Bone

G178 BONE AND MUSCLE GEOMETRY IN THE PRE-PUBERTAL SKELETON

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Introduction: A bone's strength is determined by its size, shape, and amount of mass contained within the periosteal envelope. Therefore, to understand how bones adapt to high intensity exercise, measurements other than bone mineral density should be made; baseline peripheral quantitative computed tomography (pQCT) data from an ongoing trial have been analysed to investigate these adaptations. We hypothesise that compared with sedentary controls (n 42), gymnasts (n 44) will have larger bones with thicker cortices and therefore greater stress–strain indices (SSI, related to bone bending strength) in the radius (R) and tibia (T). Muscle cross sectional area (CSA) muscle force will also be greater in the gymnasts.

Method: Bone and muscle measurements were measured at 50% R and 65% T using pQCT (XCT-2000, Stratec, Germany); loop analysis was used to measure bone mineral content (BMC), cortical thickness, SSI, and periosteal and endosteal circumferences.

Results: Natural logs of bone and muscle variables were taken. Results are given as percent mean difference (ratio controls: gymnasts). After adjustment for sex and height gymnasts had higher cortical bone area (R:13% mean difference, p 0.04; T:7% mean difference, p 0.01), mineral content (R:14% mean difference, p 0.04; T: 7% mean difference, p 0.03), and thicker cortices (R:17% mean difference, p 0.02, T:8% mean difference, p 0.02) in both the R and T than controls. Consequently their SSI was higher in both bones (R:14% mean difference, p 0.004, T:7% mean difference, p 0.04). Compared with controls, the gymnasts also had greater muscle CSA (R:17% mean difference, $p<0.001$, T:6% mean difference, p 0.03) and grip strength (11% mean difference, p 0.03).

Conclusions: The bones of gymnasts have higher SSI than sedentary controls. This is likely to be achieved by an increase in cortical BMC and area; the increase in area itself reflects deposition of bone on the periosteal surface (NS). These extremely small adaptations have a highly beneficial effect on the strength of the bone, thus allowing the appendicular skeleton of pre-pubertal gymnasts to withstand the forces it is subjected to by muscles during activity.

G179 WHAT CAUSES RECURRENT FRACTURES IN CHILDHOOD?

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Background: Fractures are frequent in childhood with the incidence peaking around the time of peak height velocity. Previous reports have indicated a variety of potential contributors to fracture risk including low bone mass, milk avoidance, lack of habitual physical activity, asthma, high body mass index, and a high consumption of carbonated beverages.

Aims: We wished to test the hypothesis that children who suffer recurrent fractures have different underlying risk factors from those who have fractured only once.

Methods: We studied 150 children aged 4–16 years; 50 who had suffered multiple fractures, 50 who had fractured for the first time, and 50 fracture free controls. Children were seen within 2 days of their fracture. Bone mineral content and density by total body and lumbar spine DXA, anthropometry, and grip-dynamometry were measured. Milk intake, physical activity levels, asthma prevalence, and carbonated beverage consumption were recorded using questionnaires.

Results: Children who fractured had a significantly lower BMC and a BMD at all sites than controls (L2-4 BMC p 0.0002; L2-4 aBMD $p<0.0001$; TB BMC $p<0.0001$; TB aBMD $p<0.0001$). There was no difference in bone mass adjusted for body size between children with one or multiple fractures. The factors that in combination were associated with an increased risk of recurrent fracture were increased body mass index, reduced consumption of milk, and, independently, increased consumption of carbonated drinks. Lack of exercise increased recurrent fracture risk; parental attitudes to physical activity dictated children's activity patterns.

Conclusions: Children with fractures have lower bone mass for body size than children without fractures. The factors that in combination predict multiple fractures include modifiable items such as diet and exercise. There are important public health implications of this work given the current trends to lower physical activity and increased body mass index at the time when fracture incidence is at its highest.

