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Invited Plenary Abstract
P8

Bone health in chronic disease: evaluation and treatment – a paediatric perspective

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During childhood, musculoskeletal development is characterized by sex- and maturation- specific increases in trabecular bone mineral density (BMD), cortical dimensions and lean mass. Children with chronic diseases have multiple risk factors for impaired bone accrual, including malnutrition, decreased muscle mass and biomechanical loading, delayed pubertal maturation, alterations in the growth hormone axis, inflammatory cytokines, and bone-active medications such as glucocorticoids. The assessment of glucocorticoid induced osteoporosis is confounded by the effect of the underlying inflammatory disease and by glucocorticoid effects on growth and body composition. Furthermore, conventional DXA measures of areal-BMD (g/cm^2) result in an underestimate of volumetric BMD (g/cm^3) in children with decreased height for age, and fail to adequately distinguish between alterations in trabecular and cortical bone.
The comparison of two childhood diseases treated with high-dose chronic glucocorticoids illustrates the impact of the underlying disease. Childhood Crohn disease (CD) is associated with significant reductions in DXA whole body bone mineral content (BMC) and femoral shaft cortical dimensions (adjusted for age and height), as well as quantitative computed tomography (QCT) tibia trabecular volumetric BMD and cortical thickness, compared with controls. The cortical deficits are characterized by both a smaller periosteal circumference and loss of bone on the endosteal surface, with a consequent reduction in bone strength (cross-sectional moment of inertia), relative to tibia length. In contrast, steroid-dependent nephrotic syndrome (NS) is associated with increased DXA whole body bone mineral content, DXA femoral shaft cortical dimensions, and pQCT cortical thickness and strength, with minimal deficits in trabecular volumetric BMD. We propose that the markedly and persistently elevated cytokines observed in childhood CD result in direct detrimental effects on bone modeling, as well as catabolic effects on muscle. In contrast, SSNS is not associated with sustained elevations in inflammatory cytokines, and the glucocorticoid-induced obesity results in preserved lean mass and linear growth. In CD, adjustment for the lower lean mass explains the cortical bone deficits observed by DXA and QCT. Similarly, in NS, adjustment for the greater lean mass explains the greater cortical bone strength observed by DXA and QCT. Ongoing studies will address the impact of targeted anti-cytokine therapy (e.g. infliximab) and daily therapy with low magnitude mechanical stimuli as potential anabolic therapies in children with CD.