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PEDIATRIC RADIOLOGY

ORIGINAL ARTICLE

Sonographic cortical bone thickness measurement: can it predict bone mineral density in the pediatric population?

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PURPOSE

To explore sonographic cortical bone thickness (CoT) as a potential indicator of bone mineral density (BMD) measured by dual-energy X-ray absorptiometry for screening and diagnosing pediatric osteoporosis.

METHODS

A prospective study included 41 osteopenic or osteoporotic patients and 52 healthy children. Radius cortical thickness (R-CoT), tibial cortical thickness (T-CoT), and second metatarsal cortical thickness (M-CoT) were measured by B-mode ultrasound; CoT values were compared between groups and the correlation between BMD and CoT was examined.

RESULTS

There were no significant differences in R-CoT ($P = 0.433$), T-CoT ($P = 0.057$), and M-CoT ($P = 0.978$) values between the patient and control groups. No significant correlations were found between BMD T-scores and R-CoT ($r = -0.073$, $P = 0.490$), T-CoT ($r = -0.154$, $P = 0.141$), and M-CoT ($r = 0.047$, $P = 0.657$) values.

CONCLUSION

Sonographic CoT values in children do not correlate with BMD values. Unlike in adults, sonographic CoT measurements do not appear to have a role in assessing BMD in the pediatric population.

KEYWORDS

Osteoporosis, children, bone, density, cortical, thickness, ultrasonography

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Osteoporosis, once primarily associated with the elderly, is increasingly being recognized as a concern in the pediatric population.[1] Various factors, such as genetics, diet, physical activity, medications, and the presence of chronic illnesses compromising bone strength, influence the bone health of children.[2,3] Untreated reduction in bone mass can result in deformities and negatively impact quality of life, potentially leading to long-term consequences.[4] Therefore, it is imperative to identify children with osteoporosis or those at high risk of developing it.

Pediatric osteoporosis is defined by the International Society of Clinical Densitometry using two criteria. The first criterion is a "low bone mineral content or bone mineral density (BMD)," characterized by a BMD Z-score of ≤−2. The second criterion is the "presence of a clinically significant fracture history," involving at least one long bone fracture in the lower extremity, at least two long bone fractures in the upper extremity, or a vertebral compression fracture.[5] Dual-energy X-ray absorptiometry (DXA) stands as the standard reference tool for assessing pediatric BMD.[6] However, alternative radiology tools, such as the bone health index,[7] direct radiography,[8] computed tomography (CT),[6] magnetic resonance imaging (MRI),[9] and ultrasonography[10] are also recommended for diagnosing and monitoring pediatric os-

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teoporosis. Nevertheless, each of these alternative methods presents drawbacks, and current recommendations emphasize the need for novel modalities in assessing osteoporosis in children.[1]

Children with osteoporosis may present with a history of recurrent fractures, deformities, or back pain.[11] An investigation for osteoporosis in children is warranted in the presence of significant risk factors, incidentally-detected fractures, or fractures that develop after minor trauma.[2,3] Given the increasing prevalence of osteoporosis in the pediatric age group, there is a growing demand for a diagnostic imaging modality that is easy to apply, safe, and cost-effective. In this context, ultrasonography has garnered attention from researchers due to its user-friendliness, affordability, and lack of ionizing radiation. As part of these efforts, ultrasonographic parameters, such as the speed of sound and broadband ultrasonography attenuation, have been explored.[12] A recent study in adults demonstrated a significant correlation between cortical bone thickness (CoT) measurements obtained through B-mode ultrasonography and BMD values determined via DXA.[13] However, the applicability and validity of this method in the pediatric population remain unknown.

Accordingly, the focus of our investigation lies in elucidating the relationship between CoT, as measured using B-mode ultrasonography, and BMD measurements obtained through DXA. Additionally, we aim to assess the utility and validity of sonographic CoT measurements as a screening and diagnostic tool for pediatric osteoporosis. Concurrently, within the scope of our study, it is imperative to highlight the significance of cortical thickness in relation to spatial resolution in ultrasonography. Specifically, we elucidate that when cortical thickness exceeds the inherent spatial resolution, a distinct demarcation can be observed in which both the external and internal surfaces of the bone cortex manifest as separate, luminous lines within the ultrasound image. Conversely, when cortical thickness falls below the spatial resolution threshold, echoes from these surfaces overlap, resulting in a merged representation as a single conspicuously bright line within the ultrasound image. Notably, we emphasize that, in this study, echo thickness serves as a surrogate measure for cortical thickness.

