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ORIGINAL ARTICLE

Predictors of trabecular bone score in school children

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Abstract
Summary Trabecular bone score (TBS) is a DXA-based tool that assesses bone texture and reflects microarchitecture. It has been shown to independently predict the risk of osteoporotic fracture in the elderly. In this study, we investigated the determinants of TBS in adolescents.
Introduction TBS is a gray-level textural measurement derived from lumbar spine DXA images. It appears to be an index of bone microarchitecture that provides skeletal information additional to the standard BMD measurement and clinical risk factors. Our objectives were to characterize the relationship between TBS and both age and pubertal stages and identify other predictors in adolescents.
Methods We assessed TBS by reanalyzing spine DXA scan images obtained from 170 boys and 168 girls, age range 10–17 years, gathered at study entry and at 1 year, using TBS software. The results are from post hoc analyses obtained using data gathered from a prospective randomized vitamin D trial. Predictors of TBS were assessed using *t* test or Pearson's correlation and adjusted using regression analyses, as applicable.
Results The mean age of the study population was 13.2± 2.1 years, similar between boys and girls. Age, height, weight, sun exposure, spine BMC and BMD, body BMC and BMD, and lean and fat mass are all significantly correlated with TBS at baseline (r=0.20–0.75, p<0.035). Correlations mostly noted in late-pubertal stages. However, after adjustment for BMC, age remained an independent predictor only in girls.
Conclusions In univariate exploratory analyses, age and pubertal stages were determinants of TBS in adolescents. Studies to investigate predictors of TBS and to investigate its value as a prognostic tool of bone fragility in the pediatric population are needed.

Keywords Adolescence · Peak bone mass · Trabecular bone score

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Introduction

Adolescence is a critical time for bone development, and for accruing peak bone mass (PBM), a major determinant of the risk of fracture later in life [1–3]. Individuals with the highest PBM after adolescence have the greatest protective advantage when bone density declines as a result of aging, illness, and diminished sex-steroid production [4].

Although adequate intake of calcium and vitamin D is important to achieve optimal peak bone mass [4], randomized controlled trials (RCT) in children have yielded inconsistent results for their effects on bone mineral density (BMD) in the

pediatric age group [5]. Winzenberg et al. demonstrated that while there was no consistent effect of vitamin D on bone mass in children, there was however a trend for small beneficial effect on lumbar spine BMD that seemed to be driven by findings in subjects who had a low serum vitamin D at entry [5]. The meta-analysis included results from an RCT we conducted in girls that had shown that girls with hypovitaminosis D at study entry, especially at premenarcheal stages, vitamin D significantly increased lean mass, lumbar spine BMD, and trochanter bone mineral content (BMC) [6]. The effects of treatment were also noticeable on hip structural analysis (HSA) parameters in girls but not in boys [7].

Trabecular bone score (TBS), is a textural index that evaluates pixel to pixel gray-level variations in the lumbar spine dual-energy x-ray absorptiometry (DXA) image, providing an indirect index of trabecular micro-architecture. TBS is not a direct physical measurement of bone microarchitecture, but rather an overall score that has been shown to be a significant predictor of osteoporotic fracture in adults independently of both BMD and major clinical risk factors [8]. Patients with similar BMD on DXA may have different TBS values. In several cross-sectional and longitudinal studies, both postmenopausal women and men with fragility fractures had lower TBS compared to their non-fractured counterparts; women who were neither osteopenic nor osteoporotic and sustained a fragility fractures had low TBS [9, 10]. A study by Ulivieri et al. also suggested that in some cases TBS appears to outperform DXA [11]. A group of experts have suggested that a TBS score equal to or more than 1.350 in post-menopausal women is considered normal [12]. A partially degraded microarchitecture would correspond to values between 1.200 and 1.350, whereas less than 1.200 corresponds to degraded microarchitecture [12].

We took advantage of our large randomized 1-year vitamin D trial conducted on school children and did post hoc exploratory analyses to investigate the following:

1. Relationship between age and puberty with TBS, by gender
2. Relationship between anthropometric and lifestyle factors with TBS, by gender
3. Relationship between vitamin D and TBS under baseline conditions and effect of 1 year supplementation with vitamin D on TBS

Methods

Study population

Participants were students recruited from four schools in Beirut, Lebanon during the period between December 2001 and June 2002. The age range was between 10 and 17 years of age. They were randomized to receive weekly doses of either a placebo or vitamin D3 preparations. There were two doses of vitamin D3; a low dose of 1400 IU/week (equivalent to 200 IU/day) and a high dose of 14,000 IU/week (equivalent to 2000 IU/day). The randomization process, dose selection, quality assurance, and monitoring have been detailed previously [6]. Clinical and laboratory evaluation, including DXA measurements, for all study participants was performed at our center.

