IBMS BoneKEy. 2010 December;7(12):473-476
http://www.bonekey-ibms.org/cgi/content/full/ibmske;7/12/473
doi: 10.1138/20100484

MEETING REPORTS

Muscle and Bone: Meeting Report from the 32nd Annual Meeting of the American Society for Bone and Mineral Research

October 15-19, 2010 in Toronto, Ontario, Canada

Norman K. Pollock[1] and Mark W. Hamrick[2]

[1]Department of Pediatrics, Georgia Prevention Institute, Medical College of Georgia, Augusta, Georgia, USA
[2]Department of Cellular Biology and Anatomy, Institute of Molecular Medicine and Genetics, Medical College of Georgia, Augusta, Georgia, USA

Muscle-bone interactions were featured prominently at the 2010 ASBMR Annual Meeting, beginning Friday evening with the Working Group on Skeletal Aging that followed the plenary poster session and welcome reception. The Working Group included an insightful clinical overview of sarcopenia and aging by Dr. Thomas Lang, and talks by Drs. Douglas Kiel and David Karasik that synthesized many of their genome-wide association studies documenting pleiotropy for muscle and bone traits. Dr. Mary Leonard presented an overview and synthesis of her clinical studies on muscle and bone abnormalities and body composition alterations in children and adolescents, and the presentations ended with Dr. Mark Johnson's intriguing talk titled "The Muscle-Bone Endocrine Axis." This talk was particularly timely because earlier in the evening two posters from Dr. Johnson's group (1;2) showed exciting new data revealing that secreted factors from muscle cells can have profound influences on osteocytes in culture, and vice versa. The former finding is consistent with our own studies demonstrating that muscle-derived factors influence bone formation (3), and with other data from cardiovascular research laboratories suggesting that secreted "myokines" can influence a variety of metabolic processes via muscle-fat crosstalk (4;5). These data all point to a growing interest from physiologists in secreted myokines, an interest that in the future is likely to rival the interest in adipokines that has characterized the last decade. The data from Dr. Johnson's group suggesting that osteocyte-derived factors influence muscle cell morphology and function are perhaps of even greater novelty. Although researchers from Julius Wolff to Melvin Moss and Harold Frost have all provided various models for how muscle might influence bone, few if any skeletal biologists have proposed ways in which the relationship might work in reverse. This is a very exciting and important direction for the bone field, which points to an expanded role for integrative physiology in the ASBMR. We expect future studies to identify specific ligands and receptors that mediate muscle-bone crosstalk.

Perhaps further underscoring the important role of muscle in bone metabolism, the plenary symposium on Saturday morning titled "The Hip Fracture Epidemic" featured a keynote presentation by William Evans of GlaxoSmithKline titled "Muscle Quantity and Quality: Sarcopenia Contributes to Fracture Risk." Dr. Evans began the talk with an overview of his many studies on the mechanisms of age-associated muscle wasting, mechanisms that include insulin resistance, disuse, inflammation, and nutritional deficiencies. Particularly impressive from our perspective were the data linking alterations in muscle strength, growth hormone-IGF1 signaling, and protein intake. Dr. Evans' previous findings synergized nicely with new data presented at the ASBMR meeting showing that higher total protein intake was associated with greater lean mass among middle-aged men and women in the Framingham Osteoporosis Study (6), and that higher protein intake was associated with increased

bone mass and IGF-1 in calorie-restricted volunteers (7). Moreover, Chevalley and colleagues (8) observed a synergistic effect between high protein intakes and high physical activity levels on femoral neck bone mass in boys followed 8 years from early to late puberty. Collectively, these results provide an empirical foundation for the design of more effective treatment and prevention strategies for falls and fractures that incorporate both dietary and behavioral interventions. Further support for the effectiveness of such an approach was provided by the plenary poster from Schacht and Ringe (9), which investigated the effects of daily alfacalcidol (1 mcg) therapy on muscle power, muscle function, and balance performance. The investigators found that the treatment regimen significantly improved muscle function after three months as assessed using the Timed-Up and Go Test (TUG) and the Chair Rising Test (CRT). Their data, along with studies previously published by the labs of Drs. Heike Bischoff-Ferrari (10) and Kate Ward (11;12), provide further evidence that vitamin D may have significant, positive effects on muscle function that may in turn decrease the risk of falls and fractures.