Main points

- In contrast to adults, the present study concluded that sonography does not play a role in assessing pediatric osteoporosis.
- There is no correlation between sonography-measured cortical thickness values and dual-energy X-ray absorptiometry-derived bone mineral density.
- Effective evaluation of pediatric patients requires considering a combination of objective radiological and/or biochemical data, clinical risk factors, and the limitations of pediatric osteoporosis criteria.

Methods

Study design and recruitment of participants

This prospective cohort study, conducted from March to May 2023, included pediatric patients admitted to the endocrinology outpatient clinic with bone pain suggestive of osteoporosis. Ethics Committee approval was received for this study from the IRB Atatürk Sanatorium Training and Research Hospital (March 8, 2023, 2012-KAEK-15/2637). The parents or legal guardians of the participant children received a detailed explanation about the study, and written informed consent was obtained. The study was designed and conducted according to relevant ethical regulations and was performed following the Declaration of Helsinki and its later amendments.

Routine calcium level measurement was performed. Among the patients, 93 were identified as having hypocalcemia and underwent BMD and sonographic CoT measurements. Exclusion criteria included patients older than 18, refusal of BMD measurements and/or ultrasonography, missing data or laboratory results, and the presence of skeletal dysplasia or cerebral palsy. The patient group (n = 41) comprised children with osteopenia or osteoporosis based on BMD results, while the control group (n = 52) included healthy children.

Data collection

Participants' age and sex information, BMD measurement results, and CoT values were measured by ultrasonography. Blood samples were acquired from the antecubital vein to measure calcium, phosphorus, magnesium, alkaline phosphatase, parathyroid hormone, and 25-hydroxyvitamin D3 levels.

In this investigation, the Toshiba Aplio 500 device, along with its 14L5 frequency probe, was employed. During the examination, the ultrasound frequency utilized was 14 MHz, with a dynamic range set at 65, a frame rate of 6, and a single focus adjusted within the range of 45%–50%.

Bone mineral density measurement

Following blood sampling, BMD (mg/cm^2) measurements were performed from the femoral neck and lumbar spine (L1–L4 posteroanterior) in all participants using a DXA device (Explorer QDR series; USA). The T-scores were calculated based on reference BMD datasets of Turkish children aged 6–18 years. T-score results were interpreted according to the World Health Organization criteria[14] as follows: normal (T-score ≥−1.0), osteopenia (−2.5< T-score <−1.0), and osteoporosis (T-score ≤−2.5).

Sonographic cortical bone thickness measurement

The ultrasonographic CoT values of each participant were measured using the same ultrasound device (Toshiba Aplio 500; Japan) and transducer. The measurements were taken by the same radiologist from the radius, tibia, and anterior cortical areas of the second metatarsal head of the non-dominant extremity. The radius cortical thickness (R-CoT) was measured 2 cm proximal to the radiocarpal joint, the tibial cortical thickness (T-CoT) was measured 2 cm proximal to the medial malleolus to the joint level, and the metatarsal cortical thickness (M-CoT) was measured 2 cm proximal to the second metatarsophalangeal joint. The B-mode ultrasonography images were adjusted for preset and gray scale settings. After achieving optimal focus and zoom settings perpendicular to the relevant bone cortex axis, the outer and inner starting and ending points of the first and most echogenic linear lines of the bone cortex were measured in millimeters (Figure 1).

Statistical analysis

The statistical analysis was performed using SPSS version 25.0 (IBM, USA). A p-value less than 0.05 was considered statistically significant for all analyses. The Shapiro–Wilk test was employed to assess whether continuous variables followed a normal distribution. Continuous variables were reported as mean ± standard deviation or median (first-to-third quartile) based on their distribution, while categorical variables were reported as relative frequency. Normally distributed continuous variables were analyzed with the Student's t-test, while non-normally distributed variables were analyzed using the Mann–Whitney U test. The chi-square test was used to analyze categorical variables. The Spearman correlation coefficient was calculated to assess the association between BMD and bone CoT.

