IBMS BoneKEy. 2008 October;5(10):396-400
http://www.bonekey-ibms.org/cgi/content/full/ibmske;5/10/396
doi: 10.1138/20080346

MEETING REPORTS

Bone Acquisition and Pediatric Bone: Meeting Report from the 30th Annual Meeting of the American Society for Bone and Mineral Research

September 12-16, 2008 in Montréal, Quebéc, Canada

Heather Macdonald

University of Calgary, Calgary, Alberta, Canada

Pediatric bone headlined the opening of the 2008 ASBMR Annual Meeting with a plenary symposium featuring experts in the areas of skeletal growth and development, nutrition and physical activity. Building on this first-ever pediatric plenary session, the remainder of the meeting showcased numerous high-quality abstracts in the area of bone acquisition and pediatric bone. An impressive feature of these abstracts was the variety of measurement technologies currently being used – from standard DXA to MRI, peripheral QCT and high-resolution pQCT (HR-pQCT), among others. A selection of the pediatric abstracts is summarized below.

HR-pQCT – A Non-Invasive Tool to Assess Bone Microarchitecture

At last year's meeting, the first HR-pQCT data for children and adolescents were presented (1). This year, three abstracts reported pediatric HR-pQCT data. As a follow-up to their preliminary HR-pQCT analysis, the Mayo Clinic group applied micro finite element (μFE) analysis to distal radius scans and showed a linear increase in estimated bone strength across puberty with boys showing a greater increase than girls after mid-puberty (2). As cortical bone is known to contribute significantly to failure load at the wrist (3), the authors compared the proportion of load borne by cortical and trabecular bone. The proportion of load borne by cortical bone decreased during mid-puberty before rising again. This transient decrease mirrored the incidence of distal forearm fractures during adolescent growth (4). Further, an index of cortical porosity (the ratio of cortical pore volume to cortical bone volume) showed a transient increase during the peak fracture period. It remains to be seen if these deficits are apparent in children and adolescents who sustain forearm fractures.

Whereas HR-pQCT reference data have been available for adults for several years (5), the first HR-pQCT data for the distal tibia in adolescents aged 15-20 years was presented this year (6). Compared with boys, girls had higher cortical density and trabecular separation and lower trabecular density, bone volume/total volume ratio and trabecular number across all ages. These sex differences were similar to those observed by Kholsa *et al*. (5) and suggest that during adolescence, boys have better trabecular microstructure than girls. Further study is needed to determine how these differences in trabecular structure relate to bone strength. In addition, HR-pQCT investigations in younger children are warranted to see if these sex differences are present prior to and during puberty.

HR-pQCT was also used to investigate the impact of late menarcheal age, a documented risk factor for fracture in women (7), on bone strength at the distal tibia in adolescent girls (8). Girls with a later age at menarche (≥ 14 years) had a lower bone strength index than girls with an earlier age at menarche and this relationship was independent of factors such as body size and physical activity. Late menarcheal age was also associated with lower HR-pQCT-derived cortical vBMD and cortical thickness at the distal radius and tibia in healthy young adult and premenopausal women (9;10). Together these findings provide further

evidence of the important influence of estrogen exposure on bone structure and strength during growth (11).

Physical Activity and Bone Health During Growth

As summarized in the pediatric plenary symposium, there is a substantial body of evidence to support the benefits of physical activity for skeletal health during growth. However, as the majority of studies have used DXA to assess the effects of exercise on bone mass acquisition (12), there remain many unknowns about the relationship between physical activity and changes in bone structure and strength as measured with other imaging modalities. Racquet sport athletes offer a unique model with which the effects of exercise on bone structure and strength can be examined. In a 12-month prospective study of young male tennis players, the playing arm showed a 44-66% greater increase in total cross-sectional area (CSA, by MRI) and BMC of the humerus compared to the non-playing arm (13). Although these differences were attenuated after controlling for changes in muscle area and grip strength, changes in BMC were still significant, suggesting non-muscular factors such as repetitive impact associated with training contribute to the increase in bone mass and size. In fact, average training volume (hours/week) was a significant predictor of BMC and CSA, even after adjusting for muscle CSA.

