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Analysis of quantitative ultrasound graphic trace and derived variables assessed at proximal phalanges of the hand in healthy subjects and in patients with cerebral palsy or juvenile idiopathic arthritis. A pilot study

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ABSTRACT

Amplitude-dependent speed of sound (AD-SoS) and bone transmission time (BTT) are the quantitative ultrasound (QUS) variables usually assessed at proximal phalanges of the hand to estimate bone mineral status. The aim of the study was to provide a reference database for some additional QUS variables reflecting morphology of the ultrasound graphic trace according to gender, age, height, weight, and body mass index (BMI), and to assess their clinical usefulness.

Fifty-two patients (age 3.1–20.9 years) affected by cerebral palsy with spastic tetraplegia (CPST, $n=38$) or polyarticular active juvenile idiopathic arthritis (JIA, $n=14$) were examined. In addition to AD-SoS and BTT, two QUS variables derived from the morphological analysis of ultrasound graphic trace, such as energy, extrapolated from the area under the ultrasound signal received, and weighted-slope (W-slope), derived from the angular coefficient of the regression line fitting the top point of the peaks of the ultrasound signal, were measured by phalangeal QUS (DBM Sonic, IGEA). The values of all the QUS variables measured in the patients were compared with our own sex- and age-reference values ($n=1083$, 587 males and 496 females, aged 3–21 years).

The mean values of AD-SoS, BTT, energy, and W-slope were reduced ($P<0.0001$) in patients as a whole compared with normative data (-2.4 ± 1.2, -2.7 ± 1.5, -2.5 ± 1.1, -2.5 ± 1.1 Z-score, respectively). Fractured patients showed lower ($P<0.001$–$P<0.0001$) values of the QUS variables than fracture-free patients (AD-SoS, -3.3 ± 1.2 and -1.8 ± 0.9; BTT, -3.9 ± 1.7 and -1.8 ± 1.1; energy, -3.2 ± 1.2 and -2.2 ± 0.7; W-slope, -3.4 ± 1.4 and -2.2 ± 0.9 Z-score, respectively). There was no difference ($P=$NS) between patients with CPST and those with JIA. Age and height were positively correlated with all the QUS variables ($r=0.55$–0.79, $P<0.01$–$P<0.0001$). QUS variables were positively correlated among them ($r=0.74$–0.94, $P<0.0001$). Age and number of fractures were independent predictors of the QUS variables (coefficients: AD-SoS, 11.466 and -17.642; BTT, 0.049 and -0.045; energy, 1.072 and -1.303; W-slope, 0.046 and -0.067; respectively).

In conclusion, measurement of QUS variables derived from the morphological analysis of the ultrasound signal could give additional information in estimating bone mineral status in children and adolescents, probably reflecting some aspect related to bone structure.

Introduction

Some studies have shown that quantitative ultrasound (QUS) methods are a useful tool for assessing bone mineral status in children with disturbances of growth and disorders of bone and mineral metabolism or chronic diseases, and for identifying children at risk of fracture [1–3].

Two main variables are measured by QUS devices, which derive from velocity or attenuation of the ultrasound waves through the bone tissue; they are influenced by bone density, architecture, and elasticity [4–6]. Amplitude-dependent speed of sound (AD-SoS) that reflects the velocity, partly amplitude-dependent, at which the ultrasound wave cross the bone and soft tissue [7], and bone

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transmission time (BTT) that reflects the transmission time of the ultrasound wave through the bone tissue [8] are the variables currently assessed by the phalangeal QUS device [3]. Low values of AD-SoS are associated with a reduced bone mineral density (BMD) assessed by dual energy X-ray absorptiometry (DXA) [2,9]. Reduced BTT values are reported in various disorders [10–15].

Studies in post-menopausal women [16,17] and in adults with osteoporosis or primary hyperparathyroidism [18], or osteomalacia [19], have shown that, by a morphological computerized analysis of the ultrasound graphic trace, phalangeal QUS device may provide some additional QUS variables which could be useful in investigating bone structure. To our knowledge, no data on the clinical application of phalangeal QUS variables derived from the morphological analysis of the ultrasound signal are available in children.

The aim of our pilot study was to assess the clinical usefulness of some QUS variables derived from the analysis of the ultrasound graphic trace in estimating bone mineral status. For this purpose some patients affected by disorders commonly associated with a reduced BMD, such as cerebral palsy with spastic tetraplegia (CPST) and juvenile idiopathic arthritis (JIA) were examined and the results were compared with those obtained in healthy subjects.