Generally, the human literature provides much evidence for both muscle forces and gravitational forces influencing bone mass/density via mechanical loading; however, little is known about their influence on other aspects of bone strength such as geometry (*e.g.*, size and shape) and their effects solely on trabecular and cortical compartments. Two quality abstracts were presented that advance our knowledge in this particular area of research. In one abstract, investigators found in both pre-adolescent boys and girls that total body lean mass, but not muscle force or power (measured by two-footed jump via a mechanography ground reaction platform), predicted various trabecular and cortical bone geometry parameters at the tibia measured by high-resolution pQCT (13). Other researchers reported that in middle-aged adults radial muscle cross-sectional area was a stronger predictor of pQCT-derived radial bone geometry parameters at a trabecular site, whereas muscle force (measured by hand-grip dynamometry) was a better predictor of radial bone geometry parameters at a cortical site (14). One may arrive at the conclusion that the effects of muscle size and function on bone geometry and trabecular and cortical compartments may be age- and skeletal-site specific; however, since these bone data come from either a weight-bearing site or a non-weight-bearing site, study comparisons are made difficult. Given that bone geometry provides additional and possibly greater information on bone strength than density alone, it is important to re-examine the trabecular and cortical bone geometry consequences of novel exercise programs specifically designed to target muscle-derived vs. gravity-derived bone loading in all age groups. The direct effects of muscle strength on bone mass and bone geometry were further discussed by the Muscle and Bone Working Group. This group featured a number of interesting presentations relating clinical conditions associated with muscle hypofunction, such as Crohn's disease, stroke, and hemophilia, to bone loss. The participants clearly showed that, as in Duchenne muscular dystrophy, bone loss is a significant co-morbidity that accompanies muscle wasting.

Although there is growing evidence in adults that being physically active reduces osteoporotic-related fracture risk (15-17), similar data in children are lacking. In fact, in a recent 2-year prospective study of 2,692 preadolescent children, Clark and colleagues (18) found that being too physically active may perhaps increase fracture risk, despite associations of greater bone mass and size also found with higher levels of physical activity. These results would imply that having stronger bones might not compensate for the increased exposure to injuries. Opposing data were presented by Dr. Fredrik Detter, who was awarded the 2010 ASBMR Young Investigator Award (19). The study was a 5-year, population-based, controlled exercise intervention that included 2,395 children aged 7-9 years. The intervention group performed 200 minutes/week of school-based physical activity compared to only 60 minutes/week in the control group (the usual amount of physical education time per week in Sweden). There were 20 fractures per

1,000 person-years in the intervention group and 18.5 fractures per 1,000 person-years in the control group. The investigators reported these findings as a rate ratio of 1.08 (95% CI: 0.79-1.47). Overall, annual gains in bone mass and structure parameters at the lumbar spine, hip, radius and tibia, measured by DXA and/or pQCT, were significantly greater in the intervention group than in the control group. The important message that Dr. Detter stressed was that increasing duration of physical activity in a school-based program can improve skeletal strength without increasing the risk of fracture. He further noted that building stronger bones during childhood via increasing time in school-based exercise programs may also be beneficial for these children's bones with regard to preventing fragility fractures in old age. Dr. Detter and colleagues did not provide information on exercise intensity of their intervention; however, in another oral presentation, Dr. Jon Tobias provided some intriguing cross-sectional data on relationships between exercise intensity and pQCT-derived cortical bone measurements in 1,748 adolescent boys and girls (20). The investigators found that between light, moderate and vigorous levels of physical activity, only vigorous physical activity (≥ 6 METS; measured by accelerometer devices) was significantly and positively associated with cortical bone mass and structure at the tibia. Though the authors concluded that childhood exercise interventions should include high-impact, intense activities such as jogging or running in order to be of benefit to the growing skeleton, it must be noted that their study findings were derived from observational, rather than interventional, data. To exclude self-selection bias (*i.e.*, athletically-inclined youth may be genetically predetermined to posses stronger bone, thus making them more apt to participate in vigorous sports or activities), experimental work is needed to confirm benefits of vigorous vs. moderate physical activity on childhood bone health.

Together, the translational and clinical data on muscle and bone presented at this year's ASBMR meeting show that integrated studies linking soft tissue physiology, diet, and physical activity with bone metabolism will continue to lead the way in improving skeletal health.

Conflict of Interest: None reported.

Peer Review: This article has been peer-reviewed.

References

1. Lara N, Hall T, Brotto L, Biggs J, Mo C, Romero-Suarez S, Brotto M, Bonewald L, Johnson M. Muscle derived factors influence the MLO-Y4 osteocyte response to shear stress. *J Bone Miner Res*. 2010;25(Suppl 1). [Abstract]

2. Lara N, Hall T, Touchberry C, Andresen J, Brotto M, Johnson M, Wacker M, Elmore C, Romero-Suarez S, Mo C, Bonewald L, Silswal N. Bone-muscle crosstalk is demonstrated by morphological and functional changes in skeletal and cardiac muscle cells in response to factors produced by MLO-Y4 osteocytes. *J Bone Miner Res*. 2010; 25(Suppl 1). [Abstract]

3. Hamrick MW, McNeil PL, Patterson SL. Role of muscle-derived growth factors in bone formation. *J Musculoskelet Neuronal Interact*. 2010 Mar;10(1):64-70.

