and girls, there was a positive relationship between age, height and BUA (r = 0.6, $P <0.005$)

Discussion

Singapore is a multi-racial society, with a predominantly Chinese population comprising 70.9%, and the Malays and Indians comprising 18.9% and 8.6%, respectively (year 2000 census for age group 6 to 12 years). In this study, we measured BUA over the left calcaneum using the CUBA machine for Singapore children aged 6 to 12 years. We did not analyse the data for each racial group as the study was not powered to determine BUA for each racial group. Similar to other studies, we found that BUA increases progressively with age, weight and height for both boys and girls (Tables 1A and 1B). The trend of increase in BUA by age group for both boys and girls is shown in Figure 2.

Using the same CUBA machine, we compared our BUA data with that obtained from children from Taiwan,[10]

Turkey[11] and United Kingdom[12] who were also randomly selected from primary schools (Table 2, Figs. 3 and 4). It was surprising that Singaporean children have significantly higher BUA than Taiwanese children, whilst BUA measurements from Turkish and white British children were not significantly different from the Singaporean population. When we compared the demographic profile of the different populations, we found that BUA differences cannot be explained by differences in height, weight or BMI (data not included in this article) alone. Though the Taiwanese boys are heavier with higher BMI values than Singaporean boys, they have lower BUA values. In contrast, the Turkish boys who are lighter and shorter than the Singaporean boys, they have comparable BUA values with Singaporean boys of the same age group. Clearly, there are many factors which contribute to the bone strength, and the impact of genetics, nutrition, and the level of physical activity on bone accrual need to be further studied between populations.

Studies have shown that one of the major limitations of DEXA is it only measures 2-dimensional areal density, which varies with bone size. Interpretation of BMD values can thus be challenging as variables such as height and pubertal stage can influence the bone size. In order to correct for this, quantitative computed tomography (QCT) can be performed to assess the actual volumetric BMD. However, this method

Table 2. Comparison of Mean BUA Measurements for Singaporean and Children from Taiwan, Turkey and the United Kingdom by Gender and Age

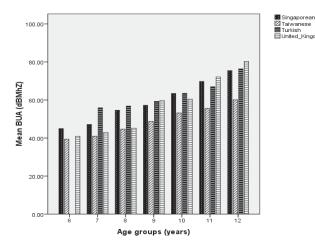| Age (yrs)	BUA of Boys (dB/MHz)				BUA of Girls (dB/MHz)			
	Singaporean (Mean ± SD) n = 417	Taiwanese (Mean ± SE) n = 1164	Turkish (Mean) n = 61	United Kingdom (Mean) n = 174	Singaporean (Mean ± SD) n = 333	Taiwanese (Mean ± SE) n = 1016	Turkish (Mean) n = 80	United Kingdom (Mean) n = 193
6 – 6.99	44.94 ± 10.94	39.4 ± 1.6	-	40.9	45.11 ± 10.84	38.5 ± 1.2	47.00	35.5
7 – 7.99	47.15 ± 8.79	41 ± 0.6	55.93	42.9	48.54 ± 10.36	40.8 ± 1.9	48.14	39.2
8 – 8.99	54.64 ± 10.57	44.7 ± 0.8	56.82	45.2	52.53 ± 9.02	44.1 ± 0.7	52.90	45.8
9 – 9.99	57.23 ± 10.55	48.7 ± 0.9	59.27	59.7	60.43 ± 11.08	47.8 ± 1.1	54.26	51.6
10 – 10.99	63.44 ± 12.72	53.2 ± 0.8	63.54	60.4	62.29 ± 9.59	50.0 ± 1.0	56.73	47.8
11 – 11.99	69.78 ± 14.41	55.6 ± 0.9	67.00	72.1	68.99 ± 13.69	53.3 ± 1.1	61.79	65.2
12 – 12.99	75.46 ± 13.08	60.1 ± 1.8	76.34	80.3	75.41 ± 19.41	61.0 ± 2.0	64.34	65.9

Fig. 3. Comparison of mean BUA Singaporean boys vs mean BUA boys of other populations.
Note: Turkish data at 6 years of age not available.

Fig. 4. Comparison of mean BUA Singaporean girls vs Mean BUA girls of other populations.

involves exposing the child to unnecessary radiation, and hence is not routinely performed. An alternative would be to use mathematical models to calculate the apparent BMD from BMD values obtained using DEXA. One study showed that apparent BMD values do not show any significant increases prior to puberty, similar to what has been reported using QCT.[13,14]

To the best of our knowledge, there have not been any studies done that have validated any mathematical methods to correct for the influence of height on BUA values. We therefore propose the use of normative values of BUA for height for children at the extremes of height (children whose height falls <3rd percentile or >97th percentile). These normative data can be used to trend the changes in BUA values for children with short or tall stature (Figs. 5 and 6).

