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MEETING REPORT

Bone acquisition/pediatric bone: ASBMR 2012

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Meeting Report from the 35th Annual Meeting of the American Society for Bone and Mineral Research, Minneapolis, MN, USA, 12–15 October 2012

Similar to previous meetings,[1–3] a large number of high-quality abstracts addressing an ample range of pediatric research questions were presented at the 2012 ASBMR Annual Meeting in Minneapolis, MN, USA. In last year's report,[3] we summarized the presented evidence related to vitamin D, obesity and physical activity in relation to bone acquisition and pediatric bone. In this 2012 report, we review selected presentations with a focus on relevant clinical outcomes—fractures and bone strength estimates during growth.

Pediatric Fractures, Trauma and Bone Microarchitecture

Several presentations at the ASBMR meeting provided new evidence related to forearm fractures in childhood and adolescence. The incidence of distal forearm fracture peaks during rapid skeletal growth and an increase in incidence has been reported during the past decades.[4] Distal forearm fracture etiology and reasons for the observed increase in the fracture incidence are poorly understood.[5] It has been hypothesized that metaphyseal inwaisting during rapid growth results in a thin, porous radius cortex that makes bone prone to fracture if a child falls.[5–7] Loading conditions placed upon bone when exposed to external forces (for example, during a fall) likely have an important role in the fracture etiology.

Using high resolution peripheral quantitative computed tomography (HR-pQCT), investigators from the Mayo Clinic assessed whether a recent fracture, either due to mild versus moderate trauma, was related to bone microstructure and estimated strength at the distal radius and tibia in boys ($n = 112$) and girls ($n = 96$) aged 8–15 years.[8] The Landin classification was used to assign trauma levels based on medical record review and an interview.[9] Children with fractures due to mild trauma (for example, from a simple fall) had, on average, 26% lower cortical area and 14% lower cortical thickness at the distal radius; conversely, bone properties in children who suffered fracture due to a moderate trauma (for example, fall from a bicycle) did not differ from controls.[8] Similar findings were observed at the tibia. Authors suggest two distinct etiologies for distal forearm fractures: (a) due to underlying skeletal deficits predisposing to fractures with mild trauma; (b) due to more significant trauma in the setting of normal bone mass and structure.[8]

Maturation, Bone Strength and Fracture Risk

Recent evidence suggests that early maturation may prove advantageous for bone mass development, especially in females.[10,11] A prospective 12-year follow-up of 124 healthy girls (baseline mean age: 8 years; follow-up mean age: 20 years) supported this premise and expanded evidence to bone strength.[12,13] At the follow-up measurement, distal radius densitometric, microstructure and strength outcomes were assessed with dual energy X-ray absoptiometry (DXA), HR-pQCT and HR-pQCT based finite element analysis (FEA), and compared between young women with fracture history ($N = 42$) and their fracture-free peers ($N = 82$).[12,13] DXA derived areal bone mineral density (aBMD) was lower in the fracture group when compared with the non-fracture group at both the radius diaphysis and metaphysis.[12,13] Trabecular density and thickness were also lower in the fracture group, resulting in a less stiff (that is, more flexible) structure with lower failure load and apparent modulus in the distal radius.[12,13] When the risk of fracture was assessed in terms of odd ratios, a 1-s.d. (standard deviation) reduction in radius stiffness or failure load doubled the risk of fracture during childhood and adolescence.[12,13] Young women in the fracture group had menarche $\sim$7 months later than non-fractured young women.[12,13] Authors estimated that if menarche was delayed by 1.2 years (1 s.d.), the fracture risk would double.[12,13] Later menarche appears to be associated with lower bone strength in young adulthood and greater risk of fractures during growing years. Prospective follow-ups of fracture incidence, incorporating baseline bone strength assessments in both sexes, are needed to address the effects on maturational timing in both sexes and to confirm these retrospective findings from young females.