Participants' baseline demographics included age, height, weight, and Tanner stages. Calcium intake (Ca), exercise (hours per week), and sun exposure (hours per week) were assessed at baseline and at 1 year by questionnaires [6]. Muscle power was measured using a squeeze grip ball that had a pressure gauge to measure grip strength. Serum 25-hydroxyvitamin D (25OHD), calcium (S-Ca), phosphorus (S-Ph), parathyroid hormone (S-PTH), and alkaline phosphatase (S-AlkPhos) were also measured at baseline and at 12 months. Pubertal status was determined by a physician using breast and pubic hair stages in girls and testicular and pubic hair stages in boys, according to the established criteria of Tanner [13]. Analyses were performed by Tanner stages derived using Tanner breast for girls and testicles for boys, as well as using Tanner hair for both genders, and results were quite comparable (data not shown). We however used pubertal status using Tanner hair in girls in Fig. 2 because of a more even distribution of girls in terms of numbers within each Tanner stage compared to Tanner breast, thus allowing more robust ANOVA analyses. We have also performed analyses evaluating girls during pre- and postmenarche and boys in early puberty defined as stages 1–2, and late pubertal stages as stages 3–5 [14].

Measurement of BMD

BMD and BMC of the lumbar spine, subtotal BMD, BMC, and composition were measured at baseline and at 1 year using a Hologic 4500A densitometer (Hologic, Bedford, MA; software version 11.2:3). The software determines BMC, fat mass, and nonfat soft tissue mass, identified in the software as lean mass [6]. In the analysis, we used subtotal body measurements, excluding the head, because inclusion of the head BMD in the calculation of total body BMD may lower the predictive value of some parameters for this variable [15]. This is in accordance with the official position of International Society for Clinical Densitometry (ISCD), that recommends the posterior-anterior (PA) spine and total body less head (TBLH), as the most accurate and reproducible skeletal sites for performing BMC and areal BMD measurements in the pediatric age group [16].

In our center, the mean±SD precision of the BMD measurements, expressed as the CV, for 280 same-day duplicate

scans performed during the study duration was less than 1.2± 0.9 % for the spine [6].

Measurement of TBS

Analyses of TBS were performed by Dr. Hans at the Bone Disease Unit at the University of Lausanne, Lausanne, Switzerland, using the TBS iNsight Software, Version 1.8 (Med-Imaps, Pessac, France) blinded from clinical outcome. TBS was evaluated based on gray-level analysis of the DXA images as the slope at the origin of the log-log representation of the experimental variogram [17], and calculation was performed over exactly the same region of interest as the BMD measurement. A research version of the commercialized TBS iNsight software was used. The TBS software was optimized for adults and not for children, and to avoid part of adult bias, built-in soft tissues correction was disabled and raw measurements were used. The TBS intra- and inter-machine precisions usually reported vary from 1.1 to 2.1 % depending on the studies and the population [9]. To date, TBS technology applies to spine DXA scans only.

Measurement of 25OHD

We measured serum 25OHD level at baseline and 12 months by a competitive protein binding radio-immunoassay using the Incstar Kit (Diasorin, Incstar, Saluggia, Italy), with intra- and inter-assay CVs less than 13 % at a serum concentration of 47 ng/ml. All samples were assayed together in the same run at the end of the study [7]. Our center participates in the international quality assurance program for the vitamin D assays; Vitamin D External Quality Assessment Scheme (DEQAS), London, UK.

Statistical analysis

Continuous variables were presented as arithmetic means and standard deviations. Values were rounded to the closest integer and one decimal for numeric measures except for BMD and TBS which were rounded to the closest three decimals. Continuous variables were checked for normality after constructing "normal P-P Plot of Regression Standardized Residual". ANOVA or independent *t* test was used to compare continuous variables across the treatment groups.

