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# Quantitative Ultrasound (Qus) of The Calcaneus in Children with Idiopathic Hypercalciuria

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## Abstract

***Background and Aims:*** Idiopathic hypercalciuria (IH) is defined as hypercalciuria with no detectable cause. Patients with IH might have low bone mineral density (BMD) with increased fracture risk and tendency to short stature. Our aim was to perform calcaneal quantitative ultrasonometry (QUS) in children with IH and relate to calciuria, body height and number of prevalent fractures (Fx).

***Materials and Methods:*** 11 children (8 girls, 3 boys; mean age 11.3±3.1 y) with IH (calciuria>0.1 mmol/kg/24h) were enrolled. The patients were not receiving any drugs known to influence bone metabolism. Fx was 1.4±1.2 per patient. Body height was recorded and QUS was measured on both heels with Cuba Clinical. The 24-h U-Ca excretion (U-Ca/24 h) was assessed and calculated in mmol/kg/24 h. Results were expressed as Z-scores ± SD and matched to values of healthy European pediatric population.

***Results:*** Body height was normal for chronological age (p=0.96). Broadband ultrasound attenuation (BUA), either age-related of height-adjusted, was normal (p=0.18 and 0.26, respectively). Velocity of sound (VOS), either age-related of height-adjusted, was low (p=0.002 and p=0.003, respectively). We found no correlations between Fx and BUA or Fx and VOS (either age-related or height-adjusted) (r =0.01 and 0.02; r =0.32 and 0.26 ). Neither were there any correlations between U-Ca and Fx (r =0.28), or U-Ca and BUA (r =0.21 and 0.32) or VOS (r =0.40 and 0.42), respectively.

***Conclusions:*** Contrary to previous observations where dual-energy X-ray absorptiometry (DXA) was used for BMD evaluation, we found only mild decrease in one QUS parameter with no relationship to fracture rate or calciuria.

Children with IH have normal values of BUA and low VOS, not related to calciuria and Fx. QUS is not a surrogate to DXA and its role needs to be further clarified.

***Keywords:*** Quantitative Ultrasound, Idiopathic Hypercalciuria, Bone Density

## Introduction

Idiopathic hypercalciuria (IH) is defined as hypercalciuria that persists after the correction of dietary imbalances and has no detectable cause (1). IH in childhood is defined by urinary calcium excretion

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exceeding 0.1 mmol/kg/24 hours and can be manifested by hematuria, dysuria, recurrent abdominal pain and enuresis. Patients with IH are also at high -risk of urolithiasis and osteoporosis. Previous studies implementing dual-energy X-ray absorptiometry (DXA) revealed low bone mineral density (BMD) in IH patients (1-12). Furthermore, increased fracture rate and tendency to short stature may also occur in IH patients (1-10). Quantitative ultrasound (QUS) of calcaneus has been repeatedly used in women with postmenopausal osteoporosis and men over the age of 65, and obtained results were considered as good indicators of bone quality and predictors of fracture rate (13, 14).

Calcaneal QUS has been so far only scarcely used for the evaluation of bone quality in patients with IH (12). Therefore we aimed to perform calcaneal QUS in children with IH and to relate QUS parameters to urinary calcium excretion, body height and number of prevalent fractures.

## Materials and Methods

### *Patients*

11 children (8 girls, 3 boys; mean age 11.3 ± 3.1 years) with IH (urinary calium excretion > 0.1 mmol/kg/24 hours in three consecutive 24-hour urine samples) were enrolled. The children were referred because of hematuria, dysuria and/or prevalent fractures and were not receiving any drugs known to influence bone metabolism. The patients were studied during 1997-2000 at the Department of Pediatrics, 1st Medical Faculty, Charles University, Prague, Czech Republic. Informed consent, in accordance with the Declaration of Helsinki, was obtained from all study patients and/or their legal representatives prior to the study procedures. The design of the work fully conforms to the standards currently applied in the Czech Republic. The serum levels of calcium, phosphate, magnesium, parathyroid hormone (S-Ca, P, Mg, PTH) and serum activity of alkaline phosphatase (S-ALP) were within normal laboratory reference ranges. Mean number of prevalent fractures was 1.4 ± 1.2 (SD) per patient in the preceding two years.

### *Procedures*

Body height was recorded on the day of the QUS measurement to the nearest ± 0.5 cm on a calibrated stadiometer. Cuba Clinical (McCue Ultrasonics, UK) dry ultrasound portable device was used to measure velocity of sound (VOS), expressed in m/s, and broadband ultrasound attenuation (BUA), expressed in dB/MHz. VOS depends on the density and elasticity of the bone, while BUA is determined by bone density and by trabecular quality, spacing and orientation (14-16). The measurements were performed at both the heels. For each individual, the mean values of BUA and VOS [(left heel + right heel)/2] were calculated to eliminate the possibility of significant intraindividual differences in QUS parameters on right and left foot as mentioned before (16). Measurement precision, based on regular weekly phantom measurements, was expressed as coefficient of variation: 3.2% for BUA and 0.18% for VOS, respectively. For the evaluation of calciuria, the urine was collected on the same day. The 24 hours urinary calcium excretion was assessed by photometry in a urinary sample from 24 hours collected urine and calculated in mmol/kg body weight/24 hours (U-Ca/24 h/kg).