Although changes in bone cross-sectional area may provide insight into bone's resistance to bending forces, there is increasing interest in region-specific changes in bone area that may be related to dominant loading direction. In female gymnasts, periosteal dimensions of the non-dominant radius measured from pQCT scans were greater along both the medial-lateral and anterior-posterior axes (14). In turn, the aspect ratio (the ratio of medial-lateral diameter to anterior-posterior diameter) tended to be greater in gymnasts compared with controls, suggesting loading-related asymmetry. Further analysis is needed to determine the effects of this asymmetry on estimates of bone strength and how this might relate to dominant loading patterns associated with gymnastics.

Also of interest in the physical activity field are novel intervention strategies such as vibration therapy that may prevent bone loss in clinical groups that are unable to participate in weight-bearing activity. In a randomized controlled trial of high-frequency, low-intensity vibration therapy, children with cerebral palsy or neuromuscular disease demonstrated greater gains in forearm BMC and aBMD and upper limb muscle strength over 6 months compared to children receiving physiotherapy alone (15). Importantly, the changes in strength resulted in increased independence among children in the treatment group. These findings are in agreement with an earlier vibration study in disabled, but ambulatory children (16) and suggest that vibration therapy may be an effective non-pharmacological treatment for bone fragility in disabled children.

Risk Factors for Inadequate Bone Acquisition

High body weight is known to be a risk factor for forearm fracture during growth (17). Although overweight children tend to have higher DXA-derived BMC than their normal weight peers, recent pQCT evidence suggests that relative to body weight, tibial bone strength is lower in overweight children, thus placing them at greater fracture risk (18). Similar relationships are present at the distal radius in young children as adiposity was found to be significantly negatively correlated with BMC, total bone area and bone strength index at the 4% site even after adjusting for body weight (19). When examined in the context of loads experienced during activity, relative bone strength (incorporating the polar strength strain index and ground reaction forces) was not significantly different between overweight and normal weight children for low-impact activities such as an active video game or walking (20). However, relative bone strength was 17-27% lower in overweight children for high-impact activities such as running and jumping, suggesting a non-protective effect of excess body weight.

On the opposite end of the spectrum, the negative effects of very low birth weight (VLBW, <1500 g) on bone acquisition are also significant. This was evident in a Finnish cohort study of VLBW young adults who, at the time of peak bone mass, were found to have almost 2 times greater odds of having a lumbar spine aBMD z-score within the osteopenic or osteoporotic range compared with normal birth weight individuals after accounting for body size (21). Similarly, the VLBW adults had significantly lower femoral neck BMD than their normal birth weight peers. These results highlight the need for early initiation of osteoporosis prevention strategies in this group.

In addition to high body weight, risk factors associated with cardiovascular disease (CVD) may also negatively affect bone acquisition. A link between CVD and osteoporosis has been reported in adults (22) and two abstracts at this year's meeting provided evidence for a similar link in children. Sixteen-month changes in tibial bone strength, estimated with pQCT, were greatest among those children with the highest arterial compliance, an indicator of good vascular function, at baseline (23). In addition, children in the highest tertile of arterial compliance had greater gains in lumbar spine BMC. Systolic blood pressure was also shown to be positively associated with bone mass in pre-pubertal and pubertal children who were classified as overweight (24). This finding is in contrast to the inverse relationship between systolic blood pressure and bone mass in adults (22) and may be related to differences in calcium and sodium dynamics between children and adults.

Vitamin D – Essential for Optimal Skeletal Development

Adverse environmental stimuli during intra-uterine life may increase osteoporotic fracture risk later in life (25). Results from the large Avon Longitudinal Study of Parents and Children (ALSPAC) confirmed earlier results from a smaller cohort (26) that vitamin D insufficiency is one such adverse stimulus. Maternal vitamin D status, estimated from background UVB exposure, was positively associated with birth length as well as total body less head aBMD, BMC and bone area at age 10 (27). In order to reduce vitamin D insufficiency in infancy, daily vitamin D supplementation is recommended (28), yet despite these recommendations vitamin D deficiency remains prevalent in many countries (29;30). This may be due, in part, to a lack of a definition of optimal vitamin D intake for infants. Currently, the optimal status of 75 nmol/L is based on adult data. In the first dose-response study using the vitamin D3 isoform, total serum 25(OH)D levels increased with both dose (from 400 to 1600 IU/day) and time (4 to 8 weeks) in breastfed infants (31). Further, compared with infants receiving 1200 or 1600 IU/day, a higher percentage of infants receiving the lower doses did not reach 75 nmol/L. Continued monitoring of these infants is required to determine optimal vitamin D intakes in relation to bone acquisition.