Pearson's correlation coefficients were used to detect the correlation between the potential predictors and TBS. Analyses were stratified by gender and pubertal stages in view of the substantial effect of puberty on bone mass and the differences in bone mass accretion during adolescence between genders. The predictors included in above analyses are the usual predictors known to correlate with bone mass in children: age, lifestyle, and anthropometric parameters. Predictors that were statistically significant at the univariate (also known as bivariate analyses or correlations) level for each gender were included in the corresponding multivariate linear regression model using stepwise linear regression model.

Pearson's correlation coefficients were also used to detect the correlation between potential predictors and percentage change in TBS at 1 year in the RCT. To explore such potential predictors, we calculated the mean value of the anthropometric and biochemical variables obtained at baseline and at 1 year, as a better integrated predictor of value over the 1 year. For the bone density and body composition variables, we used the percent changes from baseline.

P values less than 0.05 were considered to be statistically significant. All data analysis was conducted using SPSS 20 statistical software (SPSS Inc., Chicago, IL).

Least squares is a mathematical optimization technique which, when given a series of measured data, attempts to find a function which closely approximates the data (a "best fit"). It attempts to minimize the sum of the squares of the ordinate differences (called residuals) between points generated by the function and corresponding points in the data. The least mean squares (LMS) is known to minimize the expectation of the squared residual, with the smallest operations (per iteration). But it requires a large number of iterations to converge. The LMS statistical method proposed by Cole et al. [18] was used to construct the curves for the relationship between TBS and age using R software (v2.15.3).

Results

Baseline demographics

The overall study group consisted of 170 boys and 168 girls, mean age of 13.1±2 years. Girls had more advanced pubertal maturation. They also had higher TBS, spine BMC, and BMD. Conversely, boys had significantly heavier weight, higher calcium intake, sun exposure, lean mass, stronger muscle strength, and higher S-Ca and 25OHD levels. Boys and girls were comparable in the following variables: height, spine area, subtotal body BMC, subtotal body BMD, and subtotal fat mass (Tables 1 and 2).

Relationship between TBS and age

There was an overall increase in TBS as a function of age in both genders (Fig. 1). There was a suggestion for an inflection point at age 13 in boys (panel A), with a significant difference in mean TBS in those aged less than 13 years compared to those aged 13 years or more (1.324±0.086 vs. 1.368±0.099), and a proportional increment of 33 % between the two age sub-groups, $p=0.002$. Conversely, the increments were steadier, between age 10 and 17 years in girls (panel B). The

Table 1 Baseline characteristics of the study cohort, by gender

		Boys (n=170)	Girls (n=168)	p value
Continuous variables		Mean (SD)	Mean (SD)	
Age (years)		13.0±1.9	13.2±2.1	0.354
Height (cm)		154.8±13.4	152.6±9.9	0.086
Weight (kg)		51.9±16.7	47.6±11.5	0.006
BMI (kg/m^2)		21.1±4.3	20.2±3.5	0.021
Ca intake (mg/day)		775±353	677±365	0.013
Sun exposure (h/week)		9.2±5.6	7.4±5.5	0.003
Exercise (h/week)		7.9±6.9	3.8±4.8	<0.001
Muscle strength (psi)		12.6±3.6	11.2±2.2	<0.001
S-Ca (mg/dl)		10.0±0.4	9.9±0.4	0.002
S-Ph (mg/dl)		4.6±0.6	4.3±0.6	<0.001
S-AlkPhos (IU/l)		290.1±97.9	213.1±123.2	<0.001
S-PTH(pg/ml)		18.5±15.6	18.4±25.5	NS
25OHD (ng/ml)		16.5±6.7	14.2±8.1	0.003
Categorical variables		N (%)	N (%)	
Deficient vitamin D (<10 ng/ml)		21 (12.4)	57 (33.9)	<0.001
Insufficient vitamin D (10–20 ng/ml)		114 (67.1)	83 (49.4)	<0.001
Sufficient vitamin D (>20 ng/ml)		35 (20.6)	28 (16.7)	NS
Tanner stages[a]	1	45 (26.5)	28 (16.7)	0.034
	2	46 (27.1)	28 (16.6)	0.025
	3	31 (18.2)	21 (12.5)	NS
	4	30 (17.6)	47 (28.0)	0.027
	5	18 (10.6)	44 (26.2)	<0.001

[a] For boys, testicular size was used to stage pubertal status. But in girls, Tanner hair was used instead of Tanner breast because of a more even distribution of the proportions of girls in each Tanner stage

proportional increments in TBS between ages 10–11 and 16–17 years were 6.5 % in boys and 14 % in girls.