G180 BONE MINERAL STATUS IN CHILDREN AGED OVER 3 YEARS UNDERGOING LIVER TRANSPLANTATION

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Background: Children with chronic liver disease are at risk of reduced bone mineral density (BMD), which may worsen in the months following liver transplantation (OLT). Probable aetiological factors include vitamin D malabsorption, immobility, and immunosuppressive drugs.

Aim: To assess bone mineral health and vitamin D status in children over 3 years undergoing OLT.

Methods: Children with cholestatic liver disease underwent dual energy *x* ray absorptiometry (DXA) at the time of listing for OLT and bone mineral density was compared with normative values for children over 3 years. Volumetric bone density (BMAD) was calculated for the lumbar spine to adjust for body size. Bone ions, parathyroid hormone (PTH), and vitamin D metabolites were also measured.

Results: 12 children (6 male; median age 9.4 years (3.0 to 14.6 years)) underwent assessment at a median of 1.5 months pre OLT. All were ambulant and only one previously had fractures. Ten were receiving vitamin D supplements and seven supplemental feeding. Median height and weight *z* scores were −0.7 (−4.8 to 3.0) and −0.2 (−3.3 to 1.8), respectively. Ionised calcium, phosphate, and magnesium were low in 4, 7, and 3 children, respectively, but no child had a raised serum PTH. Although 9/10 and 5/10 had low 25-OH vitamin D2 and 25-OH vitamin D3, respectively, 1,25-$(OH)_2$ vitamin D was normal in all cases. Median BMD *z* score for L2 to L4 lumbar spine was −1.2 (−2.5 to 0.02) and for total body was −1.0 (−1.61 to −0.34). Median BMAD *z* score was −0.7 (−3.0 to −1.3).

Conclusions: In children aged over 3 undergoing OLT, bone mineral density, vitamin D, and PTH status were better than anticipated. Optimal bone health can be achieved in children with chronic liver disease prior to OLT using vitamin D supplementation and ensuring optimal nutrition.

G181 EVALUATION OF THE SUNLIGHT OMNISENSE QUANTITATIVE ULTRASOUND MACHINE IN CHILDREN

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Measurement of bone mass in children is performed for both clinical and research purposes, generally using bone densitometry. Quantitative ultrasound (QUS) predicts fracture risk in adults and has the advantage of avoiding radiation exposure while also being portable. We evaluated the Sunlight Omnisense QUS device in children aged 3–19 years.

Methods: Speed of sound (SOS) was measured at the distal radius and proximal tibia in 53 subjects (26 healthy controls (C), 21 with cystic fibrosis (CF), and 6 with glycogen storage disease (GSD). Duplicate measurements were made by one operator in 43 subjects (20 C, 16 CF, 6 GSD). Lumbar spine bone mineral density was measured (LSBMD; GE Lunar Prodigy).

Results: Radius SOS (SD) scores for age (machine reference data) were similar for the three groups but GSD patients had significantly lower tibia SOS scores (−1.3 (1.1)) and LSBMD SD scores (−1.6 (1.4)) than either C (SOS −0.5 (1.0); LSBMD 0.01 (1.1)) or CF patients (SOS −0.2 (0.8); LSBMD −0.43 (0.82)). Radius scores were not related to weight or height; tibia scores were negatively associated with weight (p 0.04). Correlations between SOS and LSBMD adjusted for age and sex were weak and non-significant, and agreement between techniques in categorising subjects as low or normal (SD score $<$ or >-1.0) was low (κ 0.19 for LSBMD and radius SOS; −0.04 for LSBMD and tibia SOS). Radius and tibia SOS were correlated (r 0.35, p 0.01). Percentage CV for duplicate measurements was 0.16 and 0.85 for radius and tibia, respectively.

Conclusions: Agreement between SOS and BMD in this group was low, and the two measurements identify different individuals as

abnormal. For the radius, measurements are independent of body size, so fewer small individuals may be diagnosed with abnormal SOS than low BMD. Without a gold standard, it is difficult to determine which technique is more useful in this age group, and the predictive value of both techniques for outcome needs investigation. However, the good precision of this QUS technique together with its portability suggest that further evaluation is warranted.