Materials and methods

Patients

We examined a total of 52 patients, aged 3.1–20.9 years, affected by CPST ($n=38$) or JIA ($n=14$). Clinical findings of the examined patients are given in Table 1. All patients with CPST had severe neurological disability, were on wheelchair, were moderate-to-severely mentally retarded, and lived in their family; all patients had lacked any independent motor function, even for basic postural control. No patient had chromosomal abnormalities. All patients with JIA had polyarticular active disease and they were receiving chronic corticosteroid treatment (prednisone, starting dose 1.3 ± 0.4 mg/kg per day, maintenance dose 0.6 ± 0.1 mg/kg per day, cumulative dose 830 ± 322 mg/kg; mean duration of treatment 2.1 ± 0.3 years; range 1.5–2.7 years).

The patients with CPST were diagnosed and examined at the Department of Developmental Neuroscience, and Division of Child Neurology and Psychiatry. The patients with JIA were enrolled at the Department of Pediatrics of our University.

Severity of the disease

In patients with CPST neurological disability was assessed using Gross Motor Functional Classification Scale (GMFCS) [20]. Briefly, disability corresponding to GMFCS level one and two was defined as mild, level three as moderate, and level four and five as severe. GMFCS level five includes children who lacked any independent motor function, even for basic postural control. All patients with CPST enrolled in the study were classified at level five.

Polyarticular JIA was diagnosed according to the revised International League of Associations for Rheumatology classification criteria [21]. Disease activity was assessed by using the Pediatric Total Joint Assessment, Health Assessment Questionnaire for children, and Global Assessment of Disease Activity Scale for children with JIA [22].

Moreover, in all fractured patients with CPST and JIA the severity of the injury causing fracture(s) and site(s) of fractures were recorded.

Table 1
Clinical findings of the examined patients.

Variable	CPST	JIA	*P*
N	38	14	–
Age (years)	11.0 ± 5.0	12.0 ± 2.8	0.48
Sex (males/females)	24/14	4/10	–
Height[a] (cm)	129.2 ± 27.2	140.4 ± 13.8	0.15
Weight (kg)	31.8 ± 20.6	44.5 ± 16.5	<0.05
BMI	17.0 ± 4.9	21.9 ± 5.0	<0.01

Values are given as mean ± SD.
[a] Length in patients with CPST.

Assessment of fracture findings

In patients with JIA the severity of injury was classified as slight or moderate according to Landin [23]. Slight trauma consisted of an injury caused by forces exerted by the injured individual (e.g. falling to the ground from standing on the same level, ball playing, running); moderate trauma consisted of an injury caused by forces connected to height above ground level (e.g. falling from between 0.5 and 3 m) or velocities (e.g. falling downstairs, from a bicycle or scooter, from swings or slides). Two or more fractures of the same bone caused by the same injury were recorded as one fracture.

Landin's classification [23] was not applicable in our patients with CPST. In these patients we classified the severity of injury causing fractures as very low or low. A very low trauma consisted of an injury occurring during the body passive movements needed for personal cleanliness or derived from passive physical therapy; a low trauma consisted of an injury caused by forces exerted by the injured individual, as a strong muscular spasm during a convulsion. In all patients, the sites of fractures were confirmed by examining the plain radiographs.

Age- and sex-normative data

Normative data for AD-SoS, expressed as mean ± SD, were previously obtained in 1083 (587 males and 496 females) healthy subjects, aged 3–21 years [24]. All the QUS measurements were stored in a database and they were used to calculate centile curves for AD-SoS, BTT, energy, and weighted slope (W-slope) by using a Box-Cox power transformation according to Cole [25] and Cole and Green [26] which involves normalizing the data at each age by the *LMS* method, where *L* is the distribution normal, *M* is the median, and *S* is the coefficient of variation of the distribution. Main details of all the calculations have been previously reported [27].

To allow a comparison between different ages the values of the QUS variables obtained by the *LMS* method were converted directly to *Z*-score using the formula:

$$Z-\text{score} = \frac{[\text{Measurement}/M(t)]^{L(t)} - 1}{S(t)L(t)}$$

where measurement is the child's QUS parameter assessed (AD-SoS, BTT, energy, or W-slope) and $L(t)$, $M(t)$, and $S(t)$ are values read from the smooth curves for the child's age, according to sex.

Study design

QUS variables were measured at proximal phalanges of the hand at the nondominant hand in healthy subjects and in patients with JIA and at left hand in all patients with CPST.

In all patients QUS variables were compared with our own sex- and age-reference values; a value of each variable below −2.0 *Z*-score was considered to identify a condition of altered bone mineral status according to chronologic age.

Moreover, the values of the QUS variables between patients who had a history of fractures (fractured) and those who had never fractured (fracture-free) were compared.

Anthropometric measurements

In patients with JIA standing height and body weight were measured with a wall-mounted stadiometer and a mechanical balance, respectively. In patients with CPST accurate height measurements were not possible caused by contractures or mild to severe