TBS at study entry by Tanner stages in both genders

There were significant differences in mean TBS by Tanner stages at study entry, in both genders, boys (Fig. 2a) and girls (Fig. 2b). In addition, TBS increased significantly when moving from early to late Tanner stages, with the most consistent difference being detected between early and late Tanner stages in both genders, p value<0.031 for all ANOVA post hoc comparisons (data not shown). When dichotomizing pubertal status, late-pubertal boys had significantly higher mean TBS than early-pubertal boys (1.371 vs. 1.322, p=0.01). Similarly, post-menarcheal girls had significantly higher mean TBS compared to pre-menarcheal girls (1.389 vs. 1.293, p<0.001).

Table 2 Baseline bone density and body composition characteristics of the study cohort, by gender

	Boys (n=170)	Girls (n=168)	p value
Continuous variables	Mean (SD)	Mean (SD)	
Spine BMC (g)	37.3±13.7	40.6±12.3	0.021
Spine BMD (g/cm^2)	0.661±0.126	0.733±0.139	<0.001
Spine area (cm^2)	54.8±9.7	54.2±7.6	NS
Subtotal body BMC (kg)[a]	1.4±0.4	1.3±0.3	NS
Subtotal body BMD (g/cm^2)[a]	0.747±0.113	0.733±0.089	NS
Subtotal lean mass (kg)[a]	33.1±10.1	27.5±5.4	<0.001
Subtotal fat mass (kg)[a]	13.3±8.4	15.0±7.2	0.051
TBS at baseline	1.345±0.095	1.370±0.099	0.019

[a] Measures are based on the subtotal body scan images (excluding head) as detailed in the "Methods"

Unadjusted correlations between TBS at baseline and potential predictors

TBS and demographic, anthropometric, and lifestyle factors

Age and height showed a positive correlation with TBS at baseline, both in the overall group of boys (r=0.30 and 0.23, p<0.002) and girls (r=0.66 and 0.61, p<0.001), respectively, Table 3. The correlation coefficients for both variables were higher in girls than boys and were mostly driven by findings in late-pubertal boys and post-menarcheal girls (data not shown). Weight also correlated positively with TBS at baseline in girls only (r=0.50, p<0.001), again a finding mostly driven by correlation in post-menarcheal girls (data not shown).

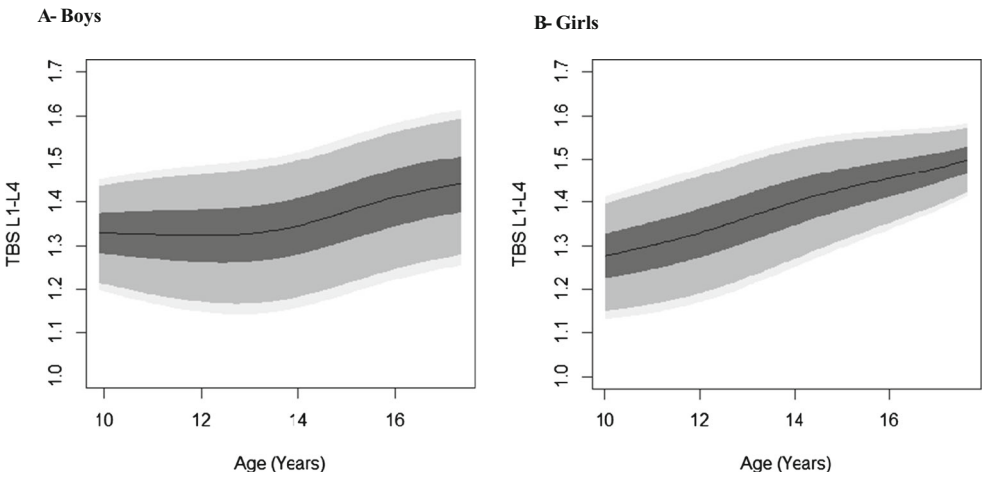

Fig. 1 TBS distribution as a function of age, at study entry, in boys (**a**) and girls (**b**). Curve fitting was implemented using the LMS using the R software (see Methods). There was a trend for a dip (inflection point) in TBS in boys at around 13 years of age with a significant difference in mean TBS between those aged below 13 years and those aged 13 years or older (1.324±0.086 vs. 1.368±0.099, p=0.002); in contrast, TBS steadily increased in girls with age