Tracking Bone Mass and Fracture Risk from Childhood to Adulthood

Prospective DXA evidence suggests that bone mineral mass (or aBMD) during growth tracks into adulthood, highlighting the importance of bone development during growing years for osteoporosis prevention.[10,12,13] This concept was addressed in a unique, 28-year follow-up of bone mineral content (BMC) from childhood to adulthood.[14] BMC from a distal forearm shaft site was measured with single photon absorptiometry in 214 children (120 boys) when they were 3–17 years old, and repeated again when the age range of the cohort was 28–44 years.[14] Bone mass in childhood or adolescence explained 23% of bone mass variance in young adult men and 41% of bone mass variance in young adult women[14] supporting the evidence of bone mass tracking. Part of the unexplained variance in bone mass accrual could be due to environmental factors.

Researchers from the Mayo Clinic investigated whether fracture risk tracks from childhood to adulthood.[15] This question was addressed with a retrospective follow-up study of 1776 Minnesota residents who had their first distal forearm fracture at, or before, 18 years of age, linking with data of fractures in adulthood.[15] From 1086 boys and 690 girls with pediatric forearm fractures, there were 144 men and 74 women who had a fracture due to mild-to-moderate trauma in adulthood (mean fracture age: ~50 years).[15] Increased risk of future fractures due to mild-to-moderate trauma was noted in males with pediatric forearm fracture, but not in females.[15] Authors concluded that distal forearm fractures in boys may signal an increased risk for future fractures, possibly due to persistent deficits in bone strength, continued exposure to activities with high fracture risk or a combination of these factors.[15] These findings were supported by an epidemiological study assessing gender differences in fracture risk across the lifespan in the United Kingdom.[16] Both boys and girls had similar peak incidences of forearm fractures during adolescence (71 per 10 000 for girls at age 10; 77 per 10 000 for boys at age 13). In young adulthood, however, males had more than triple the incidences of fractures (206 per 10 000 at age 20) when compared with incidences in young women (61 per 10 000 at age 20).[16] Notably, a steady increase in fracture risk was noted in women after age 65.[16] Authors requested future studies to examine differences in bone properties and lifestyle activities that may contribute to these different fracture rates between male and female individuals.[15,16] Both studies indirectly reflected the key role menopause has in subsequent fracture risk in women.

Physical Activity, Inactivity and Bone Structure and Strength

Although specific sports and vigorous activities have been associated with increased pediatric fracture risk,[17] physical activity (PA) has the potential to enhance bone mass and estimated strength during growth[18] and prevent fracture risk later in life. Gabel *et al.*[19] presented new evidence related to objective measures of PA and sedentary behavior (that is, physical inactivity), and their associations to bone structure and strength. Distal tibia microstructure and estimate strength was assessed with HR-pQCT and HR-pQCT based FEA from 55 premenarcheal and 56 postmenarcheal girls.[19] Moderate-to-vigorous PA and sedentary behavior were assessed using accelerometers.[19] Premenarcheal girls were more active and less sedentary than postmenarcheal girls.[19] In postmenarcheal girls, sedentary behavior negatively predicted the number of trabeculae in the distal tibia.[19] This finding could reflect early loss of trabeculae due to inadequate loading stimulus after menarche.

Associations between pQCT-derived periosteal circumference in the tibia shaft and levels of impact activity from PA were investigated in 675 teens (272 boys, mean age 18 years) from ALSPAC cohort.[20] Accelerometer results were partitioned into low- (0.5–2.1 g), moderate- (2.1–4.1 g) and high-impact (>4.1 g) PA.[20] In boys, moderate- and high-impact activities were positively associated with periosteal circumference (reflecting bone size).[20] In girls, conversely, moderate impact activity was negatively associated with periosteal circumference.[20] Authors suggested that observed interaction with DXA-measured total body fat may partly explain this finding in girls.[20] Further longitudinal evidence of bone structural and strength development from puberty to skeletal maturity, with careful assessment of factors associated to these changes, is needed to improve our understanding of bone development and factors predisposing to bone fragility and fractures.