In summary, the pediatric abstracts at this year's meeting highlighted the diversity of this research area. This is an exciting time for pediatric bone as the use of novel non-invasive imaging modalities becomes more widespread and permits a more comprehensive understanding of the growing skeleton.

Conflict of Interest: None reported.

References

1. Kirmani S, McCready L, Holets M, Fischer PR, Riggs BL, Melton LJ, Khosla S. Decreases in cortical thickness, and not changes in trabecular microstructure, are associated with the pubertal increase in forearm fractures in girls. *J Bone Miner Res*. 2007 Sep;22(Suppl 1):S54. [Abstract]

2. Kirmani S, Christen D, van Lenthe GH, Fischer PR, Bouxsein ML, Riggs BL, Melton LJ, Amin S, Peterson J, McCready L, Müller R, Khosla S. Microfinite element modeling reveals that transient deficits in cortical bone may underlie the adolescent peak in forearm fractures. *J Bone Miner Res*. 2008 Sep;23(Suppl 1):S51. [Abstract]

3. Muller ME, Webber CE, Bouxsein ML. Predicting the failure load of the distal radius. *Osteoporos Int*. 2003 Jun;14(4):345-52.

4. Khosla S, Melton LJ 3rd, Dekutoski MB, Achenbach SJ, Oberg AL, Riggs BL. Incidence of childhood distal forearm fractures over 30 years: a population-based study. *JAMA*. 2003 Sep 17;290(11):1479-85.

5. Khosla S, Riggs BL, Atkinson EJ, Oberg AL, McDaniel LJ, Holets M, Peterson JM, Melton LJ 3rd. Effects of sex and age on bone microstructure at the ultradistal radius: a population-based noninvasive in vivo assessment. *J Bone Miner Res*. 2006 Jan;21(1):124-31.

6. Burrows M, Liu D, Ahamed Y, Braid S, McKay HA. Evaluating bone microstructure at the distal tibia in children: an X-treme CT study. *J Bone Miner Res*. 2008 Sep;23(Suppl 1):S111.

7. Silman AJ. Risk factors for Colles' fracture in men and women: results from the European Prospective Osteoporosis Study. *Osteoporos Int*. 2003 May;14(3):213-8.

8. Burrows M, Liu D, Ahamed Y, Braid S, McKay HA. Age at menarche associated with bone strength in girls: an X-treme CT study. *J Bone Miner Res*. 2008 Sep;23(Suppl 1):S370. [Abstract]

9. Chevalley T, Bonjour JP, Ferrari S, Rizzoli R. Influence of pubertal timing on bone trait acquisition: predetermined trajectory detectable five years before menarche. *J Bone Miner Res*. 2008 Sep;23(Suppl 1):S31. [Abstract]

10. Chevalley T, Bonjour JP, Ferrari S, Rizzoli R. Deleterious effect of late menarcheal age on bone microstructure in both distal radius and tibia: no interaction with age dependent premenopausal bone loss in weight-bearing skeletal sites. *J Bone Miner Res*. 2008 Sep;23(Suppl 1):S67. [Abstract]

11. Järvinen TL, Kannus P, Sievänen H. Estrogen and bone--a reproductive and locomotive perspective. *J Bone Miner Res*. 2003 Nov;18(11):1921-31.

12. Hind K, Burrows M. Weight-bearing exercise and bone mineral accrual in children and adolescents: a review of controlled trials. *Bone*. 2007 Jan;40(1):14-27.

13. Ducher G, Daly R, Black J, Turner C, Bass S. The influence of muscle size and strength on changes in bone mass and size during growth and in response to exercise: a longitudinal study. *J Bone Miner Res*. 2008 Sep;23(Suppl 1):S235. [Abstract]

14. Dowthwaite JN, Hickman RM, Spadaro JA, Scerpella TA. The loaded distal radius: gymnastic-related cross-sectional asymmetry. *J Bone Miner Res*. 2008 Sep;23(Suppl 1):S500. [Abstract]

15. Reyes ML, Holmgren J, Hernandez M, Sanhueza E, Dixon J, Escobar R. Randomized, placebo-controlled, double blind study on high frequency low intensity vibration in bone mass, muscle strength and quality of life in children with motor disabilities. *J Bone Miner Res*. 2008 Sep;23(Suppl 1):S124-S125.