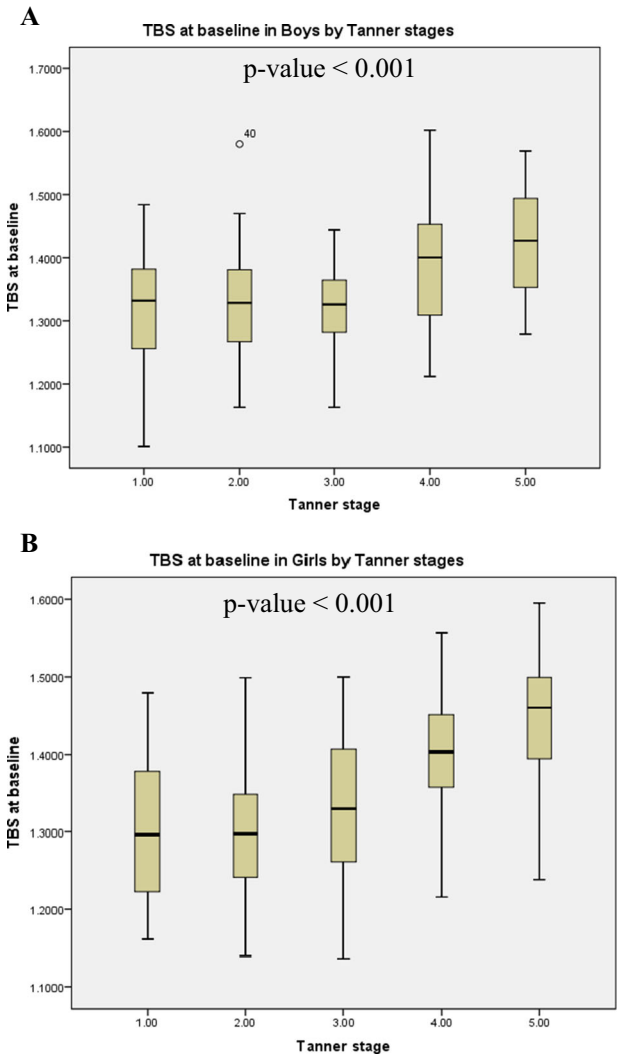

Fig. 2 TBS measures by Tanner stages in boys (**a**) and girls (**b**), at study entry. In both genders, TBS at study entry varied significantly between early and late Tanner stages with a p value<0.009. Details on differences between specific Tanner stages within each gender as derived from post hoc analyses are detailed in the text

Muscle strength and lean mass correlated positively with TBS in the overall groups of boys and girls, (r=0.305 and 0.415, p<0.001, respectively). Sun exposure, but not exercise, correlated positively with TBS at baseline in the overall group of girls (r=0.26, p=0.001, Table 3) and was also driven by correlations in post-menarcheal girls (data not shown).

TBS and BMD/BMC and body composition

TBS correlated positively with spine BMC, BMD, area, subtotal body BMC, BMD, and lean mass in both genders, (r ranging between 0.23 and 0.75, p<0.011), Table 3. These correlations were however stronger in girls than boys at both

Table 3 Correlation between TBS and clinical, densitometric, and body composition derived measures in overall study groups and by gender

Predictor	Boys		Girls	
	*R**	*p* value	*R**	*p* value
Age (years)	0.297	<0.001	0.662	<0.001
Height (cm)	0.231	0.002	0.611	<0.001
Weight (kg)	0.097	NS	0.503	<0.001
BMI (kg/m^2)	−0.061	NS	0.264	0.001
Muscle strength (psi)	0.305	<0.001	0.415	<0.001
Sun exposure (h/week)	0.111	NS	0.263	0.001
Spine BMC (gm)	0.499	<0.001	0.749	<0.001
Spine BMD(g/cm^2)	0.488	<0.001	0.718	<0.001
Spine area (cm^2)	0.438	<0.001	0.691	<0.001
Subtotal body area (cm^2)	0.144	NS	0.569	<0.001
Subtotal body BMC (kg)	0.330	<0.001	0.681	<0.001
Subtotal body BMD (g/cm^2)	0.471	<0.001	0.706	<0.001
Subtotal lean mass (g)	0.298	<0.001	0.566	<0.001
Subtotal fat mass (g)	−0.194	0.011	0.307	<0.001

*Values represent Pearson's r correlation coefficient

skeletal sites. This relationship was mostly present in the late pubertal subgroups (data not shown).

