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MEETING REPORTS

Bone Acquisition and Pediatric Bone: Meeting Report from the 31st Annual Meeting of the American Society for Bone and Mineral Research

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The 2009 ASBMR Annual Meeting showcased numerous high-quality pediatric bone abstracts. Similar to last year's meeting, a significant number of abstracts reported bone outcomes obtained with imaging modalities other than, or in addition to DXA including high-resolution (HR)-pQCT, pQCT and MRI. Highlights of the pediatric abstracts are summarized below.

Influence of Fat and Lean Mass on Bone Accrual

In light of the current childhood obesity epidemic (1) there is increasing interest in the effects of adiposity on skeletal development. Recent reports regarding the influence of fat mass on pediatric bone health are conflicting (2-4) and the same appears true for results presented at this year's meeting. One abstract reported that girls (aged 11 and 18 years) in the highest tertile of percent body fat had significantly lower bone strength index (BSI) and smaller cross-sectional area (CSA) at the tibial shaft (by pQCT) than girls in the middle and low tertiles, and the differences across tertiles were maintained at age 18 years (5). This suggests that a high proportion of body fat may negatively affect periosteal apposition and in turn, compromise bone strength at weight-bearing sites in girls. The mechanism by which fat mass exerts a negative influence on bone accrual in girls is likely related to rising levels of estrogen that are thought to inhibit periosteal apposition (2;6). In addition, interactions between leptin and estrogen during puberty may influence the fat-bone relationship (7).

Several pediatric abstracts reported positive associations between fat mass and bone outcomes (8-10). In the population-based ALSPAC study (16-year-old boys and girls, n=4427), fat mass was positively associated with cortical BMC and periosteal circumference at the tibial midshaft (by pQCT) (8). This relationship was stronger in girls than boys and suggests that fat mass may both stimulate periosteal expansion and inhibit endosteal expansion. Similarly, in a study of 397 pre- and early pubertal girls, fat mass was an independent and significant predictor of periosteal circumference and bone strength (strength-strain index (SSI)) at shaft sites of the femur and tibia, but was not associated with volumetric BMD at distal or shaft sites (9). Together these findings suggest that fat mass may influence periosteal apposition and bone strength; whether this influence is positive or negative may depend on the site assessed, maturational stage and/or sex. Further prospective studies are needed to clarify the role of fat mass in skeletal development and how this relationship may differ between normal weight and overweight children.

Importantly, when assessing the role of fat mass in skeletal development, we would be remiss not to acknowledge the strong relationship between muscle and bone. In fact, in the study of pre-pubertal girls (9), muscle CSA was the primary explanatory variable of all bone outcomes at both the distal and shaft sites of the femur and tibia. In the first HR-pQCT study to investigate the muscle-bone relationship during growth, lean body mass (by DXA) was a significant predictor of trabecular number in adolescent boys and girls and explained 14-22% of the variance in BSI (11). Similarly, lean mass was a strong predictor of trabecular microarchitecture (*i.e.*, apparent trabecular

thickness) at the distal femur in pre- and early pubertal boys and girls as measured with MRI (12). Interestingly, fat mass was also positively associated with trabecular outcomes, but these relationships were no longer significant when lean mass was taken into account.

Finally, it appears that the benefits of muscle on bone mass and strength accrual during growth may also track into midlife. In the longitudinal Saskatchewan Growth and Development Study, peak wrist flexion during childhood and adolescence was a significant predictor of bone strength indices at both the distal and shaft sites of the radius and these relationships remained significant after accounting for adult muscle strength (13). Thus, maximizing muscle strength during growth may help protect against bone fragility later in life.

Lifestyle Determinants of Bone Accrual

The benefits of physical activity for the growing skeleton are well-established (14) and this year's meeting included the first data showing the influence of weight-bearing activity on trabecular microarchitecture as measured with HR-pQCT in adolescents (15). After controlling for maturity and body size, time spent in weight-bearing activity was a significant predictor of Tb.N and trabecular BMD of the distal tibia in adolescent girls and in turn, explained 6% of the variance in estimated bone strength (BSI). Although weight-bearing activity was a significant predictor of boys' BSI, it was associated with cortical thickness and not measures of trabecular microarchitecture. In contrast, young adult men who reported participation in high-strain activities such as basketball had significantly greater trabecular BV/TV and Tb.N and reduced Tb.Sp of the distal tibia than men who participated in low-strain activities such as jogging (16). Randomized controlled exercise trials are needed to further investigate the sex- and compartment-specific effects of loaded activity on trabecular bone microstructure and strength during growth.