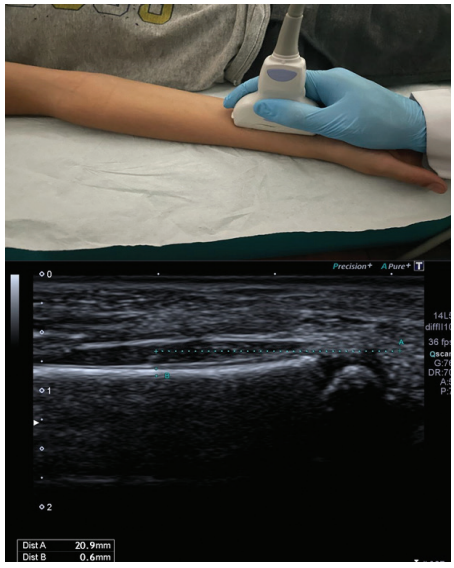

Figure 1. The cortical bone thickness measurement.

Results

The mean age of the patient group was 11.25 ± 2.76 and 12.04 ± 3.03 in the control group. The female-to-male ratios were 28:13 and 30:22 in the patient and control groups, respectively. There was no significant difference between the two groups in terms of age and sex distribution ($P = 0.197$ and $P = 0.405$, respectively). There was no significant difference between the R-CoT ($P = 0.433$), T-CoT ($P = 0.057$), and M-CoT ($P = 0.978$) values of the patient and control groups. As expected, the median T-score ($P < 0.001$) and median calcium level ($P = 0.014$) of the patient group were significantly lower than the control group, while the alkaline phosphatase level was significantly higher ($P = 0.002$) (Table 1).

We also investigated the correlation between the T-score and CoT measured by sonography. No significant correlation was detected between T-score values and R-CoT (r = –0.073, $P = 0.490$), T-CoT (r = –0.154, $P = 0.141$), and M-CoT (r = 0.047, $P = 0.657$) (Table 2).

Table 1. Summary of patient characteristics and measurements with regard to groups

		Groups		
	Total	Patients (n = 41)	Controls (n = 52)	*P*
Age	11.69 ± 2.93	11.25 ± 2.76	12.04 ± 3.03	0.197
Sex				
Female	58 (62.37%)	28 (68.29%)	30 (57.69%)	0.405
Male	35 (37.63%)	13 (31.71%)	22 (42.31%)	
Bone mineral density, T-score	–0.76 (–1.95–0.42)	–2.12 (–2.81 to –1.36)	0.38 (–0.48–1.05)	**<0.001**
Normal (T-score ≥ –1.0)	52 (55.91%)	0 (0.00%)	52 (100.00%)	
Osteopenia (–2.5 < T-score <–1.0)	29 (31.18%)	29 (70.73%)	0 (0.00%)	**<0.001**
Osteoporosis (T-score ≤–2.5)	12 (12.90%)	12 (29.27%)	0 (0.00%)	
Bone cortical thickness				
Radius	0.6 (0.5–0.7)	0.6 (0.5–0.8)	0.6 (0.5–0.7)	0.433
Tibia	0.6 (0.6–0.8)	0.7 (0.6–0.8)	0.6 (0.6–0.7)	0.057
Second metatarsal	0.5 (0.4–0.6)	0.5 (0.4–0.6)	0.5 (0.45–0.6)	0.978
Calcium	9.7 (9.3–10.1)	9.6 (8.9–10.0)	9.9 (9.5–10.1)	**0.014**
Phosphorus	4.6 (4.1–4.9)	4.8 (4.2–5.1)	4.6 (4.05–4.8)	0.089
Magnesium	2.0 (1.9–2.1)	2.0 (1.9–2.1)	2.0 (1.9–2.1)	0.850
Alkaline phosphatase	207 (124–249)	227 (167.5–430)	183 (115.5–224.5)	**0.002**
Parathyroid hormone	78.0 (66.2–95.05)	82.2 (70.5–115.6)	76.5 (61.0–86.0)	0.104
25-hydroxyvitamin D3	14.0 (9.2–18.55)	15.0 (8.1–22.0)	13.8 (10.2–16.6)	0.683

Data are given as mean ± standard deviation or median (first-to-third quartile) for continuous variables according to normality of distribution and as a frequency (percentage) for categorical variables.

Table 2. Correlations between bone mineral density and cortical thickness measurements

		Bone cortical thickness		
		Radius	Tibia	Second metatarsal
Bone mineral density, T-score	r	–0.073	–0.154	0.047
	p	0.490	0.141	0.657

r, Spearman's correlation coefficient.

Discussion

The present study's results underscore the limited utility of sonography in assessing pediatric osteoporosis, despite its use indicating intriguing relationships in adult studies. This discrepancy may be attributed to fundamental disparities between pediatric and adult osteoporosis.[2] It is paramount to acknowledge that nearly 95% of skeletal size, bone mass, and muscle mass are acquired before the age of 18.[15] While rare, untreated osteoporosis during childhood can carry adverse repercussions into adulthood.