One of the limitations of this study was that we were unable to determine the relationship between puberty and BUA in our subjects. The pubertal stage of the subjects was not assessed as the study was conducted in the schools by nurses, hence we we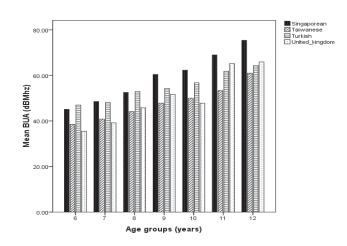re unable to accurately assess the stages of puberty for both boys and girls. Sex steroids and growth hormone levels increase during puberty, and both have been shown to increase bone mineralisation. Maximum increase in BMD has been shown to occur around the age of 13 years in girls and 15 years in boys.[13] Studies comparing BMD values between boys and girls have shown that significant differences in BMD values between boys and girls occur at the age of between 10 and 12 years.[15,16] Yet other studies have shown no significant difference in BMD between boys and girls up to the age of 13 years.[17]

Studies using calcaneal ultrasound have also yielded conflicting results. Zhu et al[18] showed that for the Chinese population, BUA values for girls were significantly higher than boys at the age of 13 years. Jaworski[19] demonstated that BUA values for boys and girls were similar up to the age of 15 years. Another study on Caucasian children by van de Bergh[20] showed that after correcting for age, pubertal stage was not a determinant for BUA values in both boys and girls.
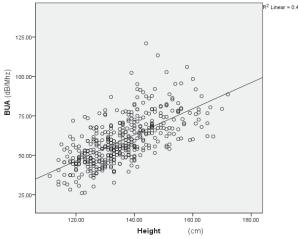
In our study population, BUA values were similar for

Fig. 5. BUA for height for Singaporean boys.

Fig. 6. BUA for height for Singaporean girls.

boys and girls up to the age of 13 years. Even though girls enter puberty earlier than boys, its effect on bone strength measured via BUA was not evident in our study. We postulate that one of the reasons could be related to the site being measured. BUA measured at the calcaneum may be influenced to a greater degree by other factors such as the weight of the child or the intensity of the child's physical exercises rather than sex hormone levels. Also, BUA values may not increase in a linear fashion in relation to pubertal stage. If we were to extend the study by a few years, we may be able to see the divergence of BUA values between boys and girls at a later age.

Bone health is an aspect that is often neglected in the management of paediatric chronic diseases. Measuring BMD is not routinely performed as it subjects the child to ionizing radiation, and the test requires the cooperation of the child. In addition, BMD accounts for only 60% to 70% of the variation in bone strength.[21] Conversely, QUS is a useful diagnostic modality, as it can be readily performed in the outpatient setting, and is able to provide information on bone microarchitecture, which also contributes to overall bone strength (and hence fracture risk) in the patient. BUA is thus a useful and complementary tool for screening and monitoring bone strength in children at risk of fractures due to their chronic illnesses or treatment.

To have an accurate assessment of the impact of chronic illness or medication on bone strength, BUA values should be compared with norms from the local population. This set of normative data will allow for a more accurate assessment of bone strength using BUA in our paediatric population.

Currently, there are no established guidelines to define osteoporosis in children based solely on DEXA.[22] The International Society for Clinical Densitometry's position statement on bone densitometry in children states that the diagnosis of osteoporosis in children and adolescents should
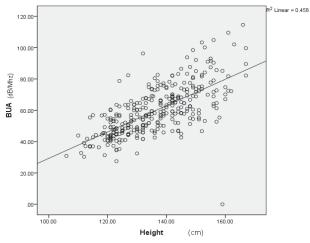
not be made on the basis of densitometric criteria alone, but should include the presence of a clinically significant fracture.[23] However, many children may be at risk for osteoporosis, either as a result of their chronic illnesses or due to the medication they are taking. In this group of children, there should ideally be a safe and easy method to monitor the impact of the disease or medication on bone health before fracture occurs.

DEXA is not an ideal tool for serial monitoring of BMD as it is costly, difficult-to-perform, and radiation is involved. QUS though not the gold standard, is portable, fast to perform, and is radiation-free. We would recommend using the QUS as a monitoring tool for children at risk of developing osteoporosis. QUS can be performed together with the first DEXA scan. QUS can then be performed on a regular basis. Should the trend show worsening of BUA values, DEXA can then be performed. This will minimise the inconvenience and radiation exposure to the child compared to regular DEXA scans in those at risk of osteoporotic fractures.

Conclusion

The calcaneal QUS is a useful and convenient screening tool to assess the bone strength in children. Similar to anthropometric charts, BUA measurements should be compared with local normal reference data, so as to achieve a more accurate assessment. To the best of our knowledge, this is the only Singapore normative data for calcaneal QUS, and it will serve as a useful reference for the assessment and identification of children who are at increased risk of fractures, especially for children who have chronic illness or are on steroid therapy. This reference data will be a precious source of information for all future studies which examine factors contributing to bone strength in Singapore children, with the ultimate aim of maximising their potential to achieve peak bone mass and to optimise bone health.

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