Further study is also needed to determine whether there is an interaction between exercise and nutrition on bone accrual (17). In pre-pubertal girls, calcium supplementation in combination with participation in high-impact activity (gymnastics) was associated with greater increases in BMC (by DXA) compared with high-impact activity alone (18). In contrast, an additive effect of calcium supplementation was not apparent for femoral neck bone geometry estimated with hip structural analysis (HSA). These findings are similar to earlier intervention trials that reported greater gains in bone mass (19;20), but not bone geometry (20), with both exercise and calcium supplementation than with either exercise or calcium alone. In contrast, exercise during pre-puberty in combination with a high protein intake appears to benefit not only bone mass, but also bone size and trabecular microarchitecture at weight-bearing sites in boys (21).

Childhood Fractures

Fracture incidence is almost twice as high in children as in adults (22) and this is thought to be due, in part, to a transient deficit in bone mass relative to longitudinal growth during the adolescent growth spurt (23). Similar to results presented at last year's meeting (24;25), one HR-pQCT abstract suggested that the high incidence of forearm fractures during childhood growth may also be associated with greater cortical porosity of the distal radius, particularly in boys, during early puberty (26). This finding supports an earlier pQCT study that highlighted the lag time between increases in distal radius bone strength and increases in forearm length and body weight that may lead to a greater fracture risk during periods of rapid growth (27).

Whether childhood fractures have a negative effect on bone health and fracture risk later in life remains unclear (28-30). One abstract reported that adolescent boys with a history of fracture had significantly lower trabecular vBMD and trabecular number (by HR-pQCT) and a higher degree of trabecular separation at the distal tibia than boys who were fracture-free even after adjusting for important confounders such as body size and physical activity (31). These

findings are in agreement with earlier DXA studies in girls (28;29) and suggest that childhood fractures may be associated with persistent bone fragility. However, based on results from the University of Saskatchewan's Pediatric Bone Mineral Accrual Study, it would appear that childhood fractures do not compromise bone health in young adulthood (32). Bone mass (by DXA) was not significantly different between individuals with a history of fracture and those who were fracture-free either in adolescence (1 year post-peak height velocity) or in young adulthood. This result supports the recent report from the European Prospective Osteoporosis Study showing that childhood fractures do not predict fractures in adulthood (30). Thus, a longer duration of follow-up may be required to determine whether deficits in trabecular microarchitecture associated with fracture persist beyond adolescence.

Clinical Populations and Treatment

With more widespread use of 3D imaging tools in pediatric studies we are able to explore how particular diseases and treatments influence the cortical and trabecular bone compartments (33). For example, in children and adolescents, pre-dialysis chronic kidney disease (CKD) was associated with significant reductions in cortical BMD and marginal endocortical bone loss at the tibial shaft (by pQCT) (34), consistent with the effects of elevated PTH levels on cortical bone. In contrast, pre-pubertal CKD patients had elevated trabecular BMD Z-scores, which may indicate abnormal resorption of secondary spongiosa proximal to the distal tibia growth plate. Prospective studies are required to determine if these disease-related effects on cortical and trabecular bone are reversible or if they influence fracture risk in children with CKD.

A number of factors associated with inflammatory bowel disease (IBD) may compromise skeletal development including inflammation and corticosteroid therapy. In young IBD patients who reported at least one clinical fracture, trabecular vBMD and parameters of trabecular microarchitecture (by HR-pQCT) were significantly lower than in those patients without a history of fracture, but cortical bone outcomes were not significantly different between groups (35). Thus, alterations in cancellous bone remodeling may influence bone fragility in this group.

In summary, the intriguing findings reported at this year's meeting covered a wide range of topics and highlighted how, with the continued use of novel imaging modalities, we can explore, in more detail, bone acquisition and the many factors that influence bone health during growth.

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