Pediatric osteoporosis often arises as a complication of underlying diseases or as a side effect of medications.[16] Furthermore, given the higher frequency of fractures resulting from behavioral factors in childhood, distinguishing whether these fractures are pathological or a natural consequence of high-energy trauma becomes more challenging.[17] Nevertheless, specific scenarios warrant suspicion of pediatric osteoporosis. For instance, any child presenting with back pain should undergo evaluation for occult vertebral fractures through lateral spine X-rays to exclude osteoporosis. Similarly, pediatric osteoporosis should be considered when fractures occur following low-energy trauma.[2,3] In addition to these challenges, the limitations of pediatric osteoporosis criteria necessitate the comprehensive evaluation of pediatric patients, incorporating objective radiological and/or biochemical data, as well as clinical risk factors. Identifying patients at high risk for low BMD or with low BMD is critical to administering effective treatment. However, presently, DXA remains the predominant modality for assessing pediatric osteoporosis, highlighting the need for radiological tools that can overcome its limitations, such as cost, availability, and radiation exposure. This study investigated whether a correlation could be established between sonography-measured CoT values and BMD results obtained via DXA. However, our findings did not establish a significant relationship between these two parameters.

Ultrasonography presents potential as an alternative to BMD assessment, with the most explored ultrasonographic parameters being speed-of-sound (or ultrasound velocity) and broadband ultrasonography attenu-

ation.[12] Previous studies have demonstrated significant correlations between CoT determined by CT or direct X-ray and bone mass and BMD.[18,19] In line with these investigations, Gokcek et al.[13] noted that ultrasonographic R-CoT and T-CoT values played prognostic roles in predicting patients with abnormal T-scores measured by DXA. Nevertheless, our study found no significant differences in R-CoT, T-CoT, and M-CoT values between the patient and control groups. While there is insufficient evidence in the literature to make recommendations regarding the utility of ultrasonography in predicting fractures in children,[16] Hartman et al.[12] suggest a significant positive correlation between lumbar DXA and radius speed-of-sound, asserting that ultrasound evaluation of the radius and tibia can yield results comparable to DXA for screening pediatric osteoporosis.

The management of pediatric osteoporosis involves two crucial stages: identifying high-risk children for low BMD and diagnosing osteoporosis.[2,3,6] In children with suspected osteoporosis who present with fractures, deformities, or bone pain, detailed laboratory examinations are conducted for diagnostic purposes. Radiological evaluations, including DXA and, if necessary, conventional lateral spine radiographs, are ordered for these patients. Despite its various limitations, DXA is still considered the reference standard technique for assessing bone quality and detecting pediatric osteoporosis due to its standardized results. However, the use of DXA in the pediatric population is inherently limited due to ionizing radiation exposure.[16] Additionally, DXA measurements may underestimate BMD in children with short stature or delayed puberty. Furthermore, the effects of growth retardation are not considered for children younger than 5 years.[20] Various factors, including movement during scans, scoliosis, body size, ethnicity, bone age, and pubertal development, can influence BMD results.[1] Moreover, DXA lacks the ability to distinguish between trabecular and cortical bone or provide information about bone geometry.[1] Despite its status as the primary modality for osteoporosis investigation, DXA may not be the most suitable tool for detecting changes in bone mass.[1]

The limitations of DXA have driven researchers to explore alternative or supplementary diagnostic tools. The bone health index measured via radiogrammetry,[7] direct radiography for detecting occult vertebral fractures,[8] quantitative CT (qCT),[6] MRI,[9] and quantitative ultrasonography (qUS)[10] are among the radiological tools used or recommended for pediatric osteoporosis diagnosis. However, the bone health index has a high false positive rate and a weak correlation with BMD,[3] while direct X-ray serves as a semi-quantitative method used solely to identify occult vertebral fractures and confirm suspected osteoporosis.[8] Alternatively, MRI and qCT offer the advantage of separately evaluating cortical and trabecular bone, with qCT having proved to be an alternative diagnostic tool in children with severe scoliosis or joint contractures.[1,3] In comparison to DXA, qCT BMD provides more valuable information about bone features, enhancing our understanding of skeletal defects associated with fracture risk.[1] Nonetheless, the higher radiation exposure associated with qCT limits its use in pediatric osteoporosis diagnosis.[1] Despite multiple studies exploring these modalities and their listed advantages, DXA remains the gold standard in the majority of healthcare centers. Ultrasonography stands out due to its lack of ionizing radiation emission, portability, non-invasiveness, affordability, ability to establish normative values for pediatric patients without radiation concerns, and capacity to measure other bone properties such as elasticity, microarchitecture, and thickness.[12,21,22] However, while qUS is generally accepted for osteoporosis screening in adults, given its effectiveness as a fracture risk indicator in postmenopausal women,[16,23] the same cannot be stated for its use in the pediatric population.[10,16]