4. Pedersen BK. The diseasome of physical inactivity--and the role of myokines in muscle--fat cross talk. *J Physiol*. 2009 Dec 1;587(Pt 23):5559-68.

5. Walsh K. Adipokines, myokines and cardiovascular disease. *Circ J*. 2009 Jan;73(1):13-8.

6. Sahni S, McLean R, Kiel D, Broe K, Tucker K, Cupples L, Hannan M. Higher total protein intake associated with greater lean mass and more favorable ratio of low lean-to-fat mass ratio in middle-aged men and women: The Framingham Osteoporosis Study. *J Bone Miner Res*. 2010;25(Suppl 1). [Abstract]

7. Sukumar D, Ambia-Sobhan H, Zurfluh R, Stahl T, Shapses S. Insulin-like growth factor and bone mass is

influenced by higher protein intake during one year of caloric restriction. *J Bone Miner Res*. 2010;25(Suppl 1). [Abstract]

8. Chevalley T, Bonjour J, Rietbergen B, Ferrari S, Rizzoli R. Positive impact of both physical activity and protein intake before puberty on biomechanical strength at weight bearing skeletal sites 7.8 yrs later in healthy boys. *J Bone Miner Res*. 2010;25(Suppl 1). [Abstract]

9. Schacht E, Ringe J. Alfacalcidol improves muscle power, muscle function and balance in elderly patients with reduced bone mass. *J Bone Miner Res*. 2010;25(Suppl 1). [Abstract]

10. Bischoff-Ferrari HA, Dawson-Hughes B, Staehelin HB, Orav JE, Stuck AE, Theiler R, Wong JB, Egli A, Kiel DP, Henschkowski J. Fall prevention with supplemental and active forms of vitamin D: a meta-analysis of randomised controlled trials. *BMJ*. 2009 Oct 1;339:b3692.

11. Ward KA, Das G, Berry JL, Roberts SA, Rawer R, Adams JE, Mughal Z. Vitamin D status and muscle function in post-menarchal adolescent girls. *J Clin Endocrinol Metab*. 2009 Feb;94(2):559-63.

12. Ward KA, Das G, Roberts SA, Berry JL, Adams JE, Rawer R, Mughal MZ. A randomized, controlled trial of vitamin D supplementation upon musculoskeletal health in postmenarchal females. *J Clin Endocrinol Metab*. 2010 Oct;95(10):4643-51.

13. Moore S, Liu D, Burrows M, Race D, Egeli D, McKay H. Muscle parameters are related to bone strength and microstructure in children: a high-resolution pQCT study. *J Bone Miner Res*. 2010;25(Suppl 1). [Abstract]

14. Lorbergs A, Farthing J, Baxter-Jones A, Kontulainen S. The role of muscle properties in predicting pQCT estimated bone strength at the radius in midlife. *J Bone Miner Res*. 2010;25(Suppl 1). [Abstract]

15. Gregg EW, Cauley JA, Seeley DG, Ensrud KE, Bauer DC. Physical activity and osteoporotic fracture risk in older women. Study of Osteoporotic Fractures Research Group. *Ann Intern Med*. 1998 Jul 15;129(2):81-8.

16. Jaglal SB, Kreiger N, Darlington GA. Lifetime occupational physical activity and risk of hip fracture in women. *Ann Epidemiol*. 1995 Jul;5(4):321-4.

17. Kanis J, Johnell O, Gullberg B, Allander E, Elffors L, Ranstam J, Dequeker J, Dilsen G, Gennari C, Vaz AL, Lyritis G, Mazzuoli G, Miravet L, Passeri M, Perez Cano R, Rapado A, Ribot C. Risk factors for hip fracture in men from southern Europe: the MEDOS study. *Osteoporos Int*. 1999;9(1):45-54.

18. 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 Jul;23(7):1012-22.

19. Karlsson M, Nilsson J, Detter F. A five years exercise intervention programme in 7-9 year old children improves bone mass and bone structure without increasing the fracture incidence. *J Bone Miner Res*. 2010;25(Suppl 1). [Abstract]

20. Tobias J, Sayers A. Habitual vigorous physical activity increases cortical bone mass in adolescents, unlike light or moderate activity which are without effect. *J Bone Miner Res*. 2010;25(Suppl 1). [Abstract]