Whereas TBS correlated negatively with fat mass in boys including the overall group (r=−0.19, p=0.011) and the early pubertal subgroup (r=−0.43, p<0.001), this correlation was positive in girls, both in the overall group (r=0.31, p<0.001) and in the post-menarcheal subgroup (r=0.29, p=0.001).

Relationship between TBS at baseline and potential predictors on multivariate analysis

Height and lean mass were positively correlated with each other in both genders, (r=0.83–0.9), thus we constructed our stepwise linear regression models with and without height as one of the predictors of TBS. However, this did not change the coefficients of the predictors that were retained in the model as detailed below.

In boys, after adjusting for age, height, and pubertal stage; spine BMC (β=0.007), lean mass (β=−0.005), and fat mass (β=−0.003) remained as independent predictors of TBS, p<0.002. In girls, adjusting for sun exposure, height, pubertal stage, and subtotal lean and fat mass; age (β=0.009) and spine BMC (β=0.005) remained independent predictors of TBS, p<0.023, (Table 4). We chose spine BMC to include in the model because it had the strongest correlation with TBS among densitometric and body composition variables. These analyses were carried using actual Tanner stage as opposed to pubertal categories (early vs. late), and the coefficients and p values obtained were the same (data not shown).

Effect of vitamin D supplementation on TBS parameters at 1 year

There were no differences in any of the baseline characteristics (clinical, biochemical, densitometric, and TBS) between treatment groups within each gender (data not shown). We could not detect any significant effect of vitamin D supplementation on TBS values in both genders and by sub-group analyses by pubertal stages (data not shown). Because of the lack of any effect of vitamin D supplementation on TBS at 1 year in both genders, this allowed us to explore the relation between baseline demographic, antropometric, lifestyle, body composition and BMD variables with TBS and percent change TBS at 1 year, similar to what was implemented for baseline TBS in the previous sections.

Table 4 TBS and potential predictors on multivariate analysis

Variable	Coefficient (95 % CI)	p value
Boys		
Spine BMC (g)	0.007 (0.005; 0.009)	<0.001
Lean mass (kg)	−0.005 (−0.08; −0.02)	0.001
Fat mass (kg)	−0.003 (−0.04; −0.01)	0.002
Girls		
Spine BMC (gm)	0.005 (0.004; 0.006)	<0.001
Age (years)	0.009 (0.001; 0.016)	0.023

TBS percent change by Tanner stages and correlational analyses

There were significant differences in TBS percent change by Tanner stages at 1 year, in girls, with a biphasic pattern, but not boys, although a trend for steady increments was present in boys (Appendix). Significant correlations were observed between percent change in TBS and age, height, weight, BMC, and body composition parameters. These were however less consistent in their trends and significance, both within gender by pubertal status and between genders (data not shown).

Discussion

In these post hoc analyses, we have defined several predictors of TBS in school children. These include age, pubertal stage, anthropometric, lifestyle, body composition variables, and both BMD and BMC in both genders. The overall relationships between these parameters and TBS were mostly driven by correlations in the late pubertal stages. On multivariate analysis, spine BMC in both genders, age in girls, and subtotal body lean and fat mass in boys remained independent predictors of TBS. One-year vitamin D supplementation did not show an effect on TBS in both genders and by pubertal stages.

Lumbar TBS is an age-dependent variable [10]. Indeed, in our study age was shown to be an important determinant of TBS. In a study by Del Rio et al. [19] which included 2659 girls and 1468 boys aged between birth and 19 years, TBS increased with age and reached a plateau at age 13 years in girls. In our study, girls had a steady increase in TBS with age; however, there was an apparent inflection point in boys at the age of 13 years. This dip in TBS was evident when boys were dichotomized into two age groups: less and more than 13 years with the difference being significantly higher in the latter (1.324 vs. 1.368). In girls, age remained an independent predictor of TBS at baseline after adjusting for other significant covariates. The difference between Del Rio's findings and ours could be due to the large difference in sample size between the two studies, in the age group, we studied, but it could also reflect ethnic and environmental differences, and possibly interactions between genetic and environmental factors.