The potential for pediatric osteoporosis and an increased fracture risk can be influenced by factors such as genetic disorders, lifestyle, chronic diseases, specific medications, calcium and vitamin D intake, and weight-bearing exercise.[3] While many pediatricians may not opt for further osteoporosis examination in children who experience bone fractures due to severe trauma, fractures resulting from mild trauma merit investigation for osteoporosis. However, reluctance to undergo DXA measurements, primarily due to radiation exposure, necessitates further studies to evaluate different modalities for their role in detecting osteoporosis. Achieving this requires screening tests that are minimally affected by external factors, exhibit high sensitivity and specificity, are easy to administer, have minimal or no side effects, and, most importantly, possess a high level of applicability and validity in the pediatric population. Despite the demonstrated utility of sonographic CoT measurement in adults,[13] there is a notable absence of evidence supporting its effectiveness in pediatric patients, as confirmed by this study.

Limitations of the study encompass various aspects that warrant consideration. First, a noteworthy limitation is the preponderance of osteoporotic patients within the study's patient group, constituting 12 of 41 patients. This preeminence of osteoporosis in the patient cohort has implications for the study's generalizability and the interpretation of its findings. Notably, osteoporosis signifies an advanced stage of bone loss compared to osteopenia, reflecting the severity of bone health issues within this subset of pediatric patients. This skewed patient group composition introduces a potential bias when drawing comparisons between the patient and the healthy control groups. Given the majority of osteoporotic patients in the study, any findings pertaining to CoT and its association with BMD may be disproportionately influenced by the characteristics specific to osteoporotic patients, potentially deviating from the broader pediatric population's characteristics according to varying degrees of bone health.

The above imbalance raises concerns about the applicability and representativeness of the study's conclusions for the wider pediatric population. Moreover, it may have ramifications for the statistical analyses and correlations involving CoT and BMD, as the patient group's composition may skew the results towards osteoporotic traits. Consequently, it is imperative to acknowledge this patient group's predominance as a notable limitation when discussing the study's findings and their relevance to the pediatric population as a whole.

Furthermore, it is crucial to acknowledge that all patients included in the study exhibited symptoms and laboratory findings that prompted suspicion of osteoporosis, leading to the recommendation of DXA measurements. Consequently, there exists the possibility that some bone properties of the control group may have exhibited similarities to those of the patients, potentially introducing confounding factors into the comparisons. Additionally, despite efforts to maintain similarities in age and sex distribution between the groups, factors such as body size, weight, physical activity, and other uncontrolled variables may have significantly influenced bone thickness measurements. Future studies could benefit from the inclusion of a control group comprised exclusively of volunteers, which may help mitigate potential biases.

Moreover, the grouping of osteopenic and osteoporotic patients for comparative analyses was necessitated by the limited number

of patients in each category. Although separate statistical analyses were conducted for subgroups, these efforts did not yield significant differences or noteworthy findings. This limitation underscores the challenge of conducting more nuanced analyses due to sample size constraints.

Finally, the study's primary focus on investigating the relationship between ultrasonographic CoT and BMD led to the inclusion of a restricted number of variables. Detailed data pertaining to patients' clinical characteristics, the specific type and etiology of osteoporosis, the presence of chronic rheumatological diseases, fracture history, occult bone fractures, and long-term follow-up complications were beyond the study's scope. These omissions highlight the need for future research endeavors to consider a broader array of factors and variables in the investigation of pediatric osteoporosis.

In conclusion, it is evident from our results that sonographic R-CoT, T-CoT, and M-CoT measurements did not differ in child patients with osteopenia or osteoporosis compared to healthy controls in our population. Similarly, no correlations were found between sonographic R-CoT, T-CoT, M-CoT values, and BMD T-scores obtained via DXA. In contrast to the adult population, sonographic CoT measurements appeared to be unassociated with BMD in children, and, accordingly, these measures cannot be used to assess BMD in the pediatric population.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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