The role of adolescent PA in adult bone structure and strength was assessed in a 20-year follow-up study.[21] Participants (39 male and 53 female individuals; mean age 29 years) were grouped by their adolescent PA *Z*-scores into inactive, average, active tertiles and pQCT-derived bone properties were compared between the groups.[21] At the tibia, adult males who were active during adolescence had 13% greater estimated bone strength and 10% greater total area than their inactive peers.[21] At the radius, active males had 17% greater estimated bone strength and 13% greater total area when compared with their inactive peers.[21] Adult females who were active during adolescence had 9% larger cortical area at the tibia when compared with their inactive peers.[21] Comparisons were adjusted for adult bone length and muscle size.[21] Greater PA level in adolescence seems to be associated with larger tibial bone size in both sexes and stronger bones in men at the tibia and radius. There were no between-group differences in trabecular bone properties, which suggest that trabecular bone properties were not associated with adolescent activity or possible benefits were not maintained to adulthood.

Although prospective follow-up studies provide important evidence to characterize bone development and associated factors (such as body composition, PA and nutrition), randomized controlled trials (RCTs) are needed to test whether these factors can provide desired changes in bone properties. In the final paragraphs, we summarize findings from three interesting exercise interventions in children and adolescents.[22–24]

A RCT conducted in Canberra, Australia, assessed the effects of generalized school-based physical education (PE) on bone and muscle mass, bone structure and strength in primary school-aged children.[22] This was a 4-year cluster RCT involving 365 boys and 362 girls in grade 2 (~8 years) from 29 primary schools. All children received 150 min per week of PE from classroom teachers. However, in 13 schools, 100 min per week was replaced by two specialized PE classes that emphasized more vigorous exercise and games integrated with static and dynamic postural activities involving muscle strength and function.[22] In girls in the specialized PE group, the 4-year gains in cortical area were, on average, 10% greater at the radius and 5% greater at the tibia diaphysis.[22] Observed results were independent of bone length, weight, pubertal status and the random effect of school.[22] In boys, the only positive effect was observed in cortical density at the mid-tibia (2.4% versus 1.3% in the non-specialized PE group).[22] There were no between-group differences in estimated bone strength, trabecular, or muscle properties in either sex.[22] These results suggest that specific bone loading activities need to be incorporated into PE classes to enhance bone strength during growth. Some support to this premise was provided from another school-based exercise intervention in girls.[23] Ries *et al.*[23] tested if a fitness-focused exercise intervention previously shown to improve fitness, body composition, insulin sensitivity and markers of inflammation would enhance bone mineral accrual in elementary or middle-school aged girls. No differences were observed in aBMD changes over 9 month fitness-focused intervention between the exercise and control groups.[23]

Another RCT assessed the efficacy of vibrations from a vibration platform, referred to as low-magnitude mechanical signals (LMMS), for enhancing bone properties in patients with Childhood Crohn Disease (CD).[24] This was a 12-month double-blind placebo-controlled trial involving 138 CD patients (8–21 years) randomized to either 10 min of daily of LMMS (30 Hz, 0.3 g) or a placebo device.[24] Lumbar spine QCT scans were obtained at baseline and 12 months, and tibia pQCT scans were obtained at baseline, 6 and 12 months.[24] An intention-to-treat analysis revealed a 0.27 greater mean change in trabecular density *Z*-score in the lumbar spine in the active LMMS arm.[24] There were no between-group differences in trabecular or cortical outcomes in the tibia.[24]

In summary, the ASBMR 2012 meeting provided new information related to pediatric forearm fracture etiology and additional evidence that earlier maturation may be beneficial for bone strength and lower fracture risk. Longitudinal studies suggested tracking, from childhood to adulthood, both bone mass and fracture risk and PA-related bone benefit in bone size and estimated strength. Exercise interventions demonstrated some site- and sex-specific adaptations in bone, suggesting that specific bone loading activities are needed to enhance bone strength development during growth.

Conflict of Interest

The authors declare no conflict of interest.