16. Ward K, Alsop C, Caulton J, Rubin C, Adams J, Mughal Z. Low magnitude mechanical loading is osteogenic in children with disabling conditions. *J Bone Miner Res*. 2004 Mar;19(3):360-9.

17. Goulding A, Jones IE, Taylor RW, Williams SM, Manning PJ. Bone mineral density and body composition in boys with distal forearm fractures: a dual-energy x-ray absorptiometry study. *J Pediatr*. 2001 Oct;139(4):509-15.

18. Wetzsteon RJ, Petit MA, Macdonald HM, Hughes JM, Beck TJ, McKay HA. Bone structure and volumetric bone density in overweight children: a longitudinal study. *J Bone Miner Res*. 2008 Aug 6; [Epub ahead of print].

19. Ducher G, Daly R, Naughton G, Eser P, English R, Patchett A, Gravenmaker K, Seibel M, Javaid A, Telford R, Bass S. Overweight children are more at risk to sustain a forearm fracture due to poor bone strength relative to body weight. *J Bone Miner Res*. 2008 Sep;23(Suppl 1):S491. [Abstract]

20. Novotny SA, Wetzsteon RJ, Pickett KA, Hughes JM, Cousins JM, Petit MA. Bone strength in overweight children is adapted to mechanical loads from walking, but is low for higher loading activities. *J Bone Miner Res*. 2008 Sep;23(Suppl 1):S498. [Abstract]

21. Hovi P, Andersson S, Järvenpää A, Eriksson JG, Strang-Karlsson S, Kajantie E, Mäkitie O. Preterm birth and bone mineral density in young adulthood: the Helsinki Study of very low birth weight adults. *J Bone Miner Res*. 2008 Sep;23(Suppl 1):S30. [Abstract]

22. Cappuccio FP, Meilahn E, Zmuda JM, Cauley JA. High blood pressure and bone-mineral loss in elderly white women: a prospective study. Study of Osteoporotic Fractures Research Group. *Lancet*. 1999 Sep 18;354(9183):971-5.

23. Hughes JM, Petit MA, Reed KE, Macdonald HM, Cousins JM, Warburton DR, Lewanczurk RZ, Scott JM, McGavock JM, Haykowsky MJ, McKay HA. Arterial compliance is associated with change in bone strength in children: a 16-month prospective study. *J Bone Miner Res*. 2008 Sep;23(Suppl 1):S133.

24. Tylavsky FA, Hare M, Richey P, Velasquez P, Cowan P, Somes G. Elevated systolic blood pressure is positively related to bone mass measurements in overweight pre-pubertal and pubertal children. *J Bone Miner Res*. 2008 Sep;23(Suppl 1):S502. [Abstract]

25. Cooper C, Westlake S, Harvey N, Javaid K, Dennison E, Hanson M. Review: developmental origins of osteoporotic fracture. *Osteoporos Int*. 2006;17(3):337-47.

26. Javaid MK, Crozier SR, Harvey NC, Gale CR, Dennison EM, Boucher BJ, Arden NK, Godfrey KM, Cooper CC; Princess Anne Hospital Study Group. Maternal vitamin D status during pregnancy and childhood bone mass at age 9 years: a longitudinal study. *Lancet*. 2006 Jan 7;367(9504):36-43.

27. Sayers A, Tobias J. Background UVB exposure in pregnancy and skeletal development in childhood. *J Bone Miner Res*. 2008 Sep;23(Suppl 1):S30. [Abstract]

28. Health Canada. Vitamin D supplementation for breastfed infants: 2004 Health Canada Recommendation. Ottawa: Health Canada; 2004. Available: http://www.hc-sc.gc.ca/fn-an/alt_formats/hpfb-dgpsa/pdf/nutrition/vita_d_supp_e.pdf

29. Ward LM, Gaboury I, Ladhani M, Zlotkin S. Vitamin D-deficiency rickets among children in Canada. *CMAJ*. 2007 Jul 17;177(2):161-6.

30. Holick MF. Resurrection of vitamin D deficiency and rickets. *J Clin Invest*. 2006 Aug;116(8):2062-72.

31. Trussler K, Rodd C, Gallo S, Vanstone C, Khamessan A, L'Abbe M, Weiler H. Vitamin D dose response study in Canadian infants. *J Bone Miner Res*. 2008 Sep;23(Suppl 1):S31. [Abstract]