G182 BONE HEALTH ASSESSED BY DUAL *X* RAY ABSORPTIOMETRY (DXA) AND QUANTITATIVE ULTRASOUND (QUS) IN GLYCOGEN STORAGE DISEASE

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Introduction: Glycogen storage diseases (GSD) may be associated with poor bone mineralisation due to factors including chronic lactic acidosis and poor diet. Most previous studies have measured peripheral bone mass.

Aim: To assess bone health in patients with type I and type III GSD and relate measurements to disease type, body size, and fracture history.

Methods: Bone mass was measured using dual *x* ray absorptiometry (DXA; GE Lunar Prodigy) at the lumbar spine (LS; L2-4), whole body (WB), and left hip in 29 patients (18 male) with GSD (14 type I, 15 type III) aged 3.8–41 years (mean 21). Speed of sound (SOS) was measured at the distal radius and proximal tibia using QUS (Sunlight Omnisense; n 15).

Results: Mean weight and height were 0.20 (SD 1.25) and −0.95 (1.19). Age matched bone mineral density (BMD) were −1.69 (1.45) for LS, −1.18 (1.28) for WB and −0.80 (0.89) for total hip. 54%, 30%, and 13% of patients had BMD <−2.0 for LS, WB, and hip, respectively. 33%, 38%, and 38% of the adult patients (n 16) had T scores in the osteopenic (<−1.0) range for LS, WB and hip, respectively, with 40%, 25%, and 6% in the osteoporotic range (<−2.5). For SOS, 7% had standard deviations <−2.0 at the radius and 20% at the tibia. SOS was unrelated to body size. To assess the effect of body size, percentage expected bone mineral content (BMC), bone area (BA), BMD, and bone mineral apparent density (BMAD) were calculated. Percentage expected values were lowest for BMC (LS mean 72.3%, (19.8); WB 76.8% (14.5)) and highest for BMAD (LS mean 89.0% (12.8); WB 98.8% (8.5)) but percentage expected BMAD was <100% for LS ($p<0.001$). There were no significant differences between patients with type I or III GSD or between those with (38%) or without a history of fracture.

Conclusions: Patients with GSD types I and III are short and have low bone mass, with a significant proportion of adults classified osteopenic or osteoporotic by DXA. Small skeletal size contributes to low bone mass but there was evidence of reduced LS mineralisation after adjusting for size. Fewer patients are classified as abnormal by radial QUS than by DXA, possibly because this technique is not affected by body size.

G183 THE ASSESSMENT OF BONE BY QUANTITATIVE ULTRASOUND IN PRETERM AND TERM NEONATES

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Quantitative ultrasound (QUS) is a non-invasive and portable method currently used in estimating bone strength in adults. Our aim was to assess the feasibility of QUS for studying bone health in term and preterm infants. Infants born between 24–42 weeks gestation were eligible for inclusion. Following LREC approval, informed consent was sought from parents. Babies were recruited from three maternity units in Glasgow. Speed of sound (SOS) measurements were performed in the first week of life using the Sunlight Omnisense 7000P ultrasound machine and compared with the reference range provided by the manufacturers. A total of 108 infants (58 male), with a median gestation of 37 weeks gestation (range 24–41 weeks) participated in the study. Mean intraobserver coefficient of variation (CoV) for repeat measurements at the same site (tibia) was 1.1%. Mean interobserver CoV for measurements by two observers at the same site (tibia) was 1.2%. In 20 infants measurements were performed at both tibia and radii. There was no significant difference between radial and tibial measurements (p 0.5.) The median CoV for simultaneous measurements at all four sites was 2.4%, left and right radius was 1.8%, right radius and tibia was 1.5%, left radius and tibia was 1.6%, and left and right tibia was 0.7%. The 68 term (median gestation 40 weeks) infants had a median tibial SOS of 3079m/s, quartiles 3010, 3141 m/s. There was no correlation between sex and SOS in this group. The 46 preterm (median gestation 32 weeks) infants' median tibial SOS was 2953 m/s, quartiles 2890, 3013 m/s. This difference was statistically significant $p<0.0001$ from the term group. Increasing gestation is associated with increasing tibial SoS. All of our results were within the manufacturers' reference range. The Omnisense 7000P is easy to use, and able to measure SOS in neonates with reproducible results. Its utility in assessing bone health in preterm infants as well as other infants at risk of adverse bone health deserves further exploration.