References

1. Macdonald H. Bone acquisition and pediatric bone: Meeting Report from the 31st Annual Meeting of the American Society for Bone and Mineral Research: 11-15 September 2009 in Denver, Colorado. *IBMS BoneKEy* 2009;**6**:450–454.
2. Bonjour J-P. Bone acquisition/pediatric bone: Meeting Report from the 32nd Annual Meeting of the American Society for Bone and Mineral Research: 15-19 October, 2010 in Toronto, Ontario, Canada. *IBMS BoneKEy*, 2010;**8**:55–64.
3. Kontulainen S, Kawalilak C, Johnston JD. Bone acquisition/pediatric bone: Meeting Report from the 33rd Annual Meeting of the American Society for Bone and Mineral Research: 16-20 September, 2011 in San Diego, California, USA. *IBMS BoneKEy* 2011;**8**:486–489.
4. Khosla S, Melton 3rd LJ, Dekutoski MB, Achenbach SJ, Oberg AL, Riggs BL. Incidence of childhood distal forearm fractures over 30 years: a population-based study. *JAMA* 2003;**290**:1479–1485.
5. Rauch F. Bone growth in length and width: the yin and yang of bone stability. *J Musculoskelet Neuronal Interact* 2005;**5**:194–201.
6. Kirmani S, Christen D, van Lenthe GH, Fischer PR, Bouxsein ML, McCready LK *et al.* Bone structure at the distal radius during adolescent growth. *J Bone Miner Res* 2009;**24**: 1033–1042.
7. Nishiyama KK, Macdonald HM, Moore SA, Fung T, Boyd SK, McKay HA. Cortical porosity is higher in boys compared with girls at the distal radius and distal tibia during pubertal growth: An HR-pQCT study. *J Bone Miner Res* 2012;**27**:273–282.
8. Farr J, Amin S, Kirmani S, McCready L, Achenbach S, Melton LJ *et al.* HRpQCT reveals cortical thinning and deficits in bone microstructure in children and adolescents with a distal forearm fracture due to mild but not moderate trauma. *J Bone Miner Res* 2012; **27**(Suppl 1). (Available at http://www.asbmr.org/Meetings/AnnualMeeting/AbstractDetail.aspx?aid=76a3297f-adad-4860-89dc-25a7032fca81).
9. Landin LA. Fracture patterns in children. *Acta Orthop Scand* 1983;**202**:1–109.
10. Jackowski SA, Erlandson MC, Mirwald RL, Faulkner RA, Bailey DA, Kontulainen SA *et al.* Effect of maturational timing on bone mineral content accrual from childhood to adulthood: evidence from 15 years of longitudinal data. *Bone* 2011;**48**:1178–1185.
11. Gilsanz V, Chalfant J, Kalkwarf H, Zemel B, Lappe J, Oberfield S *et al.* Age at onset of puberty predicts bone mass in young adulthood. *J Pediatr* 2011;**158**:100–105.
12. Chevalley T, Bonjour J-P, van Rietbergen B, Rizzoli R, Ferrari S. Fractures during growth in healthy females: relation with bone structural alterations and importance of pubertal timing. *J Bone Miner Res* 2012;**27**(Suppl 1). (Available at http://www.asbmr.org/Meetings/Annual Meeting/AbstractDetail.aspx?aid=eec6d464-b8aa-4ef6-bb81-94912eb7958d).
13. Chevalley T, Bonjour JP, van Rietbergen B, Rizzoli R, Ferrari S. Fractures in healthy females followed from childhood to early adulthood are associated with later menarcheal age and with impaired bone microstructure at peak bone mass. *J Clin Endocrinol Metab* 2012;**97**: 4174–4181.
14. Buttazzoni C, Rosengren B, Skåne M, Tveit M, L Landin L, Nilsson J-Å *et al.* Tracking pre-pubertal bone mass predicts peak bone mass—a 28 year prospective observational study of 214 children. *J Bone Miner Res* 2012;**27**(Suppl 1). (Available at http://www.asbmr.org/Meetings/AnnualMeeting/AbstractDetail.aspx?aid=6c5a7c2d-4ff4-44f1-ac8d-802838b55932).