To eliminate the influence of age, the obtained results of body height, BUA, VOS and U-Ca/24 h/kg were expressed as standard deviation scores (SDS) or Z-scores by the equation SDS = (actual individual value – mean value for age)/standard deviation for age. Czech anthropometric parameters from a 1991 survey (17) and previously obtained QUS values of the healthy Czech paediatric population (206 boys and 203 girls 5-18 years old) were used as reference data for the Z-score calculation. The QUS results were also calculated as height-adjusted values with the use of height-matched standards obtained from the above mentioned reference paediatric population.

**Table 1.** Body height, quantitative ultrasound parameters and calciuria (expressed as Z-scores) compared to reference values

| Parameter | mean | SD | P (versus reference values) |
|---|---|---|---|
| Height | -0.02 | 3.10 | 0.96 |
| BUA | -0.33 | 0.76 | 0.18 |
| BUA height adjusted | -0.43 | 1.20 | 0.26 |
| VOS | -1.46 | 1.14 | **0.002** |
| VOS height adjusted | -1.54 | 1.31 | **0.003** |
| U-Ca/24 h/kg | +3.02 | 2.04 | **0.0001** |

**SD**, Standard Deviation; **BUA**, Broadband Ultrasound Attenuation; **VOS**, Velocity of Sound; **U-Ca/24h/kg**, 24 hour urinary calcium excretion.

U-Ca/24 h/kg results were matched to values of healthy European paediatric population (18).

***Statistics***

The results of body height, U-Ca/24 h/kg, BUA and VOS measurements are reported as Z-scores (mean ± SD). The statistical analysis was performed by t-test. Correlation analysis was performed to compare the relationship among respective parameters. For all results, $p < 0.05$ was required for statistical significance.

## Results

Body height was normal for chronological age. BUA, either age or height related, did not differ significantly from the reference values. VOS (both age-related and height-adjusted) was decreased (Table 1). We found no correlations between fracture rate and BUA (either age-related or height-adjusted) or fracture rate and VOS (age-related or height-adjusted). There were no correlations between U-Ca/24 h/kg and fracture rate, or U-Ca/24 h/kg and BUA or VOS, either age-related or height-adjusted, respectively (Table 2).

## Discussion

We did not observe growth retardation in our group of patients, which is contrary to other observations including our previous report of another group of children with IH (1-3), but is consistent with other findings (8, 19). It seems likely that growth retardation is more severe in complex hereditary tubular disorders than in isolated ones, such as IH (1, 19).

The present study demonstrates low VOS in children with IH and normal values of BUA. These parameters were not related neither to calciuria or fracture rate. This is in contrast to studies implementing DXA, where low BMD, closely related to high urinary calcium excretion were observed (1-11 ). However, we are aware of the fact that our sample of IH patients is too small to draw general conclusions. So far, there is only one published study where both QUS and DXA were used to evaluate bone status in 17 children with IH (12). The results yielded normal QUS parameters (expressed as stiffness) and low BMD values measured by DXA in comparison to reference values (12), bearing similarity to our results and also to BMD studies in IH. The explanation of low VOS and normal BUA in our patients might result from the fact that VOS reflects bone density, while BUA is dependent on trabecular quality, spacing and orientation. Based on available evidence, we suggest that children with IH have normal or

**Table 2.** Correlations between quantitative ultrasound parameters, calciuria and fracture rates, respectively (R and p-values)

| Parameters | Fracture rate | U-Ca/24 h |
|---|---|---|
| BUA | R = 0.01 | R= 0.21 |
| | p = 0.98 | p = 0.35 |
| BUA height adjusted | R = 0.02 | R = 0.32 |
| | p = 0.98 | p = 0.26 |
| VOS | R = 0.32 | R= 0.40 |
| | p = 0.26 | p = 0.20 |
| VOS height adjusted | R = 0.26 | R = 0.42 |
| | p = 0.31 | p = 0.19 |
| Fracture rate | NA | R = 0.28 |
| | | p = 0.30 |

**BUA**, Broadband Ultrasound Attenuation; **VOS**, Velocity of Sound; **NA**, Not Applicable; **U-Ca/24h/kg**, 24 hour urinary calcium excretion

only slightly decreased QUS parameters and low BMD measured by DXA. The mechanical properties of bone are not exactly reflected by bone density, however BMD, as assessed by DXA, remains an important predictor of fracture risk.

QUS might give important information concerning bone quality in adult patients, in particular in the postmenopausal women, as QUS parameters are related to bone density and most probably to bone quality (12-16). However, the applicability of QUS in the assessment of bone strength or fragility in the paediatric population remains unclear and is clearly not a surrogate to DXA. In conclusion, children with IH have normal values of BUA and low VOS that are not related to calciuria and fracture rate.

## Conflict of Interest

None declared.

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