G184 VITAMIN D DURING PREGNANCY AND GROWTH IN EARLY INFANCY

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Background: Studies in vitamin D deficient pregnant women have shown that supplementation influences postnatal growth with infants of supplemented mothers being longer and heavier at the age of 1 year irrespective of postnatal vitamin D supplementation.

Aims: The aims of this study were to determine whether endogenous variation in maternal vitamin D as assessed by cord blood 25 hydroxy vitamin D (25 OHD) concentrations was associated with variation in body size during the first 6 months of life.

Methods: 110 pregnant women were recruited into the study. Cord blood vitamin D was measured in 101 and the infants measured at birth, 3 (n 87) and 6 (n 89) months. Details concerning maternal history, parental heights and weights, mode of feeding and postnatal vitamin D supplementation, and ethnicity were recorded. 88 mothers were white Caucasian.

Results: Serum 25 OHD levels for the group as a whole were low (mean median 15.4 nmol/l) with 71% being below 20 nmol/l, one of the suggested thresholds for vitamin D insufficiency. Ethnicity and prenatal vitamin D supplementation were associated with differences in cord blood 25 OHD. The only growth parameter that showed a relationship with cord blood 25OHD was head circumference *z* score at 6 months of age.

Conclusions: No definite association between body size at birth, 3 or 6 months and cord blood 25 OHD could be shown. The values recorded for 25 OHD in this study were generally lower than those recorded previously and approximately one third of those of healthy, non-pregnant women using the same assay. These low values may indicate a general increase in the population prevalence of vitamin D insufficiency possibly relating to the increased use of sun screens and covering up during the summer months. Low vitamin D intake in infancy is associated with reduced bone mass and an increased risk of type 1 diabetes in later life. Vitamin D supplementation studies are warranted in pregnant women in the UK.

G185 VITAMIN D STATUS OF RESIDENTIAL CHILDREN WITH EPILEPSY

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Background: Residential children and adolescents with epilepsy may be at increased risk of developing vitamin D deficiency due to long term anticonvulsant (AC) use, reduced sunshine exposure, or insufficient dietary vitamin D intake.

Methods: A cross sectional study of 33 residential children/adolescents (16 boys; median age 16.6 years and range 8.8 to 19.7 years) on chronic AC therapy (25 took non-enzyme inducing ACs (NEAC) and 7 were on regimens that included enzyme inducing ACs (EAC)) was undertaken during June 2003. Serum concentration of 25 hydroxyvitamin D (25(OH)D; deficiency <12 ng/ml) was measured and related to duration and type of AC therapy, dietary intake of vitamin D (3 day food diaries), and mobility status.

Results: Median serum 25(OH)D level was 24.5 ng/ml (range 13 to 59). Serum 25(OH)D concentration was not related to duration of AC use (r 0.13) and was not different in subjects on NEAC and EAC (23.7 ng/ml *v* 25 ng/ml; p = 0.9). Median serum 25(OH)D concentrations in those with impaired mobility (n 5; 16.7 ng/ml) was significantly lower (p 0.04) than in those with normal mobility (n 19: 24.9 ng/ml). The median daily intake of vitamin D was 1.7 μg (range 0.7 to 7.0; <20% recommended nutrient intake). The median 25(OH)D in four subjects receiving vitamin D supplements (29.2 ng/ml), who were

equally distributed in the two mobility groups, was significantly higher (p 0.01) than in 24 unsupplemented subjects (24.4 ng/ml)

Conclusions: None of the epileptic subjects was vitamin D deficient during summer. The vitamin D status was higher in more mobile subjects (presumably due to increased sunshine exposure) and those receiving vitamin supplements. Vitamin D status did not depend on whether the AC therapy used was enzyme inducing or non-enzyme inducing.