15. Shreyasee A, Melton LJ, Achenbach S, Atkinson E, Dekutoski M, Kirmani S *et al.* A distal forearm fracture in childhood increases the risk for fracre during adulthood in men, but not in women. *J Bone Miner Res* 2012;**27**(Suppl 1). (Available at http://www.asbmr.org/Meetings/AnnualMeeting/AbstractDetail.aspx?aid=6e6fc7d5-12f0-4b64-a386-b9e987723ee5).
16. Haynes K, Denburg M, Shults J, Leonard M. The greater fracture risk in adolescent males extends through mid-adulthood in the United Kingdom. *J Bone Miner Res* 2012;**27**(Suppl 1). (Available at http://www.asbmr.org/Meetings/AnnualMeeting/AbstractDetail.aspx?aid=48bb2aa2-c27a-4476-a929-0eb8be474108).
17. Clark EM, Ness AR, Tobias JH. Vigorous physical activity increases fracture risk in children irrespective of bone mass: a prospective study of the independent risk factors for fractures in healthy children. *J Bone Miner Res* 2008;**23**:1012–1022.
18. Nikander R, Sievänen H, Heinonen A, Daly RM, Uusi-Rasi K, Kannus P. Targeted exercise against osteoporosis: A systematic review and meta-analysis for optimising bone strength throughout life. *BMC Med* 2010;**8**:47 Review.
19. Gabel L, McKay H, Nettlefold L, Race D, Macdonald H. Lean body mass mediates associations between physical activity, sendentary behavior, and bone microstructure in post-menarcheal girls. *J Bone Miner Res* 2012;**27**(Suppl 1). (Available at http://www.asbmr.org/Meetings/AnnualMeeting/AbstractDetail.aspx?aid=c2cfd0a7-d87a-4e67-be89-e4b9289809c8).
20. Deere K, Sayers A, Rittweger J, Tobias JH. The response of cortical bone to high impact activity is attenuated in girls: findings from a cross-sectional PQCT study in adolescents. *J Bone Miner Res* 2012;**27**(Suppl 1). (Available at http://www.asbmr.org/Meetings/AnnualMeeting/Abstract Detail.aspx?aid=11e8a97c-a87a-485a-bbb1-cc56136315ff).
21. Duckham R, Baxter-Jones A, Bailey D, Faulkner R, Johnston J, Kontulainen S. Physical activity in adolescence may be associated with larger total and cortical area and greater bone strength. *J Bone Miner Res* 2012;**27**(Suppl 1). (Available at http://www.asbmr.org/Meetings/Annual Meeting/AbstractDetail.aspx?aid=5f20a15e-128d-4d39-b86c-dedc5331139c).
22. Daly R, Ducher G, Cunningham R, Hill B, Telford R, Eser P *et al.* Effects of a specialized school physical education program on bone structure and strength: a 4-year cluster randomised controlled trial. *J Bone Miner Res* 2012;**27**(Suppl 1). (Available at http://www.asbmr.org/Meetings/AnnualMeeting/AbstractDetail.aspx?aid=ba787e5e-9241-4525-9604-a418297b73b3).
23. Ries D, Carrel A, Wang S, Scerpella T. School based intervention improves fitness but not bone accrual in 8-14 year old girls. *J Bone Miner Res* 2012;**27**(Suppl 1). (Available at http://www.asbmr.org/Meetings/AnnualMeeting/AbstractDetail.aspx?aid=5346e2ad-c1fc-4e89-afc5-8e60ee0b11d4).
24. Leonard M, Shults J, Zemel B, Hommel K, Brown K, Mahboubi S *et al.* Effects of low magnitude mechanical signals (lmms) on bone density and structure in pediatric crohn disease: a randomized trial. *J Bone Miner Res* 2012;**27**(Suppl 1). (Available at http://www.asbmr.org/Meetings/AnnualMeeting/AbstractDetail.aspx?aid=1836275d-5904-4f47-a523-3038f650ffa4).