Understanding the factors associated with TBS may shed light on predictors of bone architecture in children and adolescents. In this study, we have tried to explore the predictors of TBS based on the information published in the previous

studies; however, little is known about TBS in children and most of the analyses were exploratory.

Much of the knowledge of predictors of TBS was derived from studies done on adult population. Leslie et al. investigated the clinical factors associated with lumbar spine TBS in 29,407 women aged >50 years from the Province of Manitoba, Canada [20]. Recent glucocorticoid use, prior major fracture, rheumatoid arthritis, chronic obstructive pulmonary disease, high alcohol intake, and higher body mass index were associated with reduced value of TBS [20]. A study by Kolta et al. evaluated the predictive value of TBS in patients with osteoarthritis involving 1254 postmenopausal women [21]. They found that a significant negative correlation between TBS and age (r=−0.40) and also with BMI (r=−0.22, p<0.001) and height (−0.025) [22]. Another study done on a Lebanese population aged 20–90 years, El Hage et al. showed a negative correlation between TBS and age in an older population (r=−0.39, p<0.001) [23].

In our study, TBS correlated with BMI both in the overall group of girls (r=0.26) and post-menarcheal sub-cohort (r=0.209), p<0.015. In boys, it was only significant in the early-puberty sub-cohort (r=−0.428, p<0.001). Compared to adult population which found a significant correlation between spine BMD and TBS (r=0.27) [24] and (r^2=0.04) [25], in our pediatric population, there was a significant correlation in both boys (r=0.48) and in girls (r=0.72). Our results therefore support the presence of correlation between TBS and densitometric and body composition variables which were documented in several previous studies done on adult participants [26, 27]. The positive correlation with age in young groups, as we and Del Rio et al. have shown, and the negative correlation in adult years spanning to the older ages are similar to that seen with BMD and suggests deterioration of bone structural architecture.

Change in TBS in response to osteoporosis therapy has been explored in several studies [12, 26, 28–30]. All of these studies however were in adult populations. Although we have previously shown significant effect of vitamin D supplementation on lean mass, bone area, total hip BMC, areal BMD, and hip structural parameters (narrow neck and intertrochanter regions and cross sectional area at the intertrochanter and shaft regions in this same population [6, 7], this was not mirrored by any significant change in TBS parameters. The above could be explained by the small sample size/low power, and the fact that the very modest differences between treatment arms, if any, may be too small compared to the substantial changes incurred by puberty. It may also reflect the fact that vitamin D supplementation in this age group may affect density/mineralization but not architecture. This may also reflect the fact that vitamin D may preferentially affect cortical more than trabecular bone, as shown in the main trial [6] and the hip structural analyses [7]. However, data on the effect of vitamin D on bone in the meta-analysis did not confirm such preferential effect [5].

We acknowledge several limitations in this study. Although data is from a previously published randomized clinical trial, all analyses performed herein were post hoc and exploratory. We did not adjust for multiple testing; however, most of the clinically important predictors exhibited a good-moderate linear correlation with TBS, thus adjusting for multiple testing is unlikely to change our findings. Nevertheless, we acknowledge that in view of the exploratory nature of our study, we did not adjust for multiple testing. Other limitations include the fact that we compared our results to the only study on TBS in children by Del Rio et al., the results of which are still unpublished, and that we may not be able to generalize our findings in the Lebanese adolescents to other populations at large. Finally, TBS applicability on children as is now may not be optimal. If further developments are done on children, a specific optimization would have to be performed, and likely as for DXA, a pediatric version would have to be released.

To our knowledge, this is the first study to explore possible predictors of TBS in a pediatric cohort. While the prognostic ability of TBS in adults has become well recognized in adults, further studies are needed to investigate determinants of TBS and elucidate its implications to bone health and fragility in children.

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Conflict of interest Khaled Shawwa, Asma Arabi, Mona Nabulsi, Joyce Maalouf, Mariana Salamoun, Mahmoud Choucair, and Ghada El-Hajj Fuleihan declare that they have no conflict of interest. Didier Hans is co-owner of the TBS patent and has corresponding ownership shares into medimaps group as well as chairman of the Board